Design Science and Innovation

Karupppasamy Subburaj
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Revolutions in Product Design for Healthcare

Advances in Product Design and Design Methods for Healthcare

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Design Science and Innovation

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Preface

The general design methods, processes, and evaluation strategies face challenges when applied to solve a healthcare design problem due to the rigid nature of regulatory compliance and the cost of taking a design to the market. The pathway to the market from the stage of identifying a need is riddled with death valleys, including but not limited to material choice, manufacturing and testing protocol and standards, clinical trials, and regulatory compliance. Recognizing those valleys in the early stage of the design process would allow the designer to be vigilant of every decision made and its impact down the line. The book entitled **Advances in Product Design for Healthcare** covers the best practices, advanced design methods to capture, document, and validate clinical challenges at the early stage of the design process, and mitigating design strategies to address those challenges without compromising the cost, effort, safety, and quality of the device. The editorial team compiled a comprehensive collection of technical notes, research articles, design frameworks, case studies, state-of-the-art literature reviews, and impact studies covering the topics mentioned above to offer a coherent resource for the readers. In addition, we have structured the book to provide foundations and frameworks first, then application of science, technology, and innovations in healthcare product design. Designers, clinicians, ergonomists, ancillary healthcare professionals, manufacturing enterprises, and young research scholars will benefit from this book and understand the real potential of healthcare product design innovations.

Singapore, Singapore — Karupppasamy Subburaj
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Contents

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Chapter 1
User-Involved Design of Digital Health Products

Loick Menvielle, Myriam Ertz, Julien François, and Anne-Françoise Audrain-Pontevia

1 Introduction

The growing importance of eHealth in the healthcare sector is only paralleled with the concomitant rise in various user concerns and issues. Such issues include concerns regarding lack of security, privacy, and other issues related to technological literacy and perceived self-efficacy (García-Ordás et al. 2020; Ally et al. 2017). Given the ambivalent nature of such development and to ensure appropriate user acceptance and continuance, health organizations need increasingly to reshape their views on how they design and promote medical technology in the form of eHealth to patients. This chapter adds to the growing literature on this topic (e.g., Eysenbach 2001) by proposing to allocate a broader importance to the user in the product design development process. More specifically, drawing on the concepts of patient value, co-creation of patient value, and the Service-Dominant Logic (S-DL) (Lusch and Vargo 2014), this chapter proposes a user-involved design of digital health product that places patients and their perception of value in digital objects at the center of all attention.

Therefore, the chapter explores the theoretical foundations and maps fundamental axioms of a user-involved product design in the healthcare sector. The remainder of this chapter is organized as follows: the first section presents an overview of the digitalized healthcare sector, emphasizing eHealth and two of its key constitutive technologies, including mobile health (mHealth) and Healthcare Internet of Things (HIoT). The subsequent sections outline the concepts of perceived patient value and

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co-creation before discussing the Service-Dominant Logic (S-DL) as a key theoretical foundation to understand co-creation processes in services. The chapter further discusses privacy and ethical concerns before proposing outlooks for future research and ending with a set of concluding remarks.

2 Digitalization of the Healthcare Sector: An Overview

2.1 eHealth and Its Digital Technology Nexus

eHealth. The field of eHealth has a history of more than 20 years. eHealth implies everything that comes blends information communication technology (ICT) and health care. Specifically, the term eHealth is used to describe a broad range of digital health technologies and interventions used by various stakeholders across diverse settings (Shaw et al. 2017). According to Eysenbach (2001), "*eHealth is an emerging field in the intersection of medical informatics, public health, and business, referring to health services and information delivered or enhanced through the Internet and related technologies*." This definition entails that the field of eHealth includes three different domains (Shaw et al. 2017): (1) the use of eHealth technologies to monitor, track, and inform health, (2) the use of digital technologies to enable health communication among practitioners and between healthcare professionals and clients or patients, and (3) the collection, management, and use of health data sources. In addition, eHealth technologies covered by the different domains are very diverse and include, for instance, telemedicine, mHealth, robotic surgery and healthcare Internet of Things.

However, it is possible to approach their usage either from a patient-oriented usage or from healthcare professional orientation. For instance, healthcare professionals use telemedicine or robotics to assist them in the care of their patients while patients use mobile devices or Internet of Things devices to monitor and track their health or to communicate with their healthcare professionals. In line with the objectives of this chapter, the following subsections will discuss mobile health and Healthcare Internet of Things usage from a patient-oriented perspective.

mHealth. According to the World Health Organization, mobile health or mHealth is defined as "*medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices.*" mHealth is one of the major dimensions of eHealth. mHealth specificity comes from mobile devices to support clinical diagnosis and/or decision-making regarding health management, improve clinical outcomes from established treatment pathways through behavior change, improve patient compliance, act as autonomous digital therapeutics, and acquire education regarding health (Rowland et al. 2020). mHealth has the potential for significant development due to the increasing availability of smartphones and other devices connected to the Internet (e.g., wearables). The global market of mHealth has grown rapidly in recent years,

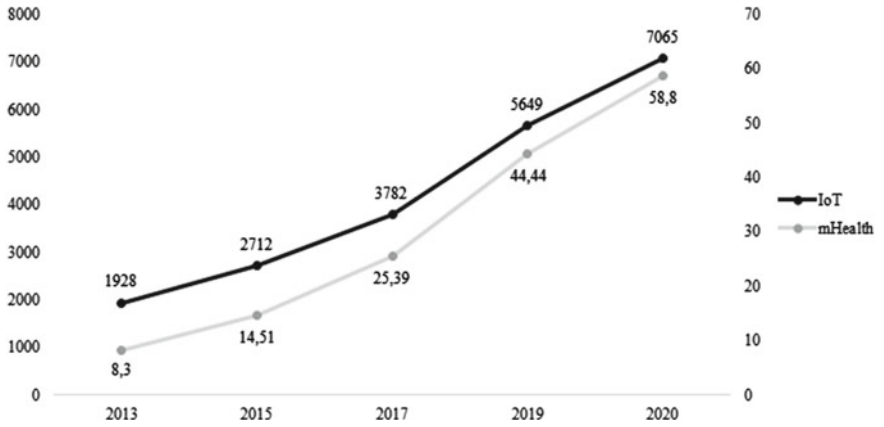

Fig. 1 Market value of Internet of Things and mHealth worldwide from 2013 to 2020 (in billion of US dollars) *Source* Adapted from Statista (2021a, b) Hoffman et al. (1999), Sivathanu (2018)

rising from $8.3 billion in 2013 to $58.8 billion in 2020 (see Fig. 1). In 2021, the adoption rate in the USA for the smartphone is 85%, compared to 35% in 2011. In addition, 56% of physicians have discussed mHealth with patients in the USA, and 26% of physicians have been asked by a patient about mHealth (PwC Health Research Institute 2019).

Healthcare Internet of Things. The global market of the Internet of Things has experienced strong growth in recent years, rising from $1.928 billion in 2013 to $7.065 billion in 2020 (see Fig. 1) One of the vital applications of the Internet of Things (IoT) is medical in the area of healthcare. IoT in healthcare is also a major dimension of eHealth. These digital health technologies are attractive because they allow the personalization of clinical healthcare, reduce hospitalization costs, reduce the time taken to diagnose a health condition, and provide efficient, high-quality care (Habibzadeh et al. 2020). IoT applications in healthcare settings include remote and real-time monitoring of patients, chronic illness management, physician–patient interaction, patient engagement, elderly care, and influencing patient behavior, to name but a few (Dantu et al. 2021). The IoT market in healthcare settings is growing fast and should be worth between $3.9 trillion–11.1 trillion in 2025 (McKinsey Global Institute 2015). By 2020, 40% of IoT-related technologies will be health-related, constituting a $117 billion market that will surpass any other domain (Dantu et al. 2021).

2.2 Patients' and Users' Attitude Towards eHealth: The Central Role of Trust

Trust plays a crucial role in consumers' perception of risk, whether it is trust in a person or an organization or trust in the technology to keep the information secure (Hoffman et al. 1999). Applied in healthcare settings, patients' perception of risk is of fundamental importance to eHealth, especially as it arises from security and privacy concerns regarding personal information. Examples of personal information include name, date of birth, medical records, and individuals' biological and/or physiological information. Perceived risks regarding security and privacy of personal information for patients constitute a strong barrier for its usage (Sivathanu 2018), and privacy perspectives regarding healthcare IoT usage are found to have a negative effect on the intention to use Healthcare IoT (Karahoca et al. 2018). Privacy-related and security issues are also a crucial concern for vulnerable groups of patients such as children, the elderly, invalid, and disabled patients.

In fact, although the implementation of eHealth-based interventions is both feasible and highly effective for those patients (García-Ordás et al. 2020; Ally et al. 2017), the use of eHealth with those patients remains questionable because it is not certain to what extent their consent is genuinely informed. This lack of trust regarding healthcare IoT usage for patients thus attenuates the supposed benefits of its usage, such as better therapy compliance, or self-management of their health condition (Zhang et al. 2014). Thus, it becomes imperative that personal information be protected from all breaches to gain trust from patients. Technological solutions are frequently designed to secure personal information. For example, it may be considered necessary to encrypt information during transmission to preserve personal information confidentiality (Sahama et al. 2013). In addition to Dólera Tormo et al. (2013), identity management solutions should also clarify who owns user data and how its spread is controlled to further build trustworthy associations between care providers. These are but a few suggestions about how to foster trust regarding eHealth technologies. Despite tremendous advances in alleviating trust and privacy concerns, it should be stressed that trust remains a key tenet of eHealth success.

2.3 Patients' New Role in Healthcare Delivery

The literature on self-extension (Belk 1988) describes how consumers cathect objects with meaning and extend their identities from themselves into objects and other people. Through self-extension, physical and digital possessions contribute to consumers' identities and function to extend their sense of themselves, bringing more meaning to their lives (Belk 1988). Specifically, the concept of self-expansion has been used to explain consumers' experience with IoT (Hoffman and Novak 2018). Self-extension refers to the significant processes in which users develop an attachment to IoT (Hoffman and Novak 2018). Applied in the healthcare settings, patients'

experience with HIoT may also create a patient identity where the identity has a special place. Indeed, living with a chronic disease symbolizes an important change for patients and impacts their social and professional lives. Suffering from diabetes or other chronic diseases affects all perspectives and projections into the future that individuals usually have. By allowing patients to be responsible for managing their chronic illness through the use of digital health technologies, it is envisioning a new role and identity for them in the medical process (Galvin 2002).

3 Value and Co-Creation

3.1 From Consumer Value to Patient Value

Value perceived by users is viewed as a critical construct for firms in the healthcare and service literatures. The main reason for the strong emphasis on consumer perceived value relies on its direct implication for organizational performance (Medberg and Grönroos 2020). Today, perceived value is identified by both firms and healthcare organizations as a strategic imperative and is a major focus for these organizations (Moliner 2006). The service literature highlights that creating consumer value helps organizations to propose a continuous stream of products and/or services that offer unique benefits to their consumers. From the patient/consumer perspective, a high perceived value towards an object, product, or service, is expected to be positively related to satisfaction and trust towards the object, which in turn triggers consumer loyalty. A substantial number of studies in the relationship literature have shown that perceived value is a fundamental determinant of consumer attitudes and behaviors and that it is also a primary motivation for consumer patronage. Hence, a strong focus on perceived value contributes to nurturing profitable long-term relationships with the consumers, which durably impacts the profitability and growth of the firm.

Because consumer perceived value expresses the patient/consumer evaluation of a product, a service, or an organization, patient/consumer perceived value provides meaningful information for organizations regarding the design of the product or service they propose, and importantly their strategy. Healthcare services are intangible, perishable, variable in nature, and inseparable because they require that the producer and the consumer both contribute to its production. Hence, the delivery of services in healthcare requires a focus on the patient throughout the process. This considered, paying attention to patient-perceived value is a key indicator to reach this aim.

However, although the importance of defining, measuring, and tracking consumer perceived value is widely acknowledged, there is a lack of a unique conceptualization of perceived value. Indeed, the service literature identifies two main definitions of perceived value, depending on the approach, which can be either utilitarian or behavioral. The utilitarian approach, which is derived from the psychological perspective

of value, defines value as "*any increase in wealth […] that will result in an increase in utility*" (Bernoulli 1954, p. 25). In contrast, in the behavioral perspective, which relies on exchange theory, perceived value is defined as resulting from a social interaction that contains an exchange ratio.

This approach is widely used in the service literature and in the healthcare one. Furthermore, the behavioral perspective is also rooted in the expectancy utility theory, which considers that consumer perceived value is derived from the consumer subjective evaluation between the utility of service and the disutility of using the service (Boksberger and Melsen 2011). Furthermore, it relies on the economic assumption that consumers tend to maximize their value from a service. This approach is initially focused on consumer's price perception of a service. However, further developments brought a wider conceptualization of perceived value given as the ratio or trade-off of the total benefits received to the total sacrifices made (Qian et al. 2011; Boksberger and Melsen 2011). In the same vein, patient-perceived value can be defined as the overall assessment of the utility of medical service based on the perceptions of what is received and what is given, i.e., as the ratio between the overall benefits gained from the medical service and the total costs associated by the patient to the medical care (Sales-Vivó et al. 2021; Audrain-Pontevia and Menvielle 2018).

3.2 From Patient Perceived Value to the Co-Creation of Patient Value (CcPV)

The study of patient-perceived value, which started in the 90s, has experienced a shift in paradigm in the mid-2000s, following the service-dominant logic (SD-L) presented as a new dominant logic in marketing (Vargo and Lusch 2008). In the SD-L approach, value creation is conceived as being phenomenological and experiential in nature. This approach also enhances the critical role of the consumer in the process of value creation, which does not solely depend upon the firm. Vargo and Lusch (2014) and Amrani et al. (2017) summarized this as follows: "the customer is always a co-creator of value." The SD-L paradigm not only highlights the importance of consumers in the value creation process but also underlines the importance of usage and relationships, which contrast with the transactional perspective of marketing. Yet, the construct of value co-creation remains elusive to define (Sales-Vivó et al. 2021). There is no agreed definition of VcC. However, the literature in marketing reaches a consensus on the collaborative, interactive, and reciprocal nature of VcC. The SD-L approach also clearly states that VcC requires a customer focus in an "ecosystem of agents in the company's environment" encompassing both suppliers and customers (Sales-Vivó et al. 2021, p. 3). Hence, in this perspective, value stems from consumers' evaluation and depends upon the interactions the consumer has with a network of actors who contribute to creating the value delivered to the consumer.

In the healthcare context, the development of new technologies has considerably changed how healthcare services are delivered. For example, peer-to-peer online

health communities, which are given as virtual platforms that enable members to interactively discuss health-related matters in order to get knowledge or psychological support, anonymously[1] and with no geographical boundaries (Audrain-Pontevia and Menvielle 2018), have given patients the opportunity to manage their healthcare actively. Similarly, Health Internet of Things (HIoT), defined as objects generating information synchronized via wireless network (Wi-Fi or Bluetooth) to a mobile phone, tablet, or manufacturer's website (Amrani et al. 2017), provide patients with opportunities to track and monitor their disease. HIoT has considerably altered the process of value delivery in healthcare services. They offer patients the opportunity to participate more and better in the management of their disease, hence in the creation and process of the health service delivery.

For example, the application *Freestyle* provides diabetic patients with a wearable monitoring device to self-manage their chronic disease while continuously sending information to the physician. In their early developments, research shows that these new technologies used in eHealth to support the patient provide them with more information on their disease, which positively affects their feeling of being socially supported and empowered (Audrain-Pontevia et al. 2019). Audrain-Pontevia and Menvielle also highlight that patient social support and empowerment gained through online health communities affect the bond that patients have with their physician. Importantly, online health communities seem to have the potential to enhance patient's compliance to the recommended treatment (Audrain-Pontevia et al. 2019). While empowering the patient, these new technologies challenge the traditional and paternalistic paradigm of the patient–physician relationship (Menvielle et al. 2016). In the past, physicians used to have more information than the patient. As a result, the patient was more passive and did not always contribute to the creation of the value delivered. The new technologies introduced in healthcare, like HIoT, provide patients with information, support, and tools to self-manage their disease, enabling patients to co-create the value delivered.

In complementary of the previous examples, various pathologies benefit innovative technology solutions in healthcare, empowering patients and improving their health for chronic diseases (diabetes, heart disease) but not only. Solutions designed with and for patients contribute to redeploy of a new relationship between patients, caregivers, and medical staff. The is the case of solutions such as LifePod, which enables aged patients to independent lives, providing them regular reminders (eat, drink, sleep, take medication), encouraging them to socialize and to maintain a certain level of independence and reducing hospitalization and fending off the degradation of mental health. These solutions redeploy links and relationships of stakeholders involved in the process of health delivery. Even if major connected health devices require connectivity, some solutions are particularly relevant to provide care without direct access to Wi-Fi. Vera solution (Virtual Exercise Rehabilitation Assistant) provides assistance for patients' rehabilitation and represents a solution fully

[1] World Health Organization encourages compliance with code of ethics, rules, and norms to ensure patients' data protection for more truthful and non-deceptive e-health devices.

designed with all constraints identified for patients: ease of use, ease of access whenever and wherever without Internet access.

4 Marketing and Healthcare Shifting Toward a New Paradigm

4.1 The Emergence of Service-Dominant Logic

Our economy and society have tremendously evolved, making it more complex, interconnected, and networked. To tackle this intricacy of the healthcare sector in the digital age, theory grounded on services is essential to analyze and contextualize the delivery process. In this context, the Service-Dominant (S-D) logic seems to play a promising role in decrypting the sector's challenges, identifying stakeholders' role in the medical process, and identifying their interactions (Lusch and Vargo 2014). Maglio and Spohrer (2008, p. 18) recognized that "*service-dominant logic may be the philosophical foundation for service science, and the service system may be its basic theoretical construct*." In analyzing services, Vargo and Lush (2009) elaborated a framework transcribing the evolution and role of all parties involved in service delivery and co-creation. Five axioms and foundational premises (FPs) were identified on a total of 11 (Vargo and Lusch 2016). Table 1 presents these core axioms.

The S-D logic considers transactions and exchanges as a collective construction process. Customers and producers of services contribute to value creation and producers are no longer market-oriented (*market to*) but cooperation-focused (*market with*). The evolution of society contributed to a shifting paradigm, moving from tangible to intangible goods and promoting interactions and inter-connectivity between the deliverer and the user of a service. The S-D logic contrasts with traditional business models. It departs from the Good-Dominant logic (G-DL), characterized by product centricity and the capability only held by firms to innovate and create

Table 1 The axioms of S-D logic

Identification	Description
Axiom 1/FP1	Service is the fundamental basis of exchange
Axiom 2/FP6	Value is co-created by multiple actors, always including the beneficiary
Axiom 3/FP9	All social and economic actors are resource integrators
Axiom 4/FP10	Value is always uniquely and phenomenologically determined by the beneficiary
Axiom 5/FP11	Value co-creation is coordinated through actor-generated institutions and institutional arrangements

Source Vargo and Lush (2008)

value. In G-DL, customers are considered as inexperienced, not knowledgeable, consuming, and destroying value. The S-D logic contributed to establish and open another perception of the situation. Applied to the service industry, the foundations of this new logic encouraged the inclusion of all stakeholders, involving customers in dialogue, embracing learning, and identifying that value is not an individual process (Lusch and Vargo 2009). The conceptual approach reverses the marketing vision from a consumer-centric model to a network-oriented model (Peñaloza and Venkatesh 2006). These changes reflect changes in society in all aspects as has been well emphasized in the collaborative economy literature, which underscores the economy like a "*mesh*" in which consumers co-create value with each other and with organizations (Gansky 2010). No industry has been spared, least of all the health sector, especially with the democratization of technology and the Internet.

4.2 Co-Creation and Service-Dominant Logic

Four meta-theoretical foundations grounded the S-D logic: actor-to-actor networks, resource liquefaction, resource density, and resource integration (Lusch and Nambisan 2015). The actor-to-actor networks refer to the ability accessible to all actors to contribute to innovation or value creation potential. Producers and customers/users are considered equal, oriented to a network-centricity perspective. The resource liquefaction highlights the evolution of information technologies, reshaping the manner to deliver services and the nature of services itself (Robey et al. 2003), "*open up innovation opportunities*" (Lusch and Nambisan 2015, p. 160).

Even though the two previous meta-theoretical foundations of actor-to-actor networks and resource liquefaction seem to be coherent with the evolution of services and the growing consideration of customers/users in the area of services, the two last components raise similarly growing interest in the field of our investigations. First, resource density emerges as a key variable in IS, law, or healthcare, for example. Second, technical solutions, connected devices, algorithms, and artificial intelligence have broadly contributed to producing new insights and models of reflection. However, this is not without raising queries about transparency or involving users in concept design to sustainable usage of the IT solutions and services using digital tools. The last meta-theoretical foundation of technical solutions underlines the importance of stakeholders' integration. The value provided in service creation and delivery is the outcome of combined resources. Thus, service innovations are enriched by integrating much resource-oriented usefulness based on market demand and integrating users' expectations and reinforcing their role in value creation. Henceforth, customers/users are considered to play an unavoidable role in the design of services, moving from a passive consideration to a central actor for co-creation practices.

This framework, as essential to analyze and understand the evolution of services, refers back to three interrelated components: (1) Service ecosystem, where actors operate in a suitable environment for exchanges and co-creation; (2) Service platform, accelerated with digital tools, which enhance the efficiency of exchanges,

opening the access to a large range of resources and accelerating innovation; (3) Value co-creation, as the outcome between service suppliers and beneficiary of service, taking into consideration the role played by different actors in the service ecosystem and considering their knowledge as a vector of co-creation. Actors involved in the service creation "*integrate their knowledge resources with those obtained from one or more other actors, which leads to new service innovation opportunities*" (Lusch and Nambisan 2015, p. 169). Customers/users are fully considered co-producers in the service delivery process, maximizing resource allocation to reach a higher level of expectations (Bovaird and Loeffler 2013). Furthermore, co-creation and customers/users' implications reinforce the quality of exchanges and relationships between firms and customers. The actual value is not focused on money but on value created to answer a specific need. This meets customers/users' expectations, advocating for a direct relationship between suppliers and users, being involved in design offers, obtaining greater transparency, which is essential as a key source of trust in the relationship between stakeholders (Vargo and Lusch 2017). Applied across various industries, the S-D logic contributed to a positive impact. For example, in education, Javis et al. (2014) have identified the benefits of using this approach, fostering student engagement and reinforcing the learning experience. In innovation studies, Vargo et al. (2015) reconciled diverging perceptions on innovation based on their model for reflection. In information system/computer science, Yan et al. have mobilized the S-D logic to design a collaborative system for a manufacturer, increasing their competitiveness via this approach. Hence, what about healthcare? Does the S-DL approach spare this sector? Research and investigations seem to be promising in this regard.

4.3 A New Paradigm in Healthcare in the Digital Age

The spread of IT and the democratization of medical information on the Internet have significantly modified "*traditional habits and relationships*" that patients could hold with their physician during a consultancy. Dr. Google—the artifact symbolizing the evolution of democratization of medical knowledge to a large scope of patients, has contributed to design a new structure for care delivery, involving patients in the medical process or acknowledging specific medical competencies that complement practitioners' proficiencies (Menvielle et al. 2018).

Furthermore, the digitalization of health fosters new relationships between patients and medical staff. In fact, the knowledge acquired by patients on the Internet, medical social media, or online health-supportive communities increase the changing paradigm (Menvielle et al. 2018; Simon et al. 2017). Patients are not only seen as for treatment but as an entity in their own right. They claim choices, express their expectations, particularly in the case of patients suffering from chronic diseases. According to Gummesson et al. (2018, p. 239), "*the patient as an active resource, not a person to whom the professional does something, but one who the professional does something with.*" This consideration is the fundamental value proposition contributing to

provide the best treatments and medical solutions for them. This phenomenon was accelerated by the dissemination of accessible medical information on the Internet. Co-creation in health embodies a new step in the delivery of care, raising a new logic of service. Thus, the co-creation approach is characterized as a source of cross-fertilization of ideas based on multiple experiences met by stakeholders bringing benefits for all parties. This has profoundly changed the nature of the relationship held by patients and medical staff.

Even if there are opposing sides to using digital tools, significant benefits should be cited: an improvement in patients' level of knowledge towards a disease, the increase in their commitment during a consultancy, and more generally during the patient's journey, contributing to make patients more empowered and more compliant to the treatment. Using a health digital tracker, for example, provides benefits to users of this solution, enhancing their quality of life and increasing their autonomy, which is the case for patients suffering from chronic disease such as diabetes or heart failure. For them, the use of health digital tools contributed to increase their level of empowerment and comply with medical treatment. Furthermore, encouraging patients to share their information contributes to a debate or critical thinking about their health condition. The outcome is an increase in willingness to be co-creators and co-actors of health decisions, impacting patients' conditions (Adkins and Corus 2009). The democratization of digital tools and online health information raised users' expectations and forced health providers to change their manner of engaging patients for a new step in shared decision-making. Even if there are various benefits for patients to use health digital tools, it requires a minimum of ability to understand constraints and risks of these new medical types of equipment (privacy concerns, frauds, security risks…).

To explore the complexity of the collaboration paradigm in health delivery, McColl-Kennedy et al. (2012) identified a typology of patients that perfectly fits digital users. Five types of practices were highlighted: team management, insular controlling, partnering, pragmatic adapting, and passive compliance. These styles of cooperation depend on the level of interaction that patients have with practitioners, medical staff, and, more globally, all stakeholders involved in the health delivery process. The second variable refers to the level of activities. It characterizes patient involvement and the manner to co-create value with others. This results in the ability to combine complementary treatments, produce, and share information, contribute to redesigning medical protocol, and state with healthcare actors how to deliver care, etc.

5 Patients' Key Concerns

5.1 Why Privacy and Ethical Concerns are So Significant for Patients

It is obvious that the digitalization of healthcare has modified the patient–physician relationship. Even if computers, IoT, and all digital solutions managed to care for patients bring benefits, these processes raise ethical issues grounded on data and its use. More and more IT users become aware of data privacy concerns, impacting the fundamental individual rights of users/patients. However, for some segments of users, digital solutions could contribute to exacerbating existing social health inequalities. So, providing information about data operation and practices is essential to make aware users of digital medical tools, particularly with IoT, which constantly and invisibly captures information to make subsequent suggestions, dynamic personalization, or nudge users into specific decisions or choices.

The main challenge in this context of health digitalization of health is to enable users to make informed decisions (Bender et al. 2017). The success of medical tools and IoT or, more globally, all connected health devices ties it with its durability. For sufficient connected medical devices, capture and data collection must be done regularly to provide a tailor-made solution to patients, and consequently, accelerate the advanced scientific knowledge. In this framework, transparency plays an essential role in the use and patients' involvement. Empowering patients with more controls on medical devices improves their level of trust and use, contributing to the dissemination and sustainable use of technology.

Providing users with more significant information access led them to a higher perception of control on privacy concerns, but also to feel more involved in taking ownership of eHealth solutions. At the same time, perceived control relies on the type of information shared (personal or not) and depending on who and with whom this information will be shared. Thus, all these new technologies are more than just the use of e-solutions or e-devices in medicine (Brandimarte et al. 2013). Designing e-health requires human centricity, method orientation, and problem centricity to provide patients and users of digital solutions with the perception of sufficient benefits for patients and users of digital solutions rather than constraints. The methods supported by design thinking and marketing based on S-D logic appear consistent with validated methods based on co-construction and co-elaboration of solutions, including patient and medical stakeholders involved in the healthcare delivery.

5.2 Is It Fundamental for Healthcare Actors to Reintegrate Patients/Users' Expectations?

Ethical challenges are fundamental, particularly in healthcare, due to the blurred distinctions between private and public information. A patient who has diabetes with a continuous glucose monitor will not always pay attention to how personal information is used and for what. However, this is particularly critical within a digital context, due to the ease of access to data or the possibility of hacking them. Reintegrating patients and users of digital health solutions is consistent with co-creation concepts, close to patients' expectations, and assisting in reducing breaks and barriers they have for future adoption of these devices.

So, reintegrating and supporting a convergent approach between S-D logic and design based on privacy and ethics promotes positive outcomes for e-Health. Design thinking is based on the ability to take advantage of users' knowledge and their ability with IT. Reintegrating patients into the development of medical solutions increases confidence, commitment and ownership of these solutions. "*Successful management of chronic diseases, such as cancer, is related to the collaborative interactions*" between major stakeholders involved in the healthcare delivery (McColl-Kennedy 2012, p. 7). This is particularly true considering the role played by connected tools used in the healthcare industry, impacting positively acknowledgment towards patients. This approach is essential for a long-term use of connected devices: (1) to increase a tailored-made medicine, providing adapted care, relying on a high level of confidence towards medical tools; (2) based on the long-term adoption of connected devices, patients contributed to a better understanding of pathologies for better care. Empowering patients and medical staff who deal everyday with their pathology enable them to understand challenges experienced by patients.

5.3 A Convergent Approach for All eHealth Stakeholders: Co-Design of a New Method to Create Real Added Value for Patients/Users

Involving patients in the elaboration process of connected health devices reduces significantly clinical uncertainty and encourages eHealth adoption, for an overall improvement of health experience and patient empowerment. Co-designing connected health solutions allows the identification of patients' interests, abilities, and beliefs to use connected devices. Patients' participation in the process elaboration assimilated as facilitators for the co-creation and development of these tools to achieve tailor-made solutions. This method is profitable for all stakeholders involved in health delivery. Proceeding to co-creation may further lead to a higher level of innovation and foster critical thinking towards connected health. It gives the opportunity to go beyond the simple observation of a phenomenon. Cavoukian's (2009) investigations highlighted seven pillars for privacy by design, Table 2. Patients' implication at

Table 2 Principles of Privacy by design

Concepts	Illustrations
Proactive not reactive; Preventative not remedial	Foresee and anticipate incidents that could impact the privacy of users of connected health solutions
Privacy as the default setting	Ensure the protection of personal data and privacy in the field (i.e., health data collection is not done without the user's knowledge but benefits from its consent)
Full functionality	Integrate privacy protection into the design (i.e., privacy and health considerations should not be identified after the connected solution has been built but directly integrated)
Visibility and transparency	Guarantee the operation of the solution in accordance with the objectives (i.e., the connected object in health is then a means with a clearly identified and known objective)
End-to-end security - full lifecycle protection	Security must be achieved throughout the life cycle process of the solution (i.e., health data must be stored securely and then destroyed when no longer needed)
Respect for user privacy—keep it user-centric	Adopting a user-centered approach, taking into account individual rights (e.g., ergonomics of the connected health solution, facilitation of use and patient experience.)

the early stage is essential to scope with them the usage of medical devices. Working with them at the first stage of the design solution plays an essential role to understand and reach patients' expectations. The other stages are more inclined to validate, refine the solution, and evangelize the medical solution in patients' communities.

Privacy by design encourages the empowerment of practitioners and even the dissemination of a culture of data ethics within the company. The implementation of privacy by design requires major adaptations due to the lack of knowledge of the potential risks and the need for trade-offs between data protection and innovation depending on the context of use. This implies questioning the role of individuals in the protection of their data. The user inclusion in the design of connected health solutions would, therefore, rely on complementary solutions such as the privacy by design principle, and at the same time on dynamic learning mechanisms for the user. Thus, users would be more aware of the nature of the data collected and their use. This would enable users to understand the indirect and/or long-term consequences of the explicit or implicit disclosure of personal data; this is particularly essential in the case of HIoT or quantified-self connected solutions because users no longer monitor the information themselves due to direct and continuous transmission. This would put users in a better position to define their privacy behavior through a learning mechanism. They will not necessarily do so, but they will have the elements to adopt an informed behavior. Through empowerment, the consumer, made aware—or

"*capable*"—could thus make fully informed decisions, which could thus encourage the emergence of new shared privacy standards.

6 Outlook for the Future

The previous parts of the chapter have emphasized the key theoretical tenets that underlie a user-involved product design in the health sector. However, while patient involvement through acknowledging the patient perspective by providing patient value and ensuring a process of co-creation of patient value is indeed suggested, it remains debatable whether the patient's perspective is always desirable. More particularly, is a service-dominant logic always a better alternative? To this question, Vargo and Lusch answered themselves by emphasizing that "*goods logic is thus seen as nested in S-D logic, rather than replaced by it*" (Lusch and Vargo 2014, p. 247). More specifically, the G-D logic is preferable in "*deeply entrenched, institutionalized solutions-that is, in well-established markets*" (p. 247). Whether this is the case in the health sector remains debatable as the market is not necessarily well established for all kinds of products, services, processes, or systems. Therefore, future research endeavors might better highlight the key conditions and variables that might influence the shift to an S-D logic with stronger user involvement in product design versus the more specific G-D logic that is less reliant on user input.

Related to the previous point, the notion of value is quintessential, but many organizations in the health industry remain product-centric manufacturing companies due to their well-established and often rather captive markets (e.g., hospitals, clinics). These companies might alternate between different value logics as emphasized by Lindhult et al. (2018) such as "*product-based value logic, service-based value logic, virtual-based value logic, and systemic-based value logic*" (Lindhult et al. 2018, p. 457), while even drawing on several of them simultaneously. Yet, for the highly sensitive issues pertaining to users that are raised by eHealth, patient input is crucial, as emphasized in this chapter. SDL theory needs further specifications and refinements to better mirror those circumstances particular to healthcare. Therefore, to further bridge the gap between SDL theory and practice in the healthcare sector, researchers might further a midrange theoretical model for value creation that blends both product-centric and user-centric perspectives into a cohesive whole.

The digitalization process is well advanced in mature economies with technological infrastructures that permeate most areas of the economy. Yet, developing economies might still be at a disadvantage to implement the same level of eHealthness across their overall healthcare sector. In this regard, some technologies tend to stand out, such as mobile technology (and hence, mHealth), which is generally very vivid in emerging economies (Murthy and Naji 2020). Therefore, additional studies might further investigate how mHealth might further contribute to higher user involvement in product design in emerging contexts.

7 Conclusion

The health sector, as we have known it for many years, based on the use of organization-powered instruments and devices, is experiencing tremendous shifts due to technological advances that provide better means to monitor and treat patients remotely while improving patients' capability to self-monitor themselves and growing in empowerment vis-à-vis medical staff. However, these advances come with mixed impacts for both healthcare professionals and patients. Professionals need to be more trained and deal with new ways of doing and learning to cope with increasingly autonomous (and relatively empowered) patients, while patients' data are faced with increasing privacy, security, and overall trust concerns regarding their data management, among others. Furthermore, technical literacy and difficulties might further hinder the adoption and continuance of eHealth by patients. We, therefore, witness a growing focus on patients who tend increasingly to be considered key partners and stakeholders in the co-construction of health care services provided to them.

This chapter draws on the marketing literature on consumer value, co-creation, and Service-Dominant Logic (S-DL) to delineate and discuss the patient-centric paradigmatic shift in the healthcare sector. We namely explain the digitalized healthcare sector and how it espouses well the notions of patient value and co-creation of patient value since patients use technology to co-create the healthcare service in collaboration with the medical staff. Most importantly, the chapter underscores how patients need, therefore, to be involved in the design of those health products to better meet their expectations and mitigate potential privacy, ethical or other concerns. One key approach can be used to this end, namely privacy by design in a co-creation process, i.e., which involves the user. The solutions elaborated under such principles will better meet user expectations, especially regarding privacy issues. Finally, user-involved design and co-creation might not always be required or applicable in every case. Both approaches of involving users or not involving them are the two faces of a same coin or the two opposites on a continuum. A more nuanced approach should be taken in order to assess situations in which signal the relative shift toward more or less pronounced user involvement.

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Chapter 2
Design for e-Mental Health: Toward a New Health Intervention Research Approach

Stéphane Vial and Sana Boudhraâ

1 e-Mental Health: A Quick Overview

e-Mental health is an area of research and intervention that relies on digital technologies to provide mental health care, support, or information to complement traditional care. According to the Mental Health Commission of Canada, *"e-mental health delivers timely, effective mental health services by using the internet and other related technologies"* (Mental Health Comission of Canada 2021). E-mental health emerged in the early 2000s and has been often related to telepsychotherapy and telehealth. However, it is much wider and includes access to medical information, coordination of care pathways, prevention and follow-up, treatments, self-care, or peer-to-peer support.

For instance, the *Sleepio* app (https://www.sleepio.com, United Kingdom) helps to overcome insomnia through a digital sleep improvement program; the web-based tool *Aller mieux à ma façon* (https://allermieux.criusmm.net, Canada) aims to support mood disorders self-management; the *Ginger* app (https://www.ginger.com, United States) offers emotional support and guided self-care to employees of select employers; or the *Temstem* app (https://www.reframingstudio.com/projects/temstem, The Netherlands) helps people who suffer from psychosis to distract from the voices they hear and strengthen themselves.

In many countries such as Canada, e-mental health is seen as a means to deeply transform the mental health system (Mental Health Comission of Canada 2014) and make it easier to use, more efficient, and more equal. Research in e-mental health conducted around the world is increasing (Drissi et al. 2020). Since the beginning of the COVID-19 pandemic, digital health at large has experienced unprecedented

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growth (Golinelli et al. 2020). In particular, the potential of digital health to improve access to quality mental health care has never been greater (Torous et al. 2020).

However, the market of e-mental health services is confused and the many challenges identified in recent years in the literature have not disappeared, such as the lack of scientific validation (Anthes 2016; Torous and Roberts 2017; Donker et al. 2013; Olff 2015; Larsen et al. 2019), the privacy and data security concerns (Torous and Roberts 2017; Torous 2016; Lipschitz et al. 2019; O'Loughlin et al. 2019), the lack of availability and advertising (Lipschitz et al. 2019; Mehrotra and Tripathi 2018), or the financial interests of developers (Lal 2019).

This is why the reality of digital uses in mental health is far from the initial ambitions imagined nearly 20 years ago. Large-scale implementation faces the harsh reality of long-term adoption (beyond simply downloading a mobile app). A study based on 93 mental health apps found that overall user retention is very low, with a median 15-day retention rate of 3.9% and a 30-day retention rate of 3.3% (Baumel et al. 2019). This is what Eysenbach in 2005 called *"the law of attrition"*: in any digital health trial, a significant proportion of users drop out before completion or stop using the application (Eysenbach 2005). The limited data available about the health app market confirms this: most mobile health apps are downloaded less than 5,000 times and 46% of these apps have fewer than 1 monthly active user.

Yet, investments in digital health are massive: the average cost of developing a mobile health app is US$425,000 (Research 2 Guidance 2018). The growing market of mental health startups is impressive, approaching 1000 startups worldwide in 2020 (Hays 2020). The benefit–cost ratio of these technologies is very high and unsustainable if nothing is changed in the way they are developed. More importantly, these apps will not be associated with a decrease in mental disorders if they are not used for a sufficient period (Torous et al. 2018).

2 Why Design Methods Matter in e-Health

Several studies show that most users are willing to accept and use new technologies for their mental health (Proudfoot et al. 2010; Huang and Bashir 2017; Dragovic et al. 2018). How can we explain the low rates of use? Supported by the literature, our hypothesis is that the lack of adoption of digital health technologies is due to a lack of attention to user needs when designing these technologies (Birnbaum et al. 2015). In fact, existing solutions consider the needs of users too late or too little (Hostetter et al. 2014). There are very few examples of the involvement of people with mental disorders in the conception and design of a mobile application for them (Torous et al. 2018). The most common design methods are based on the bilateral partnership between clinicians and engineers (National Institute of Mental Health 2019) and they are not adapted to the challenges of the contemporary digital culture that systematically places the users at the center by empowering them (Cardon 2019).

However, there are design methods that allow end-users to influence the design of technologies significantly and positively. They are known under different names

such as user experience design (UX), user-centered design, human-centered design, service design, design thinking, codesign, etc. Originating from academic research, these design approaches have been developed and adopted by creative agencies, design agencies, and major companies in the tech industry, who have appropriated them for developing their digital products/services and solutions. These methods are historically derived from the disciplines of industrial design and graphic design (Moggridge 2007). They should not be confused with the disciplines of engineering design, to which they combine advantageously. The differences between engineers and designers in the way they approach the design of a technology are documented. In the initial prototyping phases, engineers seek to define specific goals to be achieved and focus on technical functioning following a linear thought pattern, whereas designers use the prototype to creatively explore the design space for new possibilities (Yu et al. 2018). Design thinking is globally recognized for fostering the emergence of innovative solutions (Brown 2008), including in healthcare (Ku 2020).

Although they are not specifically related to mental health, two of these approaches, in particular, are worthy of use in mental health: user-centered design and codesign.

User-centered design, also called human-centered design, was defined in the late 1980s by D. Norman in his book *The design of everyday things* (17,370 citations in Google Scholar) (Norman 2013). It aims to design products that are easily usable and immediately understandable, thanks to a certain number of design principles, for example, the importance of affordances (the user understands what to do just by looking). Enriched by the works of J. Nielsen on web usability (Nielsen 1999) and J. J. Garrett on user experience (Garrett 2002), user-centered design has become the standard for best practices in web design. Garrett defines it as *"the practice of creating engaging, efficient user experiences"*, which means: *"Take the user into account every step of the way as you develop your product"* (Garrett 2002, p. 17). User experience is defined as *"the experience the product creates for the people who use it in the real world",* that is, not its internal operation but *"how it works on the outside, where a person comes into contact with it"* (Garrett 2002). In the case of an app, it is the cognitive (ease of use) and emotional (affective dimension of the use) experience that the user has when facing the screen. Recognized for fostering user engagement, user-centered design tends to be called user experience design (UX design). It has become an industry standard and has been widely used in the design of social media, video games, or fitness apps. However, the principles on which user experience design is based have little or no use in mental health (Torous et al. 2018; Bakker et al. 2016).

Codesign emerged in the late 2000s. According to Sanders and Stappers' definition (4380 citations in Google Scholar), codesign refers to *"the creativity of designers and people not trained in design working together in the design development process"*. It is *"collective creativity as it is applied across the whole span of a design process"* (Sanders and Stappers 2008). It is a highly participatory process in which the user is not only a subject of study (as in user-centered design) but a full design partner who intervenes alongside the designers from the beginning to the end of the design process. Codesign is practiced in focus groups, using materials such

as post-it notes, paper models, mockups, predefined card sets, boundary objects, etc. This type of approach is not well developed in digital health (Birnbaum et al. 2015) and is very rare in mental health (Torous et al. 2018).

Both user-centered design and codesign could have a great impact on more patient-centered research in mental health.

3 Design for e-Mental Health

Design for e-mental health refers to the broad range of human-centered design creative strategies that define the structure, function, and form of a digital mental health service from a high ethical and experiential quality perspective. At first glance, it is the application of codesign and user experience design methods to the field of digital mental health intervention research. But it is much more than that. Design for e-mental health is an approach to health innovation that is rooted in transdisciplinary research and inspired by responsible innovation in health. It is an end-to-end codesign-driven methodology which involves at all stages stakeholders such as patients, families, peer support workers, mental health professionals, and more. It is a slow innovation process facing complexity, which integrates theoretical and methodological foundations that are usually separated.

3.1 Theoretical Foundations

Design for e-mental health is rooted in three theoretical foundations: technological mediation, design for social innovation, and responsible innovation in health (Fig. 1).

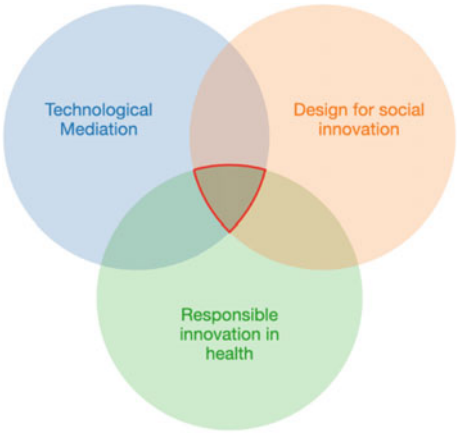

Fig. 1 The three main theoretical foundations of design for e-mental health

Technological mediation. Coming from the field of philosophy of technology, mediation theory is an approach to relations between humans and technologies based on the idea that technologies play a mediating role in the broad relation between humans and their world (Verbeek 2015). According to this approach, designers do not design things, they design human–world relations in which practices and experiences take shape. The role of design is to shape human–technology relations and, in that sense, it is a highly responsible activity. *"Designers materialize morality"*, says Verbeek (2015). They incorporate in technologies values and choices about how we want to experience the world. Design is philosophically responsible for experience (Vial 2019). In this view, the type of mental health technologies we develop determines the type of relationship we want to have with our mental health, that is, the type of practices and experiences we want to have with it. Understood in a broad sense, this includes a various range of technologies such as architectures, medical devices, or mobile apps. Design for e-mental health is a proactive approach to building digital technologies that contribute to shaping desirable relations between humans and their mental health. It proposes to rethink the experience of care, treatment, or the health system, thanks to new types of relations between humans and mental health mediated by the digital (mobile apps, internet-based services, etc.).

Design for social innovation. Coming from the field of design and based on a worldwide network of university labs, design for social innovation is a design approach focused on codesign and social change (Manzini 2015). Groups of people who cannot solve their problems alone join together in cooperative projects in order to develop sustainable social innovation at the local level and to focus on the design of less polluting services centered on collective well-being (shopping groups, materiel sharing, shared gardens, etc.). These collaborative projects are led by expert designers and rely on collective creativity, thanks to codesign. Codesign appears when *"diffuse design"* (the natural designing capacity of anybody, i.e. non-experts) meets *"expert design"* (the ability to operate as a trained designer, i.e., design professionals). Design for social innovation is *"the expert design contribution to a co-design process aiming at social change"*, says Manzini (2015). Design for e-mental health builds on design for social innovation in the specific area of e-mental health. It aims to improve population mental health and mental health services, in a more responsible and human-centered manner. It is a codesign process led by researchers and designers that involves patients, families, and mental health professionals.

Responsible innovation in health. Coming from public health, research innovation in health is an integrative framework that builds on the field of responsible research and innovation. It is a collaborative approach *"wherein stakeholders are committed to clarify and meet a set of ethical, economic, social and environmental principles, values and requirements when they design, finance, produce, distribute, use and discard sociotechnical solutions to address the needs and challenges of health systems in a sustainable way"* (Silva et al. 2018). It is comprised of nine dimensions organized within five value domains, namely population health, health system, economic, organizational, and environmental. This framework supports the development of innovations that address important challenges for the health system,

such as health equity, alternative business models that benefit more society, or eco-responsibility. Design for e-mental health is an attempt to develop responsible innovation in e-mental health by focusing on the specific ethical issues of the digital domain. For instance, it gives central importance to data privacy and cybersecurity, thanks to privacy by design methods (Cavoukian 2010), or it seeks to develop eco-responsible technologies, thanks to digital sobriety strategies (Chevance et al. 2020).

3.2 End-to-End Codesign

In design for e-mental health, codesign is used as a qualitative method of participatory action-research, within a general process of design for social innovation seen as an innovative and responsible approach to intervention research in mental health. As seen above, codesign is a process of collective creativity applied to the entire design process, involving both professional designers (expert design) and people not trained in design (diffuse design). By people not trained in design, we mean various mental health stakeholders such as patients, families, peer support workers, psychologists, psychiatrists, health professionals, health managers, and more. These stakeholders bring in the process their natural creativity (which is a personal gift universally shared) while expert designers bring *"original ideas and visions"*, *"practical design tools from different design disciplines",* and a structured design process (Manzini 2015). Imagined by the design team, the initial idea of the project becomes a shared object of collective design that keeps evolving in the form of a *"social conversation"* between the different participants (Manzini 2015) and that takes shape in an iterative way through a commented and continuously improved prototype (Fig. 2). In order to express their needs and expectations, typical activities offered to participants are ideas generation based on visual tools, discussions, and consensus-building processes (Fig. 3).

Stakeholders involvement is not ad hoc or isolated, for example only at the beginning of the project to gather insights or at the end to test the app. Participants are selected following a public call for volunteers based on various relevant inclusion criteria. They are involved from start to finish and have a say in all major decisions, from design to implementation, through several participatory mechanisms (co-creation workshops, validation meetings, priority beta testing…). Of course, this may take more time than traditional innovation processes, but it's worth it since the outcome will be the shared construction of a solution that is appropriate to the common needs and meets the shared expectations of all stakeholders.

The essential challenge is to design technologies that are in line and in close connection with the needs and realities of the end-users (represented by codesign participants, i.e., stakeholders). It is this challenge that most mental health startups fail to address, because of their obsession with going fast, too fast: they are missing a deep understanding of stakeholders needs (that they study in a superficial way through quick user research) by avoiding the difficulty of diving into the infinite complexity

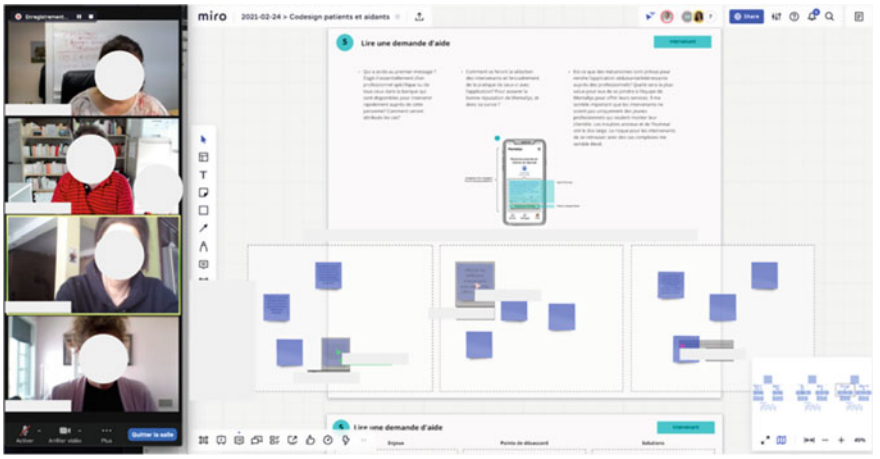

Fig. 2 A commented prototype during a remote codesign workshop with patients and caregivers: participants share their views and add virtual "post-its" on a mobile app mockup

Fig. 3 A face-to-face codesign workshop with psychologists and psychanalysts: participants describe their daily lives with patients and discuss the best options

and detail of mental health issues and practices. As well said by Paul Yock, *"the 'move fast and break things' approach that works in tech doesn't translate well to healthcare"* (Yock 2018). This is why design for e-mental health is a slow innovation process, whose motto would rather be: "move slow and break nothing". Design for e-mental health needs to welcome vulnerability with delicacy, and in that sense, it is close to the Ethics of Care (Tronto 1993). And to address the challenge of complexity in a truly relevant way, it requires transdisciplinary research.

3.3 Transdisciplinary Research

Multidisciplinarity (also called pluridisciplinarity) occurs when several disciplines offer their points of view on the same object without exchanging concepts or methods.

Table 1 Examples of transdisciplinary relations

Type of relation	Concept or method A	Concept or method B
Equivalence	Innovation through uses in sociology	User-centered approach in design
Equivalence	Technology acceptance in communication and marketing	User engagement in health research and e-health
Combination	Agile development in IT/computer science	Iterative process in design
Complementation	User eXperience (UX) in management (evaluation)	User eXperience (UX) in design (production)

Interdisciplinarity occurs when several disciplines develop a shared perspective on the same object by sharing or combining some of their concepts and methods. Transdisciplinarity occurs when multiple disciplines contribute to the development of a point of view that transcends those disciplines and becomes independent of them, possibly crossing all major scientific sectors (Darbellay 2015).

Design for e-mental health is a transdisciplinary intervention research approach.

First, it brings together several disciplines from the three main scientific sectors: (1) health research and sciences (psychiatry, clinical psychology, health technologies, public health); (2) social sciences and humanities (design, ergonomics, ethnography, communication, sociology, marketing, linguistics); (3) natural sciences and engineering (computer science, software engineering).

Second, it offers a unified point of view based on various relations between concepts and methods from the different disciplines involved. As we could observe in the initial steps of our research project Mentallys (see Sect. 4.2), these relations can be (at least) of three types: equivalence, combination, and complementation (Table 1).

The relation of *equivalence* concerns ideas or methods coming from different disciplines, but which are similar, and therefore equivalent to each other, even though they are formulated differently by each discipline.

The relation of *combination* concerns ideas or methods coming from different disciplines that benefit from being put together to form a more effective or powerful idea or method that could not otherwise exist.

The relation of *complementation* concerns ideas or methods coming from different disciplines that complement each other, i.e., that fill in their mutual gaps to constitute an exhaustive whole.

Although these relations are not specific to mental health intervention research and could apply to various other fields, we have defined them from the observation of our research process in e-mental health. They illustrate the complex nature of a transdisciplinary approach applied to mental health. Such a transdisciplinary approach is absolutely necessary for working on complex problems such as those in the field of mental health, where many different types of actors (patients, families, peer support workers, clinicians, etc.) are involved in many different processes

(clinical, institutional, financial, etc.) in many different contexts (public, private, and community).

However, the implementation of this approach is also complex. The transdisciplinary relations between ideas generate many more misunderstandings than in a classical monodisciplinary approach. The same term is understood very differently from one discipline to another (e.g., a simple word like "object" can refer to very different realities depending on whether it refers to psychiatry, design, or software development). To maintain an effective collaboration and a shared understanding of problems during co-creation workshops with clinicians or co-investigators, it is necessary to invest a lot of time in a *term mediation* work allowing each member of the team to appropriate correctly the key terms of each discipline. Such work requires a great deal of familiarity with the way of thinking and the vocabulary of each discipline. A good understanding of the relevant concepts and methods in each discipline involved makes it possible to assign to each discipline the part of the work for which it is most relevant. Therefore, one of the keys to successful design for e-mental health lies in transdisciplinary leadership, which can only be achieved through many years of experience in contact with several disciplines. The ability of design to facilitate multidisciplinary innovation projects also plays an important role (Minder and Heidemann Lassen 2018).

4 Two Case Studies: Temstem and Mentallys

In this section, we present two emblematic cases studies of design for e-mental health. First, the Temstem app (The Netherlands), which is already developed and released on app stores. Second, the Mentallys app (Canada), which is in early stage and under development. Both are using a codesign process and a design-driven transdisciplinary approach.

4.1 Helping People to Cope with Hearing Voices: Temstem

Developed in the Netherlands, Temstem is an app based on language games that aim to help people to distract themselves from the voices they hear, and to actively exercise and strengthen themselves in relation to these voices (Temstem: An app to help people cope with 'hearing voices'. Reframing studio, Amsterdam). It was codesigned by a group of designers, psychotherapists, and people who suffer from psychosis, involving a design university (TU Delft), a design firm (Reframing Studio), and a private non-profit mental health institution (Parnassia Groep).

Temstem offers to play two language games: in one of them, the user must tap the number of syllabi in a set of words during a predefined time; in the other, the user must form correct combinations of two words by linking them (Fig. 4). By playing these word games, the user activates the language production areas in the brain,

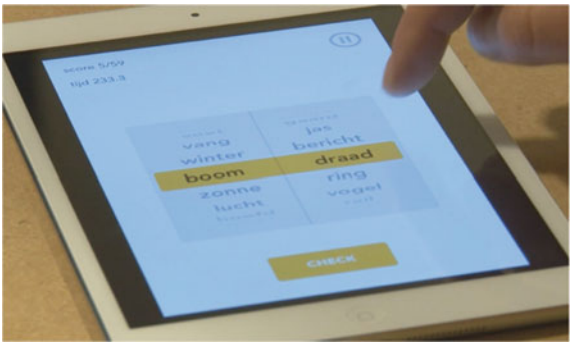

Fig. 4 Woordlink offers two sets of words that must be correctly combined

the same that becomes active when hearing voices. Playing these games cancels or reduces hearing voices, offering a way to distract from them (Fig. 5). In Dutch, the word "temstem" means "tame voices".

In order to build this app, industrial design students spent a day in the life of people with psychosis and were asked to design a product that would promote the recovery of psychosis and social inclusion. This led to the Temstem app, designed by the Reframing studio design firm. Main methods used to make this app were codesign, user experience design, game design, and ethnographic approach. The transdisciplinary approach consisted mainly in putting in dialogue the creative disciplines of design, mental health sciences, and computer engineering disciplines.

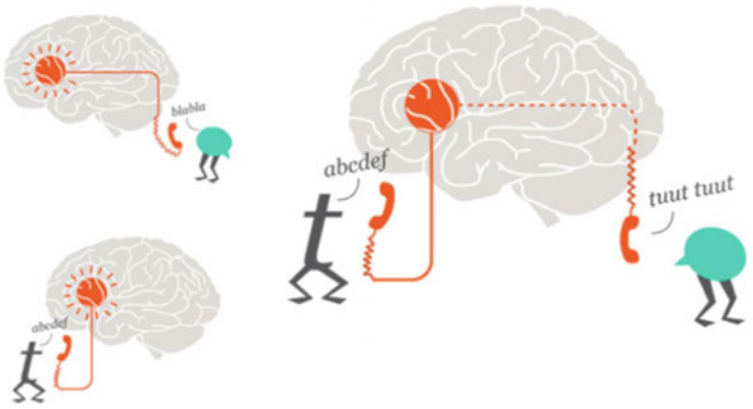

Fig. 5 Illustration of how the Temstem app helps to reduce voices by activating language areas

4.2 Improving the Experience of Accessing Mental Health Care: Mentallys

Under development in Québec, Canada, Mentallys is an app-based service that aims to improve the experience of accessing mental health care. The experience of accessing care refers to the fact that an individual initiates and follows a care path through the various mental health systems (public, private, and community), from the first steps to long-term follow-up. Mentallys seeks to open a mental health care access point in people's pockets, where their cell phones are, to drastically facilitate and simplify the experience of accessing care and services and to support the recovery process.

The project codesign process is multi-level, involving several levels of codesign with different types of participants, namely end-users (patients, families, psychologists, psychiatrists, peer support workers), transdisciplinary co-investigators (researchers from various disciplines), and expert designers (professional designers) and software developers (dev team). With each of these groups, specific codesign activities are implemented in order to maximize the benefits of the collective intelligence that inspires the project. In addition, specific codesign workshops within the lead design team are also organized (Fig. 2).

End-users are involved from start to finish in all stages of the app's design, placing their needs and perspectives at heart. They are composed of two main groups: end-users who are involved in the design at a very early stage, and end-users who test the app prototype in real-world health care environments, thanks to partnerships with public psychiatric services, a professional association, and a community organization (Fig. 6).

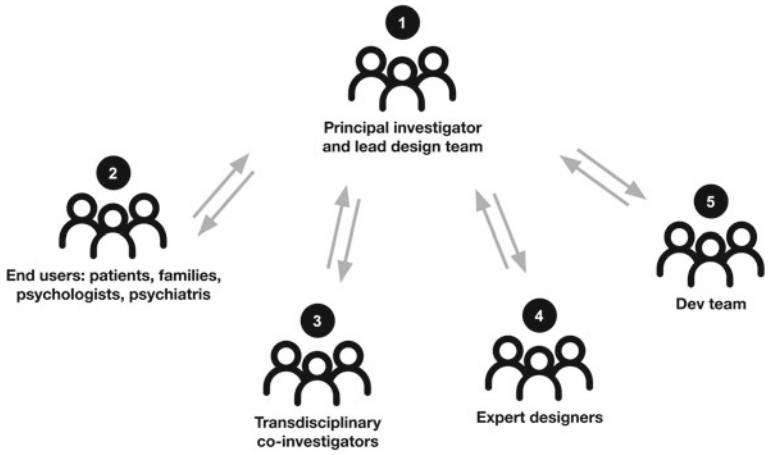

Fig. 6 Mentallys multi-level codesign process

The Mentallys app is currently under development and the project is still in early stage. However, the first series of six codesign workshops conducted between January and June 2021 with 14 end-users has allowed defining the first core of functionalities. The project involves 4 universities, 24 researchers, and more than 10 disciplines including design, ergonomics, psychology, ethnography, nursing, public health, computer science, software engineering, linguistics, marketing, and communication.

5 Conclusion

E-mental health is a growing field of research and intervention that can deeply transform our mental health experience. However, the user retention rate of digital mental health technologies is very low. The lack of design methods such as codesign and user experience design is largely responsible for this. Design methods have the power to facilitate technology acceptance and generate user adoption. This is critical when it comes to mental health.

Existing research tends to focus mainly on science, that is evaluation of the effectiveness of these technologies. This is essential, but this is not enough. A technology that is highly validated by science is *useless* if it is not *used*. Design methods help to integrate the users' needs into the design early on and stay true to them from start to finish. In that sense, design for e-mental health is a contribution to the development of high-quality standards in digital technologies for mental health.

Design for e-mental health refers to the broad range of human-centered design creative strategies that define the structure, function, and form of a digital mental health service from a high ethical and experiential quality perspective. It is an attempt to bring codesign and user experience design methods to the field of digital mental health intervention research. But it is also a new approach to health innovation that relies on end-to-end codesign and builds on highly transdisciplinary research.

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Chapter 3
Addressing Vicious Cycle of Medical Distress with Augmented Reality: State-of-the-Art Review

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1 Introduction

Stress is a body reaction to certain situations. The human nervous system coordinates the behaviors, cognitive load, emotions, and motivations. Stress triggers the autonomic nervous system that has effects on the human body. It is complex, mixed, and varies in different physiological, psychological, and behavioral indicators. General effects are increased heart rate, blood pressure, brain activity, muscular strength, metabolic rate, etc. However, stress is an essential and inevitable part of human life (Wright et al. 2007). World Health Organization already estimated that depression and anxiety disorders to be growing by the year 2020 (Kalia 2002). Stress can be related to numerous factors that affect various ranges, including forces of duties and leisure time activities. According to the holistic stress model (see Fig. 1) stress includes positive responses as well as negative ones (Simmons and Nelson 2007). "Eustress" is known as good, positive stress, besides "Distress" is negative stress that happens in difficult, unfair, and painful situations. Stress can be a risk for stress-related illnesses as well as a useful stimulant for humans' daily life that motivates individuals to move into action and accomplish targets (Fevre et al. 2003). Stress management techniques control the individual's stress level and it has a significant role to balance stressors. Stressors can be challenging or threatening events or environments that stimulate or create tension in the individual. Whether stress is a positive–negative stimulus, being aware of the stress situation eases the management process and exploiting it. The published work shows that the exposure of stressors intensity and duration presents different impacts to the stress response (Kupriyanov and Zhdanov 2014). Stress management has wide physical and psychological techniques and therapies such as practicing mindfulness with controlled breathing, stretching, organizing events schedule, exercising, or cognitive behavioral therapy (CBT), and more. CBT

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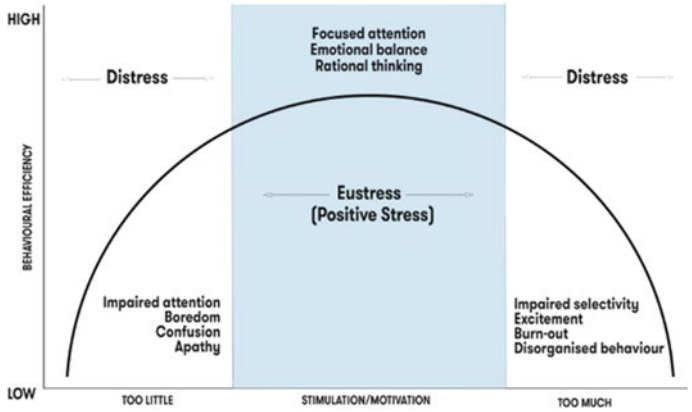

Fig. 1 The relationship of behavioral efficiency and amount of stress, too much and too little stress is distress and in the middle is eustress phenomenon

is a psychotherapeutic treatment for anxiety and phobia that can be effectively used in short-term treatment. It is centered on changing the automatic negative thoughts based on faulty or unhelpful ways of thinking that can emerge into fear and anxiety and be reshaped to more objective, positive, and realistic thoughts (Mendes et al. 2008).

Recently, AR is getting popular as it offers an alternative interface to the users (Rauschnabel and Young 2016). AR is an exciting concept that allows us to feel and live in a phygital environment that combines physical and digital content in real time, dynamically with computer-generated sensory inputs. It is estimated that AR will take place in a large part of our lives in the future.

AR provides huge opportunities in medicine such as remote guidance, surgical virtualization, medical device utilization, medical training, patient care, healthy lifestyle and therapy, and more. Using AR surgeons can precisely perform with low risk and save time in critical situations.

There is plenty of medical AR research that is studying how to use this novel technology and bring it into practical use in medicine. As revealed in the study conducted by Evangelista et al. (2020), medical augmented reality is one of the application domains with the most R&D efforts reporting an interesting number of 64 patented solutions. Among the 13 application domains identified in the study, medical augmented reality ranks fourth in terms of the number of patented solutions.

Medical distress refers to the negative stress for both surgeons and patients. This mutual distress creates a vicious cycle that creates wider complications. Surgeons' medical distress is caused by the tiring workload. The learning curve required to become surgical expertise has been an issue in the medical community. Therefore, burnout and suicide rates among the surgeons are increasing over the year. Besides, distress of patients is common in pre- and post-operative scenarios. This surgical anxiety can transform into a permanent phobia. The distress of a patient may cause surgical complication, and prolongs the recovery. Many people prefer to have online

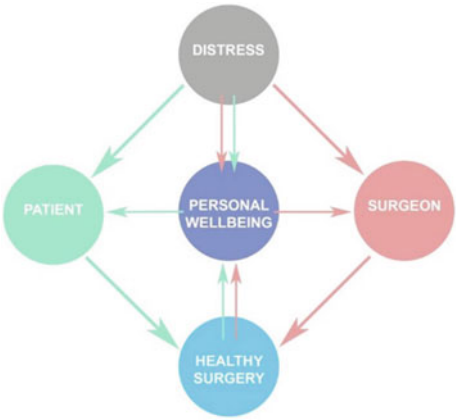

Fig. 2 Vicious cycle of medical stress; arrows means that affect the pointed event or fact

mental health services to deal with stress and anxiety. This vicious cycle of medical distress causes the deterioration of both surgeons' and patients' life quality, extra money and time loss, and worsens the overall outcome. Hence, this works aims to explore AR for addressing the vicious cycle of surgeons' and patients' medical distress (see Fig. 2). This distress situation contributes to adverse events and other undesirable consequences.

2 Related Work

The related work is divided into three main sections: the first part reviews the stress management methods and common coping strategies; the second part analyzes innovative stress management solutions using AR. During the state-of-the-art analyses the research was performed on several databases, using search terms TITLE-ABS-KEY ((“Augmented Reality” AND (“mental health” OR “stress management”))). Totally, 79 papers are found. The papers that are addressing virtual reality and the papers that are not related to patients' or surgeons' health are excluded. Finally, six papers are screened according to Table 1.

Table 1 The inclusion/exclusion criteria of the found papers

Included papers	Excluded papers
Augmented reality/mixed reality	Virtual reality
Stress and stress management	The studies that are not related to patient's health
Mental health	The studies that are not related to the surgeons' health

Finally, the third part examines the pre-operative, operative, and postoperative conditions and analyzes possible conceptual AR solutions differentiated for and surgeons' and patients' points of view.

2.1 Stress Management Methods and Common Coping Strategies

Stress happens when the individual is being affected by some events and reacts to these events physically and psychologically. Stress resistance is a mechanism that tolerates stress and is a skill to protect human well-being. Therefore, when the stress resistance is low, it affects us negatively and at important times. Having excessive stress can cause burnout while having a small amount of stress can cause boredom, and both situations are called distress situations (see Fig. 1). Instead, having the right amount of stress can create a balance situation and motivate individuals when they face stressful situations. Stress management can be obtained with several methods and techniques and is proved to have benefits for managing distress, such as yoga, mindfulness and meditation, CBT, physical activities, and more (Riley and Park 2015; Jackson 2013). Although these methods establish benefits for stress management, they are not easily applicable in daily routines and some therapies without support or expert are not easily understandable. People show significant changes in the heart rate or brain activity when they are exposed to stress. Currently, in the market, there is various stress wearables and application to detect the stress and manage it.

Fitbit Sense (2021) is a smartwatch that tracks the daily activity, sleep, and stress mood of the users and sends reports (Dempsey 2021). The watch has an electrocardiogram (ECG) sensor, a pulse oximeter, and electrodermal activity (EDA) sensor. The EDA sensor determines the response variation of skin conductance and measures the mood of the stress. The stress mood changes by the health parameters of the user and the watch reminds them to de-stress during stressful situations. The mobile application tracks these parameters and detects the stress as a percentage. However, the application reviews declared that the perceived stress in percentage is confusing and not reliable to the users.

Muse2 (2021) is a brain-sensing headband that offers stress relief, meditation, and sleep pattern tracking. It has an EEG sensor, a pulse oximeter, and a photoplethysmography (PPG) sensor. The sensors detect the electrical activity of the brain through the electrodes attached to the scalp. The headband's application shows the statistics of meditation and sleeping quality. During meditation, the user is hearing a guiding sound that translates the brain activity. If the user is concentrated on relaxation, the user is disposed to listen to calming sounds such as rain sound. On the contrary, if the user is not focused on meditation the user tends to hear the thunder sound. However, according to reviews of the application, some users don't rely on results and they think staying calm is quite easy during the meditation.

Garmin Fenix (2021) wearable is an activity tracking smartwatch that also enables stress tracking. The smartwatch understands the body autonomic nervous system (ANS) and tracks the heart rate peaks and the user activity for detecting if the user is stressed or not. The watch measures the stress numerically from 0 to 100. Between there are four categories of stress which are resting state, low-stress, medium-stress, and high-stress levels. Throughout the day the watch offers the breathing timer which is also similar to Apple Watch Breathing App.

Samsung Health (2021) application measures the stress level of the user with mobile phone built-in sensors or other wearables with sensors. The application has a wide range of wellness features that tracks workout intensity, state of sleep, heart rate, stress, the oxygen level in the blood, etc.

Wysa (2021) is a therapy chatbot designed as an additional support system to reduce stress and anxiety using artificial intelligence (AI) technology. This technology is using empathetic conversation which is based on CBT, dialectical behavior therapy (DBT), meditation, and mindfulness. Inkster et al. (2018) argued application's effectiveness and engagement levels on users with self-reported symptoms of anxiety and stress. Users that engaged with Wysa showed a higher average reduction in depression symptoms (reduction of 31%) compared with those who engaged less with Wysa (reduction of 18%).

Sanvello (2021) application is based on cognitive behavioral therapy that overcomes anxiety and stress. Composed of a series of independent learning tools, audio lessons, and related activities, the application helps users to improve their mindfulness. Moberg et al. (2019) elaborate on the application between 500 adults with mild to moderate anxiety, in one month with no constant use required. Significantly, the application decreases users' anxiety, fear and increases their self-efficacy during usage.

Teladoc Health (2021) is a teleconsultation platform that allows users to understand and solve health problems. The application collects the medical data and analyzes the records, images, and test results to confirm the accuracy of diagnoses and treatments (Litzkin et al. 1997). Study shows that 92% of patients' health issues are resolved, with ease of access to the expert, and quality healthcare.

The selected stress management products and services are compared in Table 2. It is seen that mobile applications are utilized more with smartwatches. However, these mobile applications remain limited in 2D, and they are temporary. Based on the applications' reviews some users hesitate the results and usually ignore the reports. In a daily scenario, the user doesn't pay attention to the notifications depending on their context situation. Instead, augmented reality offers a continuous user experiment that possibly has more effectiveness and better outcomes. AR provides wider perceptions and is in accordance with the real-world conditions.

Table 2 Application comparison table downloads, release date, age, and app ratings in date 14/07/2021

Application name	Downloads	Release date	Age	Device type	App ratings
Fitbit	+ 50 M	2014	3 +	Mobile App + Smart Watch	3.6 /5
Muse	+ 500 k	2019	3 +	Mobile App + Smart Headband	3.7/5
Garmin Connect App	+ 10 M	2012	4 +	Smart watch + App	4.6/5
Samsung Health	+ 1B	2012	4 +	Mobile/tablet app	3.7/5
WYSA	+ 1 M	2016	3 +	Mobile app	4.8/5
Sanvello	+ 1 M	2015	12 +	Mobile app	4.5/5
Teladoc	1 K	2019	3 +	Mobile app	No ratings

2.2 Stress Management with Augmented Reality Applications

The world of healthcare is evolving, thanks to technology developments and Industry 4.0. Health applications and wearables are becoming more common over the years. These applications enable the collection of the data of the user to increase patient health quality and quality of treatment. The meaning of healthcare pushes its boundaries such as telemedicine, mobile health, remote monitoring as well as AR&VR (augmented & virtual reality) technology which has become common to provide patients with advanced medical support. The AR allows users to interact with virtual objects and avatars in real-time environments by triggering different positive emotions and increasing users' confidence and satisfaction.

Augmented reality assists healthcare professionals to extend their skills during the operations or diagnosis by overlaying the medical information place. The patient can easily describe their symptoms and understand their actual medical state. While research on AR for mental health is scarce, AR can be a solution for reducing the symptoms of mental illness as well as treatments for specific phobias (Silva et al. 2017). Wrzesien et al. (2011) developed an application that users with entomophobia visualize hologram cockroaches around themselves through hypnosis therapy technology. After the experiment the users have become more confident to reduce their anxiety and psychological distress. Although there are still some challenges in applying AR technology in practice, it promises faster and more reliable smart solutions in the future.

Soni et al. (2020) presented a mixed reality (MR) for stress relief application for office workers and their workplace stress. The MR application aims to reduce stress with low cognitive activities such as singing, listening to music, and doodling. The AR headset changes users' surroundings with AR features. The application has a design perspective to embrace user well-being by "positive computing" (Calvo and Peters 2015). The research that has been done shows that controlled lighting, projections, and sounds have benefits to boost the performance and productivity of workers. The application continuously tracks the brain activity of the user and whenever the

user has stressful moments, the application sends a notification. Users interact with mixed reality environments and engage with virtual objects. The developers of the application claim that it may distract the attention of users while they work, and using MR in the workplace can be undesirable by employers.

Tivatansakul et al. (2013) conducted a healthcare system for supporting students and working people. The application was tested on a virtual box and a respiratory detection sensor. The user follows the instruction to breathe deeply to relax and decrease the stress level. The results show that virtual objects and music can increase user comfort and decrease their stress level.

Stuart et al. (2020) presented a study that uses AR for stress reduction for healthcare providers during the virtual medical triage training simulation. The study aimed to reduce the stress in critical situations and avoid the stress effect on their work performance. In the experiment, the participants interact with the virtual patients using HoloLens 2. The participant use the task-focusing stress management strategy and then rated their stress during the experiment on a scale of 0–10. Results show by using AR applications that healthcare professionals are stress-induced.

Healium (2021) is an AR mental fitness application that aims for self-stress awareness and self-stress relief. The company declares that the application is not a treatment for anxiety, but a self-management of anxiety. It rewards the user's ability to calm or focus for a brief time by connecting with wearables, either the Apple Watch or BrainLink Lite EEG headband (the app can function without the wearables as well). Users control the virtual forms in real time by their health parameters and change the context of the augmented environment. For example, if the users manage to keep their stress level down the threshold, more butterflies appear in the room around the users. According to the study, it has been proven that users are less anxious after the Healium AR experience (Viczko et al. 2021).

The selected AR stress management methods are compared by their device type and field of study in Table 3. The existing approaches showed the potential of augmented reality for stress management, but scientific studies on this topic are limited, especially for medical distress.

Table 3 Comparison table of AR applications by the release date, device type, and field of study

Product name	Release date	Device type	Field of study
Soni et al.	2020	HoloLens 2	Stress relief
Tivatansakul et al.	2013	Mobile App + Smart Headband	Stress relief
Stuart et al.	2020	HoloLens 2	Stress relief
Healium	2020	Phone/tablet	Self-management of anxiety
Wrzesien et al.	2015	Head-mounted-display	Phobia treatment

2.3 Managing Medical Distress with Augmented Reality

The surgeons have legal and administrative responsibilities in operative/non-operative scenarios. Surgeons' distress situations affect their technical (e.g., dexterity skills) and non-technical performance (e.g., communication skills), and stressed surgeons make more mistakes during the surgery. Moreover, this may affect negatively patients' health or may damage the surgical team's communication, and no doubt these stress situations influence negatively their well-being. On the other side, distressed patients may complicate the surgery, and delay the recovery process after the operation. Considering that the recent Covid19 global pandemic has changed the surgical guidance and procedures (Myles and Maswime 2020), the operating rooms are riskier than before. The surgeons are overloaded and the patients are worried. Medical distress can easily affect doctor–patient communication (Hulsman et al. 2010).

Surgeon and Distress. Becoming a medical expert requires strong dexterity, problem-solving ability, and nerves of steel. Doctors' work conditions differ in pre-operative, intraoperative, and post-operative scenarios. For surgeons overseeing non-operative diagnosis and de-stress their nervous patients are mandatory tasks. They must operate with maximum performance and provide post-operative treatment. To qualify as a surgeon requires several burdens that drag them into a repetitive predicament. Over workloads under pressure that are caused by long surgeries and nightshifts increase the risk of burnout among healthcare professionals. Hawton et al. (2015) emphasize the burnout risk of the doctors, especially female doctors are likely to commit suicide statistically more than male doctors.

The operating rooms are high-cost, complex, and stressful places where individual members accomplish various functions. In the schema of an optimum OR ecosystem, several rules and conditions must be provided so that the health of the patients and OR members won't be at risk. Recent findings show that the management of OR depends on focusing and reducing wasted time to provide a better experience for staff and patients (Krupka and Sandberg 2006). To optimize the performance of the ORs, there are three distinct routes to follow; reducing the time dedicated for the surgery (using the application of new technology and making surgeons work faster), scheduling the cases that fill the day efficiently, and minimizing the time between the surgeries (minimizing sterile time). Time organization is also a key factor to deal with depression. Distinguishing the meaning of events augments the eustress level of individuals. It is a core element to encourage and support surgeons in their work-life.

The surgeons' role is being the surgical team leader and providing good communication and teamwork that are fundamental to completing medical procedures effectively during the surgery. Thus, time organizations are the key factor to carry out the work efficiently. Surgimate (2021) is a surgery scheduling software for coordinating and scheduling surgeries and offers surgeons to manage their work time. However, it is limited with ordinary agenda and only reduces paperwork for the institutions. Surgeons only visualize the surgical events and send post-op confirmations.

In 2014, at St. Michael's Hospital, researchers have used "black box technology" as familiar in the airline industry for understanding and analyzing better OR conditions (Jung et al. 2020). The black box saved inputs, such as audio, OR cameras, laparoscopic cameras, patient physiology, machines, and sensors with machine learning, algorithm, and code systems. The black box derived outputs of the timeline with potential surgical events and error flags.

The black box has been tested in a month, for many surgical procedures to understand how errors lead and how to prevent errors from happening again. The research also points out the importance of communication between the surgical team and distraction by noise happening in the OR such as pagers, alarms, door sounds, or music. Some operating teams prefer to listen to music while they are operating. Some think that music has contributions such as reducing mental workload and increasing the performance capacity of the surgical team. The researchers point out that music creates distraction and weak intercommunication and may be banned in the future (Kacem et al. 2020).

In 2018, the researchers used another technology that captured the electrical activity of the surgeon's heart (Grantcharov et al. 2019). The surgeon wore Hexoskin which is a smart cloth, and with the precise physiological data, the electric impulses that trigger heartbeat were measured during surgery (Hexoskin 2021). The variation between heartbeats in the time indicated the heart rate variability (HRV) statistics and the surgeon's momentary stress levels. This variation data were then compared with the laparoscopic surgery recordings for assessment of the surgical performance. Both surgeon stress level and surgical errors were timestamped. The results reveal that during acute stress situations, surgeons make 66% more mistakes on patients. These errors can be triggered by negative thoughts or loud noise in OR. Research also includes a summary that in the United States, medical errors cause between 250,000 and 440,000 people's deaths in a year. So any change in a widespread practice that lowers the number of mistakes made by surgeons due to stress would also diminish the number of deaths.

Briefly, the day of surgeons is stringent between long surgeries, administrative workloads, long nightshift, emergency calls, and the responsibilities of hundreds of patients. They often end up with no work and life balance and are most distressed. All these factors put them in bad psychological situations. These pressure and negative distress moments cause surgeons to make multiple mistakes in surgeries, involve the death of patients, lose motivation, and even have burnout (Galaiya et al. 2020). Their psychological conditions are ignored, not cared for, or generally underestimated, which leads to making surgical errors or even creates big damage to surgeons' health.

Dastan et al. (2020) conducted a master thesis that aims to develop an AR medical tool for surgeons in pre-operative and operative scenarios. The study emphasizes that the work conditions of the surgeons have difficulty in establishing a proper work/personal life balance, and they end up tired and depressed due to the several responsibilities using the ABC strategy for stress management (Ellis 1991).

The thesis included a questionnaire between 40 international laparoscopic surgeons with 15 years of average experience in the operating room and pass their 12 h average in the OR, to better understand the non-operative and operative conditions

of surgeons. The results showed that %92 of participants agree short-term stress causes surgeons to do mistakes, %78 of participants experienced eustress in the operating room, and %62.5 of participants would like to have an external system that monitors their stress level while they operate. The surgeons preferred to play music, have a comfortable environment, take a short break some preferred self-control techniques such as taking a deep breath, having a quiet place to reduce distress. Some surgeons prefer to manage stress with good assistance, better scheduling, practicing, and surgical team collaboration, and optimum OR conditions (light, temperature, instruments, sound).

The AR-Cube product requires a smart headband that tracks the EEG parameter of the surgeons and a HoloLens 2. The surgeons through their distress parameters control the AR-Cube in real time.

The application aims for keeping the eustress level in the right range, avoid distress situations for surgeons, and boost their surgical performance and productivity by integrating them with virtual objects in real environments. The framework of application (see Fig. 4) explains the connection between the user and the AR system. A smart wearable headband takes the stress parameters of the surgeon and visualizes real-time feedback through AR glasses. The AR-Cube has non-operative and operative scenario modalities that differ from each other. The study declared that the operative scenario is more delicate compared to the non-operative scenario and focuses on the non-operative scenario.

In the non-operative scenario solution, the tool converts into a virtual calendar that organizes the surgeon's personal life and works in a pre-operative scenario. Each face of the AR-Cube has different functions such as stress calendar, surgical stress, and stress relief.

Stress calendar balances between the stressors/events. Surgical stress (see Fig. 3) provides the surgeon to see the surgical mistakes made and self-stress relief supports the surgeon to control the stress with self-relief techniques during the day. The

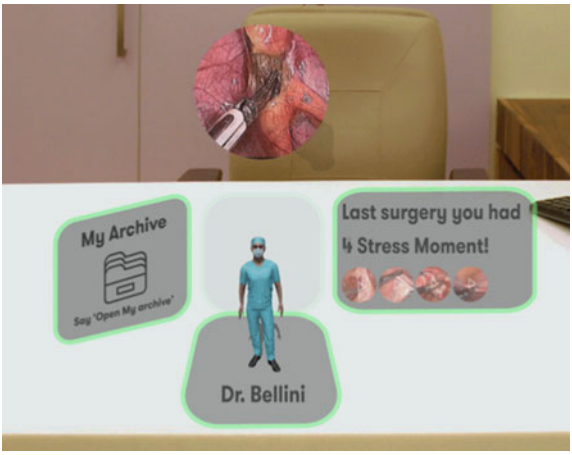

Fig. 3 The high-stress moment of the surgeons tracked and compared with surgical time. The surgeons visualize their stressful situations and are aware of how they reacted to the distress during the surgery

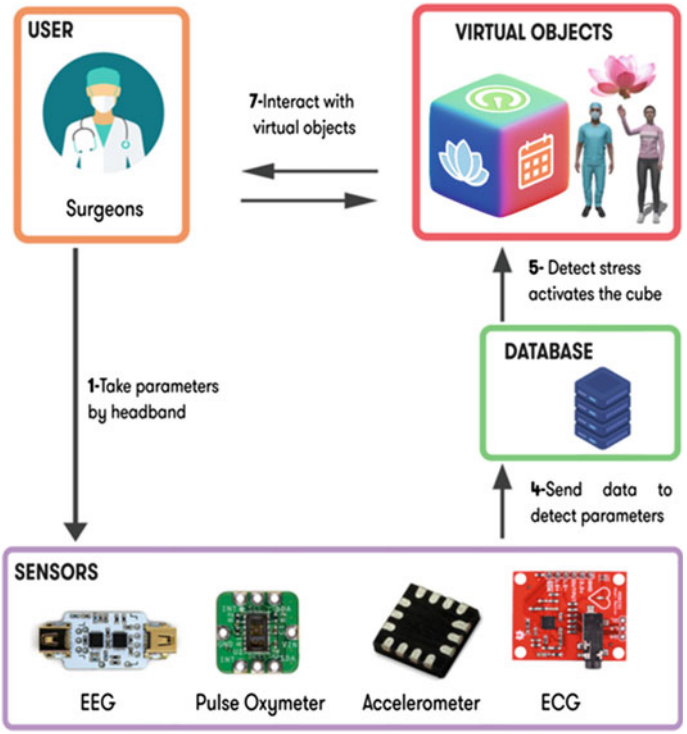

Fig. 4 The framework of the AR-Cube application used sensors and relationship between the user and virtual objects

AR-Cube takes the voice command from the user and opens itself to expand the information to the user.

Meanwhile, in surgical operation smart headband tracks the distress situation and matches with the surgical performance. Moreover, in the free time of the surgeon, the application suggests user de-stress with breathing exercises. The main goal is to make surgeons aware of their distress and how it affects their work and learn how to prevent these situations. According to the user questionnaire results, the surgeons were satisfied with the application in the pre-operative scenario. Instead of the operative scenario, they suggest the application to be improved.

Patient and Distress. Unlike the surgeon's situation, patients' anxiety and distress are more common in the pre-operative scenarios. Potent negative emotions might affect the patient subconsciously before surgical operations. Certain patients are more likely to experience problems or complications, and varies among individuals, reflecting their physiological (allergies to anesthesia, diabetes, heart disease, high blood pressure, obesity), psychological, and social differences. These factors lead patients to be stressed in pre-surgical preparation. Therefore, numerous studies address distress and fear of surgery. Nielsen et al. present a study that psychological

and physiological distress may affect post-operative recovery and the patients have higher post-surgical pain (Nielsen et al. 2007).

Oberle et al. (1990) addressed the link between anxiety, fear, anesthesia, and surgery. High-level anxiety before receiving anesthesia is associated with higher blood pressure during surgery which leads to the need for more drugs, higher infection rates, and slower recovery times. This is most likely due to stress hormones like cortisol, which increase and interfere with the body's ability to calm down and heal itself.

Ali et al. (2014) compared the effect of pre-operative anxiety on post-operative pain control and recovery from anesthesia in patients undergoing surgery. Totally, 80 patients are divided by the level of their anxiety that was measured by Beck's anxiety inventory (BAI—multiple-choice self-report inventory used to measure the severity of anxiety in children and adults). They divided patients into two types of groups: high-anxious patient group and low-anxious group, and the duration of surgery, duration of anesthesia, extubating time, and adverse effects were recorded. Although the type of anesthesia, surgical procedures, and surgical duration were identical, the results showed that pre-operative anxious patients' recovery from anesthesia was prolonged, side effects occurred, and their post-operative pain increased. The unknown side effect of a patient's surgical anxiety can even become a permanent phobia. This phobia refers to fear and anxiety that appears in upcoming surgical operations called Tomophobia.

According to the literature, people react differently to threatening and fearful situations. In the face of uncontrollable and unpredictable events, the degree of threat perception varies from patient to patient (Miller 1979). The study distinguishes two types of "coping" strategies: monitoring and blunting. The monitoring, which is also called a problem-focused strategy, relied on using active ways to directly challenge the situation that causes stress. This strategy consists of looking for information about the fearful situation to reduce the uncertainty and distress generated by the threatening event. In extreme cases, the individual can be overwhelmed by negative thoughts that invade their entire field of consciousness. The second strategy blunting, also called emotion-focused strategy is used to handle feelings of distress, rather than the actual problem situation, and it consists of resorting to distraction in the face of a threatening event. This cognitive strategy can be related to distraction, intellectualization, or even an appositive reinterpretation of events. In this case, the individual will try to seek to be entertained by different activities.

Aust et al. (2016) approved a study about coping strategies in 1205 anxious surgical patients. The patients were divided into two groups according to the coping strategy that they had to choose. 63.7% of them relied on the information that would help them to cope with their anxiety. Patients who chose a monitoring strategy indicate a positive correlation to problem-focused and social-support coping. They took information from a physician (educational) or the internet. Instead, the patients who chose the blunting strategy preferred emotional coping efforts such as mental strategies but not correlated to any anxiolytic medication. However, some patients who suffered from severe anxiety request anxiolytic medication and they refuse both coping strategies, and their needs should be taken seriously. The result is two-thirds

of patients with high anxiety levels seek information related to surgery and anesthesia while one-third avoids such information.

Ajroudi S. et al.'s master thesis (Ajroudi and Fiorentino 2020) proposed an AR application for pre-operative anxiety and stress of the patient. An online survey was distributed between patients to assist surgical phobia for their well-being and better surgical quality. Through an online survey data were collected and analyzed from 44 participants (20–60 age) that experienced high anxiety. The response showed that 81.8% prefer to have information about their surgery, 86.4% indicate that the technique of CBT can reduce their anxiety and change their perspective of negative thoughts, 52.3% of respondents say that they have chosen to play a video game that does not reduce their stress, and 86.4% of participants are satisfied with the breathing exercise to reduce their anxiety before surgery.

The proposed mobile application integrates AR, AI, and Motion Capture technologies to support the patient for the surgical preparation and provides attention, relevance, confidence, and satisfaction. The application measures the anxiety of patients' resting heart rate (RHR) and HRV parameters. The application offers a CBT session with doctors utilizing AI chatbot for reducing patients' negative thoughts and anxiety about the surgery. Communication between expert and patient is a key factor for correct diagnosis and to provide the patient with correct and positive information about surgery to avoid anxiety and distress (see Fig. 5) Furthermore, the patient answers daily questionnaires, according to the answers the application suggests to user exercises, listening to music, and talking with a friend to reduce their anxiety during the day.

Another function of the application is breathing exercise, using AR and Motion Capture technology, for implementing a virtual mirror using a frontal camera (e.g., fixed to phone or smart glasses). Users will be guided by a 3D avatar that will interact with the user. The system will detect his movement through two key joints of the extreme points of his shoulders, to understand the way the user is breathing and help the user for controlled breathing. The Motion Capture assists user breathing. When

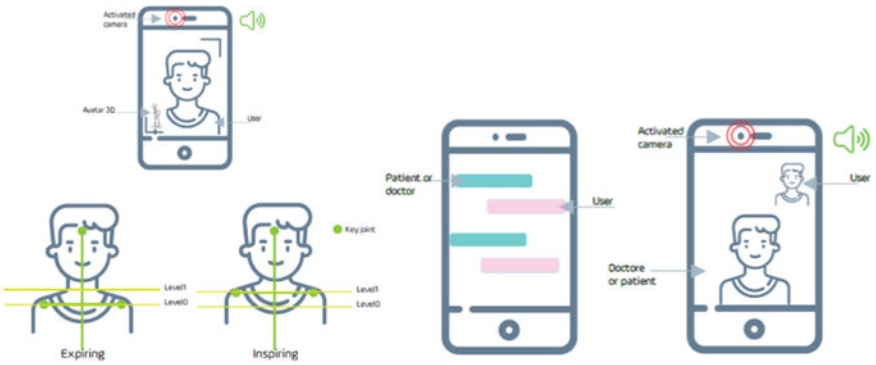

Fig. 5 The application guides the user breathing level with the frontal camera and CBT session with the doctor through the application platform

the user's key joints of the shoulder are in a normal "relaxed" position, the application detects that the user is expiring; when the joints are higher means that the user is inspiring. The application understands the rhythm of the breathing which should take five seconds for inspiration and expiration. If the users complete respiration faster or slower, the 3D avatar will interact with the user to correct their respiration.

3 Conclusion and Future Trends

Surgeries are expensive procedures, so any mistakes or unpredictable outcomes can cause extra time and money spent. The error may occur injuries to people or can cause patient death. All these conditions demonstrate that medical distress is a real problem. It is present in the healthcare structures every day affecting critical events such as surgeries and treatments. Surgeons' and patients' distress effects in both ways viciously and this problem is underestimated. There is the necessity of support in their individual lives.

AR motivates the user to interact with virtual content by making it invisible visible. One of the benefits of the AR experience is easily adaptable to people's daily life. The future technology prepares a suitable and non-obstructive place for augmented reality applications for humans. Despite all the positive aspects of AR, there are still constrained issues and limitations of spreading and adaptation of AR in personal health and awareness. The lack of flexibility limits developers to create certain content with AR.

Beyond the current methods, AR doesn't limit users' information quantity only in the screen borders but increase the human perception combining virtuality into real spaces. On the other hand, AR has a great potential to become a most spread technology. There is less information in the literature about ergonomics and user interface design. Scarce UI design causes low visibility and high effort spent that augments the cognitive stress of the user. The implementation of AR in the healthcare industry has a huge gap because of the absence of specific standards and guidelines for the creation of this medical content that needs to be delivered with user needs, ergonomics, and design principles. Therefore, the future research question will be how and when to display the visual assets to the user. Novel AR interaction methods will be implemented with a user-centered approach, which puts the feedback of the user to manage the medical distress.

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Chapter 4
Design and Modeling of a Novel Exoskeleton Suit for Load-Bearing Augmentation

Shivansh Mishra, Jyotindra Narayan, Ankit Kumar Nikum, and Rajat Singh

1 Introduction

An exoskeleton is a structure with actuators (electric, hydraulic, and pneumatic) controlled by an electronic circuit to assist in physical work (Toxiri et al. 2018) and locomotion of the wearer (Gorgey et al. 2019). Exoskeletons are famous nowadays as rehabilitation devices in therapeutic medicine (Narayan et al. 2021) and load-augmentation devices within different industrial sectors (Toxiri et al. 2018). In case of post-stroke and spinal cord injury (SCI), the exoskeleton assists the patients to regain motor strength and provides better social life by performing different activities of daily living (ADLs). Moreover, the harmful consequences of increased sitting time on cardiovascular health can be revamped by using exoskeleton devices at the expense of physical activity (Gorgey 2018). Although people with neurological disorders use either a stick or wheelchair for locomotion, they cannot assist specific tasks like natural walking and climbing stairs without an exoskeleton device (Dhand et al. 2016). Narayan et al. (2020) designed a wheelchair-based sit-to-stand exoskeleton (STSWE) model for paraplegic children. This wheelchair exoskeleton can turn into an exoskeleton when needed, with the help of gear and a dog-clutch mechanism. The basis of the design is to verify the dynamic analysis for different subjects at seat-off position using a neural network approach. On the other hand, industrial workers who perform manual handling of heavy loads through stoops and turns have an increased risk of musculoskeletal problems (Ratti and Pilling 1997). These problems can be reduced with the help of load-augmenting exoskeletons. Moreover, exoskeletons can also be used as lumber distraction devices to reduce pressure in the intervertebral

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disk in the lower spine. Lumbar traction is a physical therapy procedure used to treat lower back pain by lessening the mechanical stress on the lower back (Zaïri et al. 2021).

Based on human body mechanics, exoskeletons can be classified into three categories—upper body, lower body, and full body exoskeleton. The upper body exoskeleton augments the strength and assists the movement of the wearer's arm (Narayan et al. 2021). These can be classified based on the joint or part of the arm they assist—shoulder (Kiguchi et al. 2003), elbow (Hosseini et al. 2017), forearm (Kung et al. 2007), wrist (Pang et al. 2020), and finger (Nilsson et al. 2012). The upper body exoskeleton can also assist a combination of arm segments—shoulder-elbow (eksoBIONICS 2021; Kim et al. 2018; Pedrocchi et al. 2013), shoulder-elbow-forearm (Rahman et al. 2012), and shoulder-elbow-forearm-wrist (Yan et al. 2021; Kazerooni and Guo 1993). The lower body exoskeleton augments and assists the movement of the lower leg. They can be classified based on the assistance to the anthropometric portion of the body (hip, knee, ankle, and their combination) (Kalita et al. 2020). BLEEX (Zoss et al. 2006) and MIT exoskeleton (Walsh et al. 2007) are lower body exoskeleton which assists trunk, hip, knee, and ankle joints. HAL-5 (Sankai 2010), Walking Power Assist Leg (WPAL) (Chen et al. 2007), and a pediatric lower limb exoskeleton system (Narayan and Kumar Dwivedy 2021) assist hip, knee, and ankle joints. Exoskeleton for Patients and The Old by The Sogang University (EXPOS) (Kong and Jeon 2006) and ABLE (Mori et al. 2006) are designed and developed to assist hip joint and knee joint. There are lower body exoskeletons that assist only a single joint, viz., robotic hip exoskeleton (for hip) (Junius et al. 2017; Seo et al. 2017) and RoboKnee (for knee) (Pratt et al. 2004). A full body exoskeleton can be defined as a hybrid arrangement having features of both upper and lower body exoskeletons (Dhand et al. 2016; Fontana et al. 2014; Christensen et al. 2018). The major fraction of load is transferred from its upper body to the lower body via exoskeleton joints and, eventually, to the ground (Mattsson et al. 2018). Full body exoskeletons are basically wearable suits whose joints are aligned with the wearer's joint and structure is parallel to the wearer's body.

On the other hand, the exoskeleton can be further categorized into load-augmentation exoskeleton and rehabilitation exoskeleton based on the application. Load-augmentation exoskeletons enhance the strength of a person while lifting and carrying heavy objects for several hours (Zaïri et al. 2021; Nilsson et al. 2012; eksoBIONICS 2021; Kim et al. 2018; Zoss et al. 2006; Walsh et al. 2007; Sankai 2010; Fontana et al. 2014; Christensen et al. 2018; Mattsson et al. 2018; Martinez et al. 2007). Load-augmentation exoskeletons reduce the force and frequency of the force exerted by the load on the wearer. These are effective in industries where heavy objects are maneuvered by the workers, like the automobile industry, aircraft manufacturing, and maintenance industry. On the contrary, rehabilitation exoskeletons enable the user to perform daily locomotion tasks independently and offer therapy after trauma (Kung et al. 2007; Nilsson et al. 2012; Pedrocchi et al. 2013; Rahman et al. 2012; Narayan and Kumar Dwivedy 2021; Kong and Jeon 2006; Mori et al. 2006; Junius et al. 2017; Seo et al. 2017; Pratt et al. 2004). The literature in this work is limited to the design implementation of load-augmentation exoskeletons.

Upper body exoskeleton devices for load-augmentation purposes are Ekso Vest (eksoBIONICS 2021; Kim et al. 2018), SEM Gloves (Nilsson et al. 2012), Human extenders (Kazerooni and Guo 1993), and Intelligent Assist Device (IAD) (Martinez et al. 2007). Ekso Vest, developed by Ekso Bionics (eksoBIONICS 2021), is a passive upper body exoskeleton for assistance in overhead industrial works. It contains a moment generation and a hinge mechanism that reduces the wearer's fatigue to endure the tools' weight for an extended duration (Kim et al. 2018). Developed by BioServo, SEM Gloves (Nilsson et al. 2012) is an upper body exoskeleton that assists the wearer in grasping objects by sensing the force applied and providing feedback to the actuator. It has a fabric glove with strong Bowden cables to serve as artificial tendons and is controlled by actuators inside a backpack having a battery. The exoskeleton weighs 700 gm and can generate 3–4 N force at the fingers to augment the force of the wearer. Human extenders (Kazerooni and Guo 1993) is a 6-DOFs upper body exoskeleton developed at the University of California in Berkeley. It is operated by hydraulic actuators, controlled by the generated contact force signals between the exoskeleton and the wearer's arm. A device of a non-wearable kind, Intelligent Assist Device (IAD) (Martinez et al. 2007), is designed as a simple upper body exoskeleton to augment the load transfer capabilities using a fractional form of weights via sensors and cables.

In case of lower body, the well-known load-augmenting exoskeletons are BLEEX (Zoss et al. 2006), MIT exoskeleton (Walsh et al. 2007), HAL-5 (Sankai 2010), and treadmill-based lower body exoskeleton (Tagliamonte et al. 2013). BLEEX (Zoss et al. 2006) is a 7-DOFs lower body exoskeleton (three at hip, one at knee, and one at ankle) with the characteristic feature of portability and generating high power. The hydraulic actuators are utilized to generate high force and amplify the human capacity while carrying a heavy load. Another load-supplementing exoskeleton, developed at MIT (Walsh et al. 2007), has 6 DOFs, two at the hip, two at the knee, and two at the ankle. It can generate 130 Nm at the hip, 50 Nm at the knee, and 90 Nm at the ankle. Hybrid Assistive Leg (HAL-5) load-augmentation and rehabilitation device (Sankai 2010), designed by Cyberdyne (University of Tsukuba, Japan), enables the user to augment the load up to 70 kg. It has an operating time of 160 min. The treadmill-based exoskeleton, developed by Tagliamonte et al. (2013), exploits the 4-DOFs arrangement attached to the lower body—for hip f/e and for knee f/e at each leg. All four joints are actuated by compliant actuators (SEAs) in the sagittal plane. The compliant actuators provide 10 Nm back-driving torque and can be controlled to provide variable torque to ensure smooth operating conditions.

Karlin (2011), AXO-Suit (Christensen et al. 2018; Mattsson et al. 2018), and Body Extender (BE) (Fontana et al. 2014) and Modular Agile eXoskeleton (MAX) (SuitX 2021) are the well-known full body exoskeletons for load amplification. Sarcos (Karlin 2011) is a full body exoskeleton with rotary hydraulic actuators, enabling the wearer to walk at 1.6 m/s while lifting 70 kg of load. AXO-suit (Christensen et al. 2018) is a full body exoskeleton for assisting the elderly with locomotion and performing medium-load intensive day-to-day tasks. It is divided into upper body and lower body modules with 27 DOFs, 15 DOFs (3 at spine, 6 at each arm) in the upper body module, and 12 DOFs (6 at each leg) in the lower body

module. It provides the strength to lift and carry a 5 kg load in each arm for an hour (Mattsson et al. 2018). The body extender (BE) (Fontana et al. 2014), developed by the PERCRO laboratory, TeCIP Institute, is another full body exoskeleton for load-bearing purposes. It has 22 DOFs, 6 DOFs at each leg and 5 DOFs at each arm, all powered by electric actuators. It is a heavy exoskeleton weighing 160 kg and carrying up to 100 kg load at 0.5 m/s walking speed. Modular Agile eXoskeleton (MAX) (SuitX 2021), developed by SuitX, a US company, is a modular full body exoskeleton consisting of BackX, LegX, and ShoulderX. BackX is a passive upper body exoskeleton that reduces lower back muscle forces while lifting load. LegX provides support in the tasks which require squatting for a long time in industries. ShoulderX provides support to the shoulder and arms of the wearer carrying tools and load in overhead tasks.

It is evident from the literature that there are only a few full body exoskeletons available for load-augmentation purposes. Moreover, the design criteria of such exoskeletons are yet to be explored extensively. Therefore, in this work, the design and modeling of a novel full body exoskeleton are proposed for weight carrying capacity. Table 1 presents a vis-a-vis comparison of novel design features for different load-augmentation exoskeleton devices and the full body exoskeleton proposed in this work.

The above state of comparison demonstrates that the proposed exoskeleton design amalgamates several original features such as.

- Lightweight, as it is fabricated using rectangular hollow cross section of Aluminium 1060 alloy having high strength-to-weight ratio. Further, passive joints in the lower body module make it more lighter.
- Portability, the exoskeleton has on-board power source and therefore can be carried from one place to another easily.
- Low complexity, the number of DOFs provided is reduced to 12 (4 active and 8 passive) keeping the DOFs restricted from movement to avoid complex configuration of the exoskeleton.
- Optimized structure, iterative development of the exoskeleton structure was done with focus on wearer comfort while lifting and carrying the load.
- Active–passive actuation, a combination of active (linear actuators at shoulder and elbow joint) and passive actuators (gas springs at knee joint) are selected to optimize the duty cycle.

Furthermore, the proposed design has promising advantages as follows:

- The proposed exoskeleton design comprises upper body as well as lower body module which efficiently transfers load to the ground.
- Passive joints in the lower body module increase the duty cycle.
- The design dimensions are focused to serve the young industry workers of the country.

Firstly, the methodology for a general exoskeleton design is explained based on the literature. Thereafter, the design and development of a full body load-augmenting

Table 1 Vis-a-vis comparison between load-augmentation exoskeletons and proposed exoskeleton

Exoskeleton	Developer	Design feature
Ekso Vest (eksoBIONICS 2021; Kim et al. 2018)	Ekso Bionics	Passive spring loaded mechanism to support load
Human Extenders (Kazerooni and Guo 1993)	University of California, Berkeley	Extender hands to grasp heavy loads, contact force of wearer control the actuators using sensors
SEM Gloves (Nilsson et al. 2012)	BioServo	Tendon-like actuators, under-actuated fingers
Intelligent Assist Device (IAD) (Martinez et al. 2007)	University of California, Berkeley	Simplest industrial load-augmentation device, non-anthropomorphic, uses wire ropes, and suction cup/hook
BLEEX (Zoss et al. 2006)	University of California, Berkeley	Higher load capacity and rotary joints
MIT Exoskeleton (Walsh et al. 2007)	MIT	Passive spring (hip, ankle) and damper (knee) mechanism
HAL-5 (Sankai 2010)	Cyberdyne (University of Tsukuba, Japan)	• Application for load augmentation as well as rehabilitation • Bio-electrical signals on skin's surface
Sarcos (Karlin 2011)	Raytheon Sarcos	Application in military missions, heavy though agile
Body Extenders (Fontana et al. 2014)	PERCRO laboratory, TeCIP Institute	Pantograph mechanism and pulley-based actuator for wide range of motion with high torque
Modular Agile eXoskeleton (MAX) (SuitX 2021)	SuitX	Modular, customizable, supports the wearer by reducing exertion, fatigue
Proposed Full Body Exoskeleton (in this work)	SVNIT Surat and IIT Guwahati	• Linear actuators (at shoulder and elbow joints) • Industrial load-augmentation device, no ceiling setup required, • Passive gas springs (damper) (knee) and four-bar mechanism for better stability

exoskeleton are described in detail using the CAD model. The finite element analysis of the critical components is carried out for different conditions. Finally, the corresponding stress and deformation results are carried out in a detailed manner. The organization of the remaining chapter is given as follows. In Sect. 2, design methodology and CAD modeling are presented. Section 3 explains the details of the FEA analysis. The related results are discussed in Sect. 4. The future directions are pointed out with the concluding remarks of the complete work in Sect. 5.

2 Design and Modeling of Full Body Exoskeleton System

The design methodology and modeling of the full body exoskeleton based on the design process are presented in this section. At first, the methodology is explained in different stages, starting from the design statement and ending at complete prototype development. Thereafter, in the subsequent subsection, the CAD model of the proposed full body exoskeleton system is presented with the details of mechanical and electric modules.

2.1 Design Methodology

The complete design process can be divided into five stages, as shown in Fig. 1. Stage1 recognizes the problem by searching for need, deciding on the device category, and research for the prerequisites. The research includes the clinical and technical study of the recent similar devices and technologies used. The output of this stage is the documentation based on the device category and to be used in further stages. Stage 2 is the proper presentation of the idea after defining mechanical modules with dimensions, connections, DOFs, and electronic modules with the circuit, referring to the documentation. The output is a conceptual design of the exoskeleton/device. Therefore, Stage 3 is the realization of the design by making CAD modules and integrating mechanical modules, actuators, and electronic modules into an assembly. Stage 4 presents the simulation of the CAD assembly using documentation made earlier, which generates a database for evaluating the prototype. This database can be used to assess and modify the prototype (physical model) for ranges of motion and

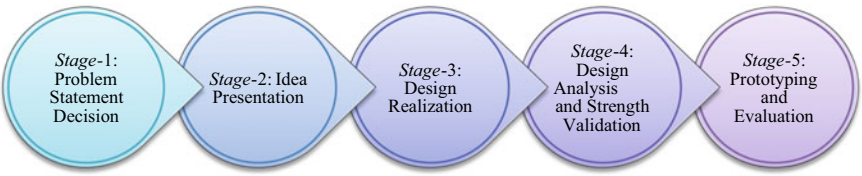

Fig. 1 Proposed methodology

mechanical failure during movement. Moreover, the design strength and analysis with a different set of boundary conditions is computed. In Stage 5, the prototyping and appropriate material selection based on strength analysis can be considered. Finally, the evaluation of the developed prototype could be performed to make decisions for future directions. For that, a survey could be carried out in the recreated or original workplace environment in the presence of experts and take feedback from them over design criteria as discussed in the literature (Rubin and Chisnell 2008). This type of survey helps to develop a statistics-based performance index of the device, which helps in the future development of the device.

This design methodology is followed up to Stage 4 for the exoskeleton design and analysis. Therefore, this work covers only computer-aided design of the mechanical modules and the finite element-based strength analysis of critical submodules. In the following subsection, the proposed design and modeling of the full body exoskeleton are presented.

2.2 Proposed Design of Exoskeleton

The device was designed considering the needs of automotive industries and manufacturing industries near the lab. A survey was conducted to determine dimensions and capacity of the exoskeleton in the industries near the lab. For that, male industrial workers of age ranging 22–28 years old (height: 5′6"–6′0") are selected. The workers of the industries were found to frequently lift and carry heavy loads of 50 kg. Consequently, they faced health issues related to back pain and fatigue. Therefore, we decided to conceive a device to relieve industry workers from lower back muscle injury by reducing the force sustained by the arm muscles. At first, (Stage 1) the state of the art used for the exoskeleton is of armor or mechanical suit to assist back [48], shoulder/arm (Kim et al. 2018), and legs [49], which can be attached to the wearer's body using straps, cuffs, or held via the handle at the hands. The shoulder, elbow, hip, knee, and ankle joints at all limbs are kept revolute joints, capturing their f/e movements. Actuator technologies for existing exoskeleton devices were studied, and electrical actuators are found suitable for their compactness, load capacity, and power source availability. The concepts of ergonomics and biomechanics of shoulder and elbow joints were studied. Similarly, other design criteria were also decided based on the design, engineering, and application gaps in the existing exoskeleton, which are presented in the Table 2. Based on the limitations, the current full body exoskeleton is designed in following stages.

Thereafter, (Stage 2), taking average of the body dimensions from the survey, the dimensions of the proposed exoskeleton design are selected according to a 5′10" healthy male. The shoulder and elbow joints for f/e movements are kept active for load augmentation, while hip, knee, and ankle joints for f/e movements are kept passive for power-saving features. The motion of the wrist supporting the forearm, shoulder joint's abduction/adduction (a/d), and the hip joint's abduction/adduction (a/d) movement are restricted. The restrictions ensured the stability of the system and

Table 2 Comparison among existing load-augmentation exoskeleton for industry needs

Exoskeleton	Description	Load capacity	Application	Limitation
EksoVest (eksoBIONIC 2021; Kim et al. 2018)	Spring-loaded mechanism, reduces fatigue, increases productivity	2.2–6.8 kg	Load lifting in warehouses, also overhead jobs in manufacturing industries and construction work	No active joints for load lifting and carrying has no support for lower body
Human Extenders (Kazerooni and Guo 1993)	6 DOFs, hydraulic actuators, direct driven, controlled using contact force signals	227 kg	Handling of heavy objects	Portability, space constraints due to hydraulic actuators
Intelligent Assist Device (IAD) (Martinez et al. 2007)	Ropes and electric actuators, simple, non-wearable	27–32 kg	Handling of parts in assembly lines in automotive industries, loading–unloading of trucks in warehouses and distribution centers	Large space, ceiling setup requirements, safety issues with possibility of slack in rope
BLEEX (Zoss et al. 2006)	7 DOFs, hydraulic actuators, Portability, high power generation	34 kg	Carrying food, rescue equipment, in rescue operations and weapons in military missions	No support to lift load in hands (upper body), high power consumption, heavy weight (75 kg including payload)
MIT Exoskeleton (Walsh et al. 2007)	6 DOFs, Spring-loaded mechanism (hip, ankle) and damper (knee), quasi-passive	36 kg	Carrying heavy loads on back in military missions, industries	No support to lift load in hands (upper body), does not bears load directly, only supports the wearer
HAL-5 (Sankai 2010)	Electric actuators, High load capacity	70 kg	Carrying heavy loads in industries, hospitals, rescue missions	High price, not affordable by small-scale industries
Sarcos (Karlin 2011)	Rotary hydraulic actuators, High load capacity, power efficient	70 kg	Carrying heavy loads in military missions	Heavy weight (90 kg), tethered power source

(continued)

Table 2 (continued)

Exoskeleton	Description	Load capacity	Application	Limitation
Body Extenders (Fontana et al. 2014)	22 DOFs, Electric actuators, High load capacity, heavy weight (160 kg)	100 kg	Carrying, handling of heavy objects	Requiring sufficient training to operate, slow speed, difficulty in handling objects
Modular Agile eXoskeleton (MAX) (SuitX 2021)	Modular, passive, lightweight (3.17 kg), customizable	~15–20 kg	Overhead tasks in industries	Does not bears load directly, only assists the wearer

avoided the complex movements in the exoskeleton. Moreover, the alignment of the exoskeleton joints with the body joints is considered, to the maximum possible extent, for the physiological safety of the user. Ergonomic factors are considered while attaching the user's body to the exoskeleton. Straps are provided at the shoulders, waist, thigh, and lower leg, and the back frame is cushioned.

As shown in Fig. 2a, b of the exoskeleton, the conceptual design is 12 DOFs, having 3 DOFs each for every upper arm and lower limb. In the upper limb, a 2-DOFs active–passive arrangement is made at the shoulder joint for f/e and i/e movements, and a 1-DOF linear-actuated mechanism is kept at the elbow joint for f/e movements. On the other hand, all 3 DOFs are kept passive for f/e movement of the hip, knee, and ankle joint in the lower limb. As explained earlier, only 12 DOFs are provided in the design to lessen the complexity of motion and for augmenting

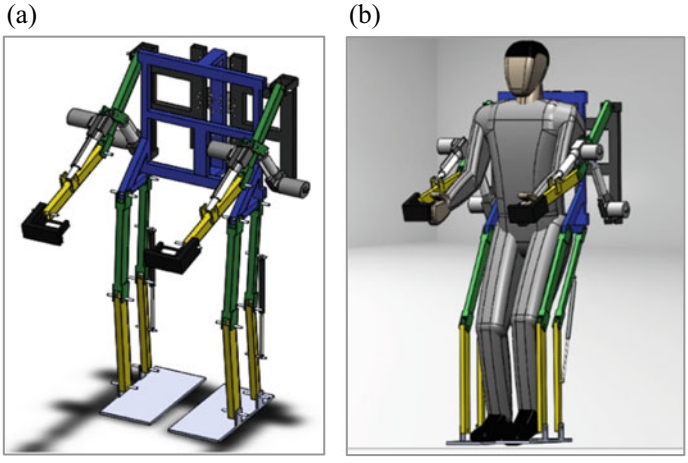

Fig. 2 Conceptual view of the proposed design **a** isometric view of the proposed design; **b** isometric view with a human dummy

the physiological safety of the user. For active joints, a linear actuator with a load capacity of 3000 N is designed at each shoulder (between the Scapula and upper arm) and each elbow (between the rear arm and forearm). Two gas springs of 20 KN/m stiffness are exploited and appended between the thigh and calf for the passive joints at the knee. Aluminium shafts of 10 mm diameter are used at the joints for revolute movement. For the i/e movement with a passive joint at the shoulder, stainless steel door hinges with holes of 6 mm diameter are used. All the joints are aligned with the wearer's joint except the passive joint of the shoulder, which is kept behind the back frame with the axis at the spine for structural rigidity and stability. A handle with a control panel and load-lifting hooks is given at the wrist to actuate the exoskeleton. The control unit (circuit of microcontrollers) and power unit (battery) are provided near the back frame.

Now (Stage 3), the realization of the exoskeleton is done by dividing it into two modules, mechanical and electronic. The mechanical module consists of arm links (forearm links, rear arm links, wrist handle), double H-frame (two H-frames supporting Scapula), back frame (back section, spine base, and waist support), and leg links (thigh links, calf links). On the other hand, the electronic module comprises actuators, buck converter, motor driver, control switches, and Li-Po battery. In this work, the mechanical submodules are presented extensively; however, only important ones in the case of the electronic module.

The CAD modeling of the proposed design is carried out using SolidWorks software. The exploded view of the exoskeleton in trimetric view is shown in Fig. 3a and the components' dimensions are shown in Fig. 3b, c. The total weight of the exoskeleton is 15.71 kg (including actuator and springs) as computed from the SolidWorks. An aluminium cuboid with a hollow rectangular cross-sectional area of $50 \times 25.4 \times 2$ mm^3 is selected for designing all links. The orientation of the cross section of links is used strategically to increase the structure's performance in bending. As shown in Fig. 3b, for the forearm links, a cuboid of length 43 cm is considered on each side. Moving from the elbow joint toward the forearm and rear arm, the extrusions are designed at the distance of 22.5 and 15.5 cm to hinge the linear actuator. The rear arm link at each side is made up of a 40 cm length box section as shown in Fig. 3b. Each forearm and rear arm link weigh about 0.37 and 0.62 kg, respectively. C-type aluminium connector with 6 mm thickness is brazed at the proximal end of the rear arm and connected with the distal end of the forearm to construct the elbow joint. Two wrist handles, each of 0.61 kg, are designed to hold and control the actuators using a control switch. Figure 3b further indicates that each H-frame is a ladder-shaped structure with inner and outer vertical links of 50 and 53 cm in length and two horizontal links of 15 cm. The mass of each H-frame is 0.97 kg. On the outer vertical link, extrusions with 10 and 7.8 mm diameter holes are provided at the upper and lower ends to form the shoulder i/e joints and shoulder actuator hinges. The back frame, having a total mass of 2.85 kg, comprises three parts—the back section, spine base, and waist support. As shown in Fig. 3c, the back section is designed as a rectangular-shaped structure having dimensions of 50×49 cm^2 and encloses a "T-shaped" arrangement. The spine base is planned with two horizontal links of 12.5 cm extruded backward and a vertical link of 59 cm. The spine base is

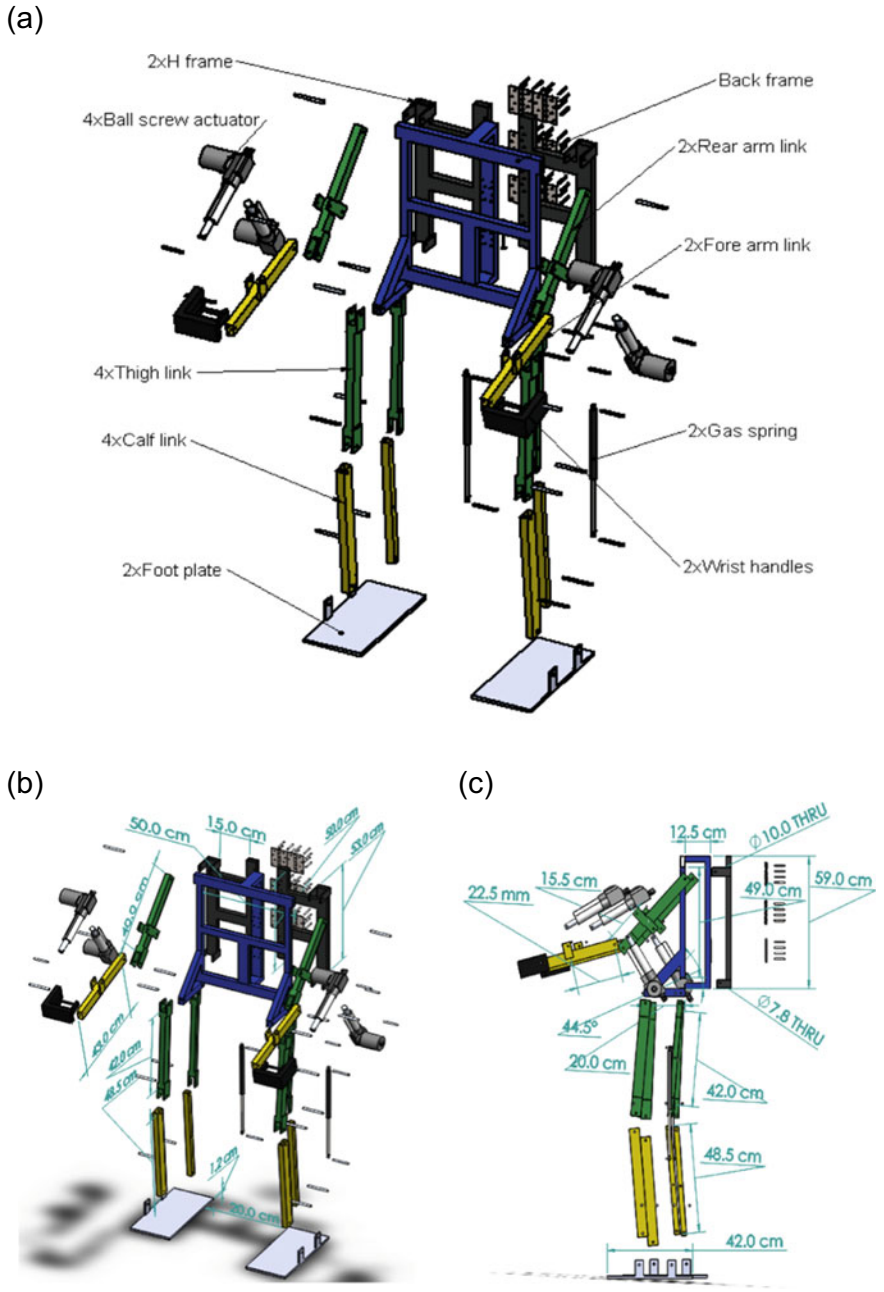

Fig. 3 Exploded model of proposed exoskeleton design with **a** submodules' names, **b** dimensions from trimetric view, and **c** dimensions from side view

provided to shift the center of mass (COM) of the exoskeleton at the plane of the back and reduces the toppling effect while loading. Waist support is made up of a horizontal link, and a slant link of length 20 cm protruded at the bottom of the back section. These are fastened at an angle of 44.5° to the back section, as shown in Fig. 3c.

Moving further to the lower body exoskeleton, both thigh and calf links for each leg are designed in the form of two distinct four-bar mechanisms. The length of thigh and calf links in the mechanism is selected as 42 and 48.5 cm, respectively, as shown in Fig. 3c. Two thigh links on one side of the exoskeleton leg weigh about 0.60 and 0.32 kg whereas the masses of two calf links on one side are 0.31 and 0.22 kg. Two C-type connectors with 6 mm thickness are brazed on both ends of the thigh link to form the hip and knee joint. Figure 3b, c shows that the foot is a rectangular plate of dimensions $42 \times 20 \times 1.2$ cm^3 and mass 0.66 kg with two hook-like extrusions as ankle joints. Furthermore, all the mechanical submodules are integrated into an assembly along with the electronic submodules. For example, the ball screw linear actuators and gas springs, shown in Fig. 3, are designed to integrate with other electronic submodules such as buck converter, motor driver, ultrasonic sensors (at the wrist to provide data of height above the ground), control switches, and Li-Po battery. These submodules are evaluated for their parallel functioning, and several iterations are made for efficient design, which could eventually lead to the final prototype in the future.

3 Design Analysis: Boundary Conditions

The design analysis (stage 4) of different mechanical submodules of the exoskeleton is carried out in ANSYS structural workbench software. The aim of this analysis is to check the failure of the critical submodules in extreme loading conditions based on the stresses and deformation. The analysis built upon these extreme conditions ensures the safety of the components during various tasks. Although the effect of interaction between the components is taken into account using the help of appropriate force transfer, the analysis is performed part by part owing to the computation limits of the system used and to reduce the complexity of the problem. Reaction forces and moments are calculated by considering equilibrium conditions at every point of time; therefore, net torque and net forces put to zero in order to get the reaction forces and moments for every submodule. Magnitude and direction of calculated forces are shown in Figs. 4, 5, 6, 7 and 8. Stress generated by application of these forces on submodules must not exceed the yield strength of the material used for the design to work perfectly. In order to observe variation of stress along the whole dimensions of submodules, the end of the submodule needs to be fixed so that the load can be transferred to another submodule. The fixing of these ends is carried out using the "Fixtures" option in ANSYS structural analysis.

The submodules are imported to ANSYS structural workbench from SolidWorks as an IGS file. Four integrated submodules such as forearm link with wrist handle,

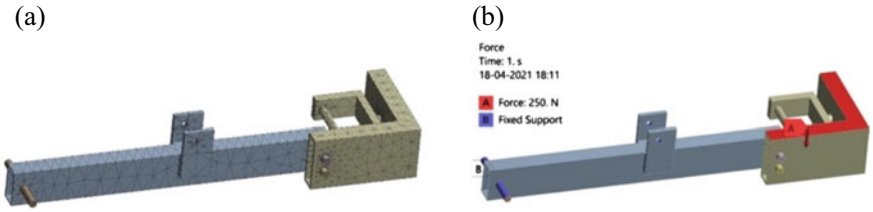

Fig. 4 **a** Mesh generation for forearm link; **b** Applied force and a fixed support

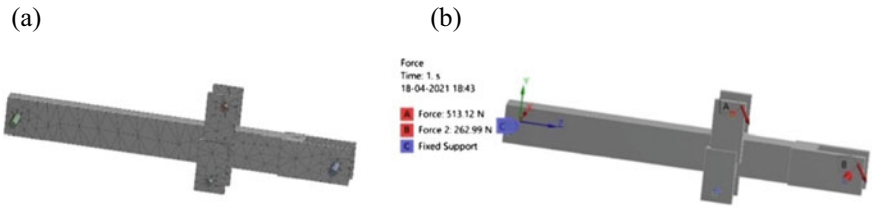

Fig. 5 **a** Mesh generation for rear arm link; **b** Applied forces and a fixed support

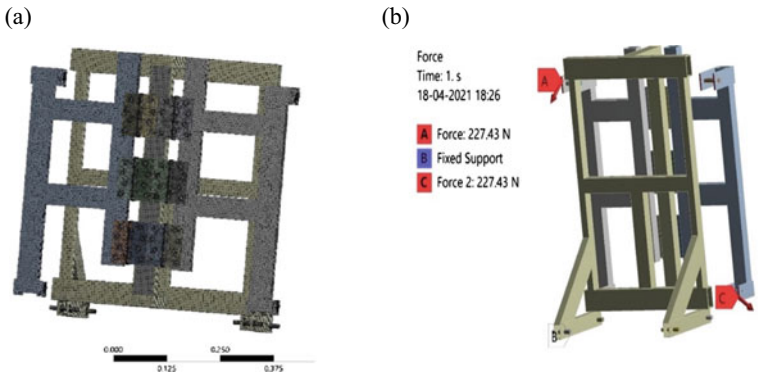

Fig. 6 **a** Mesh generation for double H-frame along with back frame; **b** Applied forces and a fixed support

rear arm link, double H-frame with the back frame, and leg links are considered critical submodules that bear significant stresses and lead to large deformations.

The forearm link and wrist handle are fastened using mild steel bolts. In the customization tab, mild steel as new material is added by referring to various standard property charts. Handles, links, and shafts are made up of an aluminium alloy 1060, and related properties are allocated in the material assignment. After assigning material to all the parts in a static-structural module, a mesh is generated in the forearm, as observed in Fig. 4a. Mesh sensitivity analysis was performed and solid elements (SOLID 187 and SOLID 186) provide better meshing results. The number of

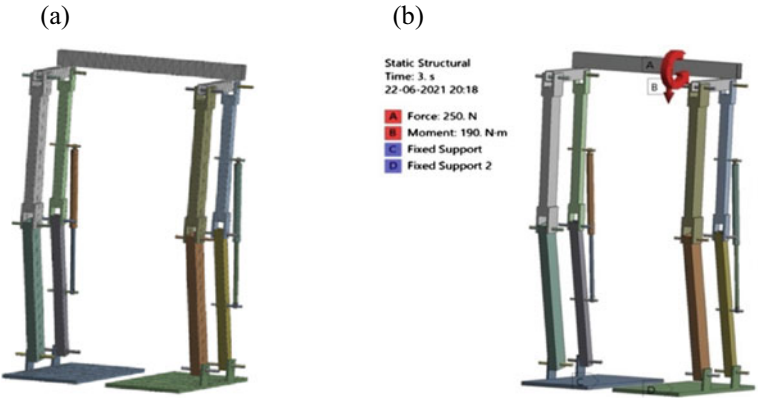

Fig. 7 When both feet are in ground contact **a** Mesh generation for leg links; **b** Applied force, moment, and fixed supports

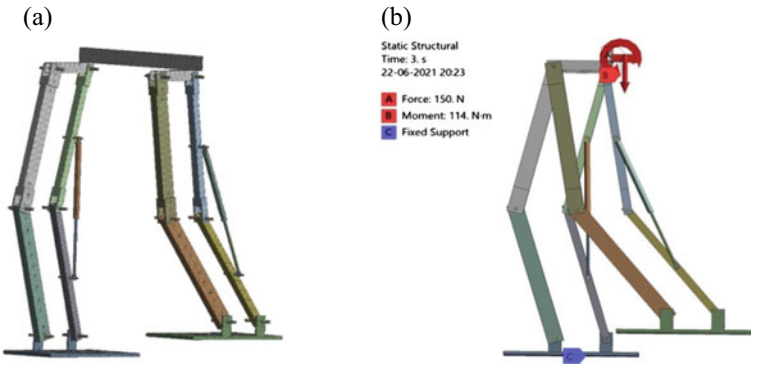

Fig. 8 When left leg swinging in the air **a** Mesh generation for leg links; **b** Applied force, moment, and fixed support

nodes for the forearm link and handle is 8021 and 5465, respectively. Corresponding number of elements (SOLID 187 and SOLID 186) for the forearm link and handle are 3947 and 2580. Additionally, number of nodes and elements (SOLID 186) for shafts are kept as 2289 and 448, respectively. As per the survey conducted in design Stage I, assuming the exoskeleton can lift 50 kg, a reaction force of 250 N downward is applied on the handle attached with each arm. The direction and magnitude of the force can be observed at point A in Fig. 4b. The rear shaft is kept as fixed support, shown at point B in Fig. 4b.

The force gets transferred from the forearm link to the rear arm link during the load lifting, making it one of the critical parts to analyze. As made up of aluminium alloy 1060, it is assigned the same material. A global coordinate system is declared for the structural analysis of the rear arm link. Figure 5a shows that the mesh is

generated with a number of nodes as 17,341 and elements (SOLID 187) as 5633 for the rear arm link. Number of nodes and elements (SOLID 186) of shafts is kept as 2551 and 501, respectively. The reactions are calculated at equilibrium conditions, i.e., by considering net force and net moment equals zero.

Conservation of forces in X-direction,

$$F_B^i + F_A^i + F_C^i + F_{ext}^i = 0 \tag{1}$$

Similarly, conservation of force in Y-direction,

$$F_B^j + F_A^j + F_C^j + F_{ext}^j = 0 \tag{2}$$

and conservation of momentum at point C,

$$l_2^i \times F_B^j + l_3^i \times F_A^j = 0 \tag{3}$$

F_A, F_B, and F_c are reaction forces at point A, B, and C, respectively, F_{ext} is 250 N, l_2, l_3, and l_1 are distance between BC, AC, and AB, respectively. The magnitude of the forces comes out to be 452.91 N at point A in the y-axis direction and 240.90 N at point A in the z-axis direction, making the resultant as 513 N. At point B, the respective forces in y- and z-directions are 227.53 N and 131.8 N, forming the resultant as 263 N. The reaction force at point A and B is shown in Fig. 5b. The rear shaft (at point C) shown in Fig. 5b is kept as fixed support.

Furthermore, the aluminium alloy is assigned to double H-frame and back frame in the material assignment. Three hinges made up of stainless steel are used to connect both H-frames. Forces are transferred from wrist handles to H-frames via arm links, and thereafter hinges start to perform the required movement. Therefore, hinges along with the H-frames and back frame are the critical components. Figure 6a shows mesh generation for double H-frame and back frame along with hinges. Respective number of nodes and elements (SOLID 187) for left and right H-frames are kept as 71,715 and 36,974, and 72,970 and 37,554. Moreover, the back frame has 21,276 nodes and 21,505 elements (SOLID 187). The magnitude of the force at points A and C is calculated using

$$\frac{(p \times e \times l_1)}{\left(2\left(l_1^2 + l_2^2\right)\right)} \tag{4}$$

where l_1 and l_2 are the distances from the reference for points A and C, respectively.

The reference is considered passing from point C, making l_1 zero and l_2 equal to the length of the H-frame itself. The e is the perpendicular horizontal distance from the wrist handle to the back section, and p is the load applied at the wrist handle, as mentioned in Fig. 6b. This formula applies to bolts and rivets when there is an eccentric force application on the system. The final calculated force at both points

A and C is 227.43 N. The shafts connecting the lower exoskeleton to the upper ones through the waist are kept as fixtures. It can be observed as point B, as shown in Fig. 6b.

The leg link consists of the thigh link, calf link, hip joint, knee joint, and ankle joint. The material is assigned as aluminium alloy 1060 in ANSYS to all the parts. A few components, for instance, the bolts and the gas springs are originally made of different materials like MS and stainless steel; however, as both the materials have strength greater than aluminium alloy 1060 the results hold valid. Both the thigh link and calf link are made of two separate links in parallel. There are a total of 12 revolute joints in the assembly. A revolute joint is originally the connection of two links with a shaft; however, in the analysis, all the revolute joints are assigned a bonded contact with the respective links for simplifying the system and making the whole system a rigid body. The rigid contact can be assumed as a weld between the joints; however, as the stresses within the region of the joint are of prime importance, the assumption does not significantly affect the results. The static-structural analysis for the submodule is done for two conditions: first, when both feet are on the ground (Fig. 7) and second when the left foot is swinging in the air (Fig. 8). The first condition depicts the situation of holding the load in a static state and the second situation can be considered as an instant when the subject is walking while lifting the load. A more reasonable approach for analyzing the second situation is to perform the dynamic analysis, which is carried out in future work. The automatic mesh option is used to carry out analysis for both conditions. As shown in Figs. 7a and 8a, the generated mesh comprises triangular elements (SOLID 187). The total number of nodes and elements are kept as 37,304 and 13,841, respectively.

The direction of the forces transferred from the upper body exoskeleton to the lower one is shown in Figs. 7b and 8b. Although the point of application of force and moment in both conditions is similar, the magnitude differs according to different walking instants. For the first case, both the legs are on the ground; therefore, both feet are defined as fixed support (at points C and D in Fig. 7b). On the other hand, for the second condition, the left leg is in the air, and only the right foot is fixed (at point C in Fig. 8b). A downward force of 250 N (at point A) is applied on the center of the horizontal spine link, and a moment of 190 Nm (at point B) is applied about the side faces on the center of the link, as shown in Fig. 7b for the first case. The second case is considered an instant dynamic condition where the load on left leg links decreases approximately 60% (Narayan and Kumar Dwivedy 2021). Therefore, a downward force of 150 N (at point A) and a moment of 114 Nm (at point B) are applied to the center of the horizontal spine link, as shown in Fig. 8b. The loading conditions are decided by using simple Newtonian mechanics. The downward force is applied to replicate the transfer of load lifted with the hand assembly which then transfers the load to the rib. The moment is the product of the weight of the load and the distance between the point of application of load and the hinge.

4 Results and Discussions

After defining material, force magnitude, force direction, and fixtures, an iterative solver is used to solve the mathematical model and provides the related results. The blue and red colors depict the variation limit of stress concentration and deformation around the critical points in the submodule. The variation in equivalent von Mises stress for the forearm link with the wrist handle is shown in Fig. 9a, with a maximum value of 41.92 MPa. Higher stress concentration is observed near the bolts, shafts, and hinges. The maximum stress values are much less than the yield limit of 270 MPa for aluminium alloy and 370 MPa for mild steel. The respective deformations observed are illustrated in Fig. 9b, with a maximum value of 0.631 mm at the tip of the forearm link. The magnitude of deformation decreases while moving away from the point of application of load.

After applying force and fixtures as boundary conditions on the rear arm link as shown in Fig. 5a, the mathematical model is solved using the default solver, i.e., power-based iterative conjugate gradient (P-ICG) solver. The rear arm link design is not complex and the stress induced due to applied forces is within the elastic limit of the material used and hence default solver works effectively in this case. As shown in Fig. 10a, the maximum value of von Mises stress is observed as 33.867 MPa near the shafts due to high-stress concentration. The maximum stress values generated are much less than the yield limit of 270 MPa of aluminium alloy. Reaction forces are

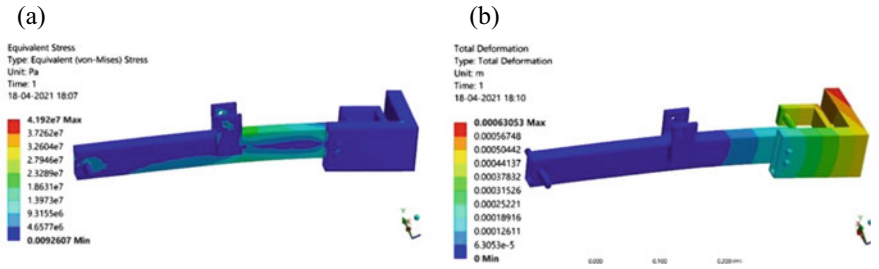

Fig. 9 Static structural analysis of forearm link **a** Equivalent von Mises stress; **b** Total deformation

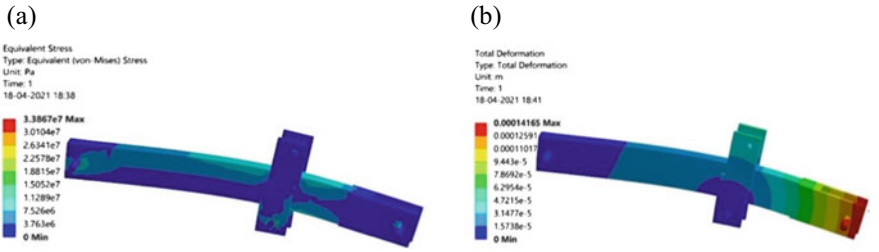

Fig. 10 Static structural analysis of rear arm link **a** Equivalent von Mises stress; **b** Total deformation

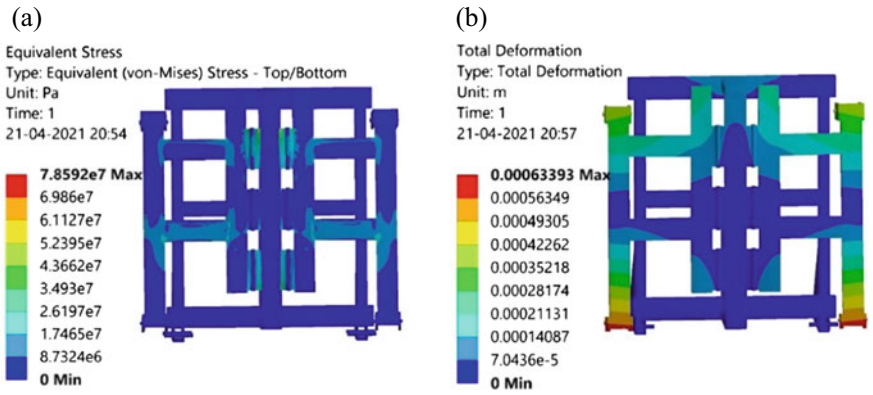

Fig. 11 Static structural analysis of double H-frame along with back frame **a** Equivalent von Mises stress; **b** Total deformation

responsible for deformation in the rear arm. Maximum deformation of 0.14165 mm is observed near the point where reaction forces act (shown as red color in Fig. 10b).

The reaction forces are calculated and applied to perform static-structural analysis on the double H-frame and back frame, as shown in Fig. 6b. Thereafter, shafts are fixed at the hip joint as a boundary condition, and an iterative solver is used to solve the mathematical model. The variation in generated von Mises stress is shown in Fig. 11a, with a maximum value of 78.592 MPa. All the forces from arm assembly are transferred to the H-frames, which are connected to the back frame through hinges. Hinges are bolted to the back frame and do not allow motion in the perpendicular direction; however, the moment due to the lifted weight tends to rotate the H-frames, which eventually rotate the hinges in the restricted direction. Therefore, the restriction of motion generates a significant value of the reaction couple, which leads to a high-stress concentration near that region. The maximum stress values generated are much less than the yield limit of 270 MPa of the aluminium alloy. Figure 11b shows the deformation in the H-frames with a maximum value of 0.63393 mm.

After applying forces with the fixed constraints, the results for the equivalent von Mises stress are presented in Figs. 12a and 13a. The corresponding results for total deformation are illustrated in Figs. 12b and 13b. It is essential to be noted that the total deformation represents the movement of the assembly in a specific direction instead of deformation within the parts. In the first case (when feet are in ground contact), the maximum stress is 140.62 MPa on the extreme side of the right hip due to localized bending of the straight beam, and the minimum stress is 0.034 Pa on the left foot as most of the stress is distributed in the system above feet. For the second case (when the left leg is swinging in the air), the maximum stress of 189.9 MPa is observed at the ankle joint of the right leg due to the maximum transfer of load on only one leg, which increases the compression force. The minimum stress of 0.039 Pa

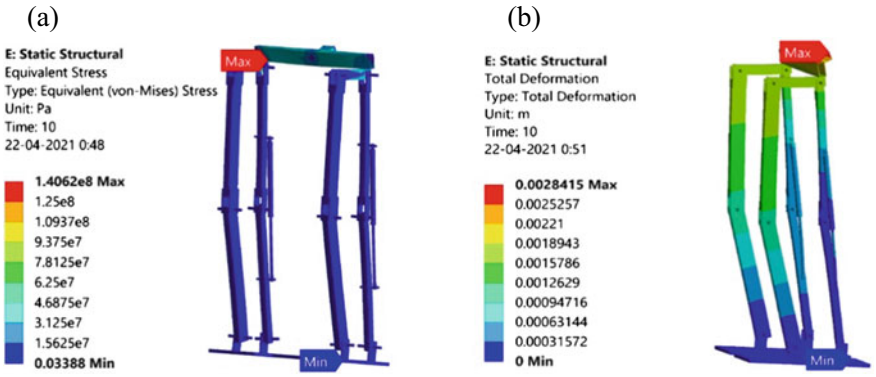

Fig. 12 Static structural analysis of leg links when both foot ground contact **a** Equivalent von Mises stress; **b** Total deformation

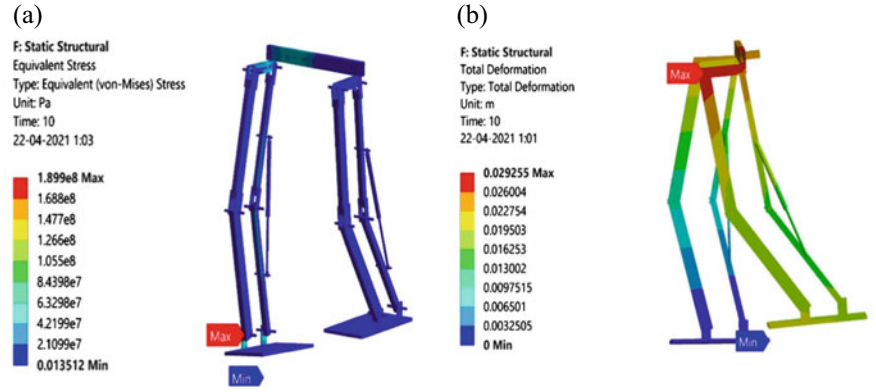

Fig. 13 Static structural analysis of leg links when left swinging in the air **a** Equivalent von Mises stress; **b** Total deformation

is observed on both feet. All the stress values observed in the system are within the yield limit of 270 MPa of aluminium alloy and do not lead to any failure.

Table 3 lists the maximum equivalent stress and maximum deformation in the critical parts in both conditions. The maximum deformation in the first case is observed as 2.84 mm on the hip in the upward direction. This deformation varies depending upon the subject's weight, which is currently not considered in this work. For the second case, the maximum deformation of 29.2 mm is observed on the left extreme of the hip in the downward direction. Here, the forces due to load and moment of load try to push down the swinging leg back to the ground. In the actual scenario, the subject wearing the suit can easily control this movement by applying force in the opposite direction. From Table 3, it is to be noted that the deformation values in the second case for leg links and joints are more significant in magnitude; however, they

Table 3 Maximum equivalent von mises stress and maximum deformation in leg links and joints (First case: both foot on the ground; second case: left leg swinging in the air)

Cases	Component stress (MPa) and deformation (mm)	Thigh link	Calf link	Hip joint	Knee joint	Ankle joint
First case	Max. von Mises stress	$3 \times 10^{-}$	31.25	140.62	31.25	15.625
	Max. deformation	2.21	0.9	2.84	1.11	0
Second case	Max. von Mises stress	21.09	21.09	126.8	58.42	189.9
	Max. deformation	29.2	16.52	29.2	19.53	19.53

do not represent the deformation within the links. Furthermore, all the maximum values are observed for the left leg links. This is due to the suspended link in the air trying to lower down with no support attached. Support, in real scenarios, is provided by the subject who wears it. Therefore, all the deformations in the system are within safe limits.

The database, as mentioned above, is obtained after the simulation (stage 4) in ANSYS static-structural workbench. The database contains the plots of stress, plots of deformation, maximum and minimum von Mises stresses, and maximum and minimum deformation values. The simulation results suggest that the aluminium alloy can withstand the stresses generated in the exoskeleton due to the loading. Thus, the analysis suggests that all the critical components are safe during these extreme loading conditions and no further design changes are required. Moreover, these results can be used to reference future development of exoskeleton devices, which may include more lightweight and high-yield strength materials like carbon fiber, functional composites, etc. The holes for joints and the hinges at the back frame have high-stress concentration, suggesting use of high-yield strength components like bearings. High-stress concentration near the hip and ankle joint indicates the provision of fillets at the right angles.

5 Conclusions

In this work, a novel design of a full body exoskeleton has been presented along with the FEA analysis. Primarily, a stage-wise design methodology has been presented to develop the practical exoskeletons following the literature. Thereafter, the novel design of a 12-DOFs full body exoskeleton device for load augmentation has been proposed, and related modules have been explained extensively. Finite element analysis (FEA) in ANSYS static-structural workbench has been performed for the critical submodules subjected to maximum loads. The generated maximum von Mises stress and deformation have been computed for different upper body and lower body submodules. All the stresses have been found to be less than the yield limit of assigned

materials, and have not shown the failure of any functional part. Moreover, the deformations have been observed within the safe limits, which concludes that the structure can safely lift 25 kg in static condition and 15 kg in dynamic condition. In future, more work can be carried out to increase the DOF of the suit to provide comfort to the user. Moreover, the design can be improved to become more ergonomic for better comfort to the user. The dynamic analysis of the design can be performed for acquiring reliable results in dynamic conditions.

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Chapter 5
Design for Additive Manufacturing of Prosthetic and Orthotic Devices

Trevor Binedell and Karupppasamy Subburaj

1 Introduction

For decades, additive manufacturing (AM) has been used for rapid prototyping. However, recent advances in the available materials, speed of printers, resolution, accuracy, reliability, cost and repeatability of AM technologies have broadened the possibilities for clinical use (Banks 2013). Additive manufacturing enables on-demand production, outsourcing possibilities, unlocks digital design tools and offers breakthrough performance across industries. The global AM materials market for the healthcare industry expects to account for $568.5 million by 2024 (Global 3D Printing Materials Market 2020). Most AM applications are still in the research and development stage in medical fields or have only just entered clinical practice within the last decade. There remains a lack of research into the clinical efficacy, effectiveness and long-term follow-up compared to traditional technologies (Mulford et al. 2016; Diment et al. 2017). AM does provide the opportunity to create customized P&O devices for various patient populations (Zadpoor and Malda 2017), but more evidence of device efficacy and effectiveness is needed to help clinicians make an informed decision before prescribing additive manufactured devices for users.

Before devices can be made with AM, the design of the device must be developed and completed. A design method known as 'personalized medicine' may be suitable for this. Personalized medicine is where the treatment approach considers such needs

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as patient preference and response to treatment, in opposition to the traditional 'one-size-fits-all' method (Anaya et al. 2016). Personalized medicine can include design concepts such as function, aesthetics, usability, durability, safety and evaluation of the needs of the clinicians and users. Consideration would also be given to the environment in which the personalized device will be used. Devices developed using the personalized medicine approach can be enhanced with AM capabilities.

Although AM is often touted as a game changer in healthcare services, the prosthetics and orthotics industry has witnessed low technology adoption. This is mainly due to a lack of technical understanding and clear regulatory guidance (Binedell et al. 2020a). It may be necessary to augment the basic P&O degree knowledge with engineering and digital-related skills to better prepare for a technology-centric future. The needs of the users, clinicians, and healthcare institutions are constantly changing and technology adoption such as AM must be timely and appropriate.

1.1 Additive Manufacturing Trends in P&O

The AM industry has expanded rapidly over the last few years, with printing innovations from medications and human organs to anatomical models and implants. Even with low adoption rates, it could be said that the most commercially successful so far have been prosthetics and orthotics. P&O is a field that treats a person's physical and functional limitations resulting from a range of health conditions and movement disorders. A limb prosthesis is an artificial limb used to replace a missing body part. These are typically classified into lower limb and upper limb prostheses. Orthoses (orthopedic braces) support, modify and augment the structural and functional characteristics of the human musculoskeletal body to improve or maintain alignment in order to facilitate efficient gait or position. They are classified according to the joints they support, such as ankle–foot-orthoses (AFO) and wrist-hand-orthosis. However, they are broadly grouped into lower limb, upper limb or spinal orthoses.

Custom P&O devices are traditionally made using artisan techniques, with the quality of the device and user outcomes based on the experience of the clinician (Totah et al. 2017). However, custom designs are challenging for an industry that relies heavily on hand skills and heavy equipment, which is costly, time-consuming, generates significant material waste, and is a labour-intensive process (Wang et al. 2020; Olsen et al. 2021). The rise of AM offers freedom of design, greater customization, less material waste and an economical device that is specific to the individual. Furthermore, digital technologies and AM permit precise reverse engineering of devices (Totah et al. 2017; Yan et al. 2018) made with conventional processes, making it possible to increase their functional performance in terms of weight (Wang et al. 2020), structural strength, topology and comfort. It has been demonstrated that customized designs improve the quality of life and user satisfaction (Wang et al. 2020; Berke et al. 2010; Gailey et al. 2008).

Well-thought-out customized designs that thoroughly research the user's needs and requirements and carefully consider the limb characteristics set the stage for

user success. These include maximizing the range of motion, providing stability throughout daily activities, and comfortably distributing the forces exerted on the limb during movement or at rest (Lake 2008). Evidence suggests that adopting a naive plug-and-play approach using optical scanning and AM for prostheses or orthoses is unlikely to produce a satisfactory result (Olsen et al. 2021; Hofmann et al. 2016), particularly if the user's expectations are not met with a positive experience when using the device. Digital technologies such as 3D optical scanning and AM are often presented in the media as ready-to-use solutions for producing low-cost, functional devices. However, public perceptions are shaped primarily by superficial media representation and advertising (Olsen et al. 2021) and often fail to consider the design elements necessary to achieve an optimal outcome.

However, when designed correctly, the results have been beneficial. Customized prostheses are made to be either functional or in the form of cosmetic limbs, and they are optimized for the user (Pullin 2009). The diversity of attitudes and attributes of a user and the appeal of AM have led to new combinations of materials and socket designs that enhance comfort and function. Prosthetic sockets can be made with AM that incorporates variable stiffness, enhancing static (sitting) and dynamic comfort. Additive manufactured sockets can also be adjustable, with panels that compress the leg using a boa cable system (Weller et al. 2015). AM can now be used to produce prosthetic interface liners with silicone that can be custom designed with additional padding, compression and stiffness.

AM in lower limb sockets has had early success in improving comfort and decreasing pressure in typically problematic areas (Chen 2016). The provision of upper limb sockets, particularly for children who require constant remoulding as they grow, may find significant advantages in using AM due to shorter expected life cycles and changing preferences for design, colours and patterns. Recently, many design aesthetics and concepts are available online that inspire the users on the possibilities currently not available with traditional practice. These are also influencing the design and use of AM for orthoses.

Additive manufactured orthoses appear to be of sufficient value to replace conventional orthoses in clinical practice (Choo et al. 2020). The use of AM has been most evident in cranial orthoses used to correct head deformities such as plagiocephaly, as well as wrist-hand orthoses, neck orthoses, insoles to support the feet and AFOs for pediatric and adult users in many parts of the world (Geoffroy et al. 2018; Cha et al. 2017). The biomechanical effects and mechanical properties of additive manufactured AFOs are comparable to traditionally manufactured AFOs, offering improved biomechanical function and comfort and dramatically affect the use and user satisfaction (Wojciechowski et al. 2019).

The use of AM for custom-made P&O devices offers opportunities to reach those in countries where service provision is minimal. The utilisation of cloud-based software means AM businesses can provide their services remotely. Many countries in Europe and the US adopt AM as part of their business models, driven by the users' needs and a demand for better devices. The remote servicing of users has seen developing nations pilot AM prosthetic sockets to meet the needs in an under-resourced environment. Although delivering a prosthesis to these areas can be efficient, for

many of the non-profit medical clinics and academic centres in the developing world surviving on governmental support and private donations, the many advanced applications of AM are just not feasible (Ibrahim et al. 2015), and barriers remain for adoption (Binedell et al. 2020a). The bottom line, though, is that we must be realistic about the uses of AM in the field of P&O. The challenges could be contextualised to an individual, department or country, with their needs specific and unique. There are still clinical, financial and technological barriers to the full-scale implementation of AM in a service system for custom P&O industry devices (Chen 2016).

2 Digital Design and AM of Prostheses and Orthoses

The standard prostheses and orthoses prescription and manufacture process involves the following steps:

(1) the *user assessment*, taking medical history and a cast of the affected limb with plaster of Paris or fibreglass bandage;
(2) *cast rectification* of the positive mould;
(3) *thermoforming* or lamination of the device;
(4) *finishing* and polishing the device;
(5) *fitting* the device to the user;
(6) *rehabilitation* and training;
(7) *review,* including up to nine visits for adjustments per year (Pezzin et al. 2004).

There are several challenges posed by the steps mentioned, including the amount of time needed and skills, material wastage due to subtractive manufacturing methods, the accuracy of measurement or fit and its associated discomfort and the quality of the final product. AM aims to improve these inefficiencies. The above figure shows the digital product cycle of prostheses and orthoses which highlights a manufacturing process that is cleaner and more efficient (Fig. 1). However, the critical factor in applying digital workflows and AM is that the end device must satisfy the functionality, comfort and aesthetics requirements while keeping the cost competitive (Wang et al. 2020).

2.1 Data Collection

Extensive data collection is necessary and can involve interviews, shadowing or immersion in the home and work environments. It is important to thoroughly document all relevant information with videos, sketches and photos. The appropriate method must be chosen within given time constraints to determine the requirements accurately. Consideration to the system and the providers in which the additive manufactured device will operate should also be collected to determine the critical success factors and value. During this phase, all stakeholders must be clearly identified, and

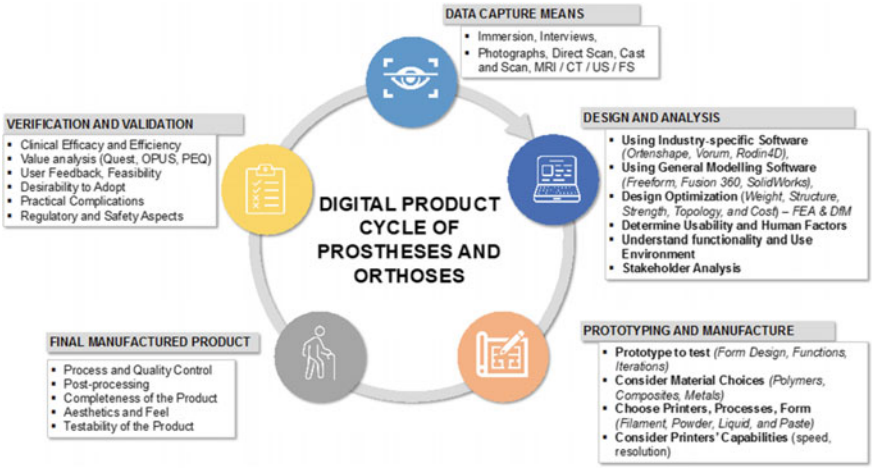

Fig. 1 Digital product cycle and workflow of AM for prosthetic and orthotic devices

their roles and influences must be documented. Users may not be familiar with digitalization and AM capabilities, potentially limiting design opportunities, and careful attention should be given to explain to the user any advantages. The design process should be user centric (Binedell et al. 2020b) throughout to ensure the functional, environmental and psychosocial needs are met to achieve a successful outcome. Other stakeholders such as the clinician, the department or hospital will have a set of non-negotiables that may require resolving to meet all requirements, however that may not be possible, and prioritization of requirements may be necessary. Finally, all the collected data should be stored, as it may be necessary to revisit this information for clarification later in the design phase.

The geometry capture of the affected limb can be completed through a variety of technologies at varying costs. Techniques range from the cheapest traditional plaster of Paris for casting, to more advanced and costly methods such as 3D optical or laser scanning and medical imaging. Medical imagery may include computer tomography (CT), magnetic resonance imaging (MRI), ultrasound (US) imaging and dual fluoroscopy. Today, a handheld scanner is commonly used to capture a cast, a previous device's geometry or direct anthropometric measurements of the limb. Handheld scanners that offer excellent geometric precision at 0.01 mm are accurate but are also heavy and costly. Low-cost alternatives such as the iSense 3D scanner for the iPad tablet have a 0.06 mm accuracy. They are much lighter to carry and maneuver when capturing the geometry, providing a sense of ease in use. 3D body scanners maybe also used as they capture highly accurate anthropometric data, decrease the duration of the process and provide fewer errors in measurement (Paper et al. 2014), although handheld scanners may be more practical. As most of the body segments scanned in P&O are rounded without deep sharp angles, the detailed accuracy of the advanced scanners may not be necessary unless there is a need to capture internal measurements of sockets for duplication. However, the simplicity and low cost of

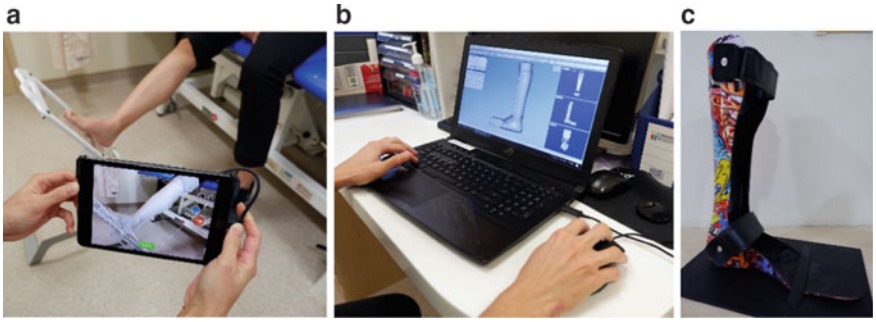

Fig. 2 A photograph showcasing a clinician capturing the geometry of the limb. **b**: Modifying the scanned data. **c**: 3D-printed AFO

using a tablet that requires less advanced skills may appeal more to the clinician (Fig. 2a).

Digital workflows may also be inaccessible to some, but with the widespread use of smartphones to leverage, the use of photogrammetry offers a possible solution. Utilizing a smartphone is a suitable platform for collecting geometric data since smartphones contain high-resolution cameras and a suite of embedded sensors that can be used jointly within an application (Cabrera et al. 2021). Photogrammetry provides a mathematical relationship between a 2D image and a 3D object. It has been demonstrated to show effectiveness in modelling transtibial amputees (Taqriban et al. 2019). However, remotely offering this alternative in resource-limited communities may prove difficult if the clinician requests the user themselves to take the photos. The camera resolution may not be high enough to ensure quality images. As with all photographs, lighting remains a crucial factor. An adequate quantity of pictures with 80–90% overlap is needed to render a static 3D model successfully (Agisoft 2020).

Although the different capturing methods provide unique information, all methods used for the limb geometry depend on posture, muscle actuation and user compliance for accurate representation. It is also essential in prosthetics to capture both the residuum and sound limbs for reference and to create an accurate cosmesis should the user require one.

2.2 Design and Analysis

The freedom to introduce design solutions that are not easily achieved or performed through traditional techniques is a major advantage of digital product cycles. An example of these is compliant features embedded in prosthetic sockets to relieve contact pressure (Faustini et al. 2005) and topology optimization of the design to obtain the desired functional performance (Liu et al. 2018). However, several practical constraints based on clinical experience and subjective feedback need to be specified to optimize the design. Essential design constraints include (Banks 2013)

maintaining the structural integrity of the design feature during loading, (Global 3D Printing Materials Market, Forecastto 2020) preserving the overall shape, which should closely follow the limb shape, (Mulford et al. 2016) remain cosmetic, (Diment et al. 2017) maintain a tight overall fit, (Zadpoor and Malda 2017) minimize void areas and (Anaya et al. 2016) prevent exposed spikes or sharp spots when compliant features are deformed (Faustini et al. 2005).

The design constraints need to be combined with the user's requirements and technical needs to determine the overall geometric design. Several geometry rectification software programs are available to complete this next step. While there are many open-source software programs, such as Meshmixer (USA), many others are propriety in nature. Freely accessible rectification software enables others to construct a model at low or no cost and it may encourage the uptake of a digital workflow, since cost has been identified as a significant barrier (Binedell et al. 2020a). Specialized commercial CAD systems have been developed for modelling: Bioshape (USA), Rodin4D NEO (France), PandoFit (Bulgaria) and Canfit (Canada), Standard Cyborg Design Studio (USA) (http://www.biosculptor.com, http://www.rodin4d.com, http://www.prosfit.com/, http://www.vorum.com, http://www.standardcyborg.com/). These software tools provide the option to alter the volume parameters of models among others. They also create a library of standard and custom-designed components of the prosthetic system being modelled, offering an opportunity for device production speed to be increased (Golovin et al. 2018). The use of templates and overlays is helpful to enhance the modelling process, and modification tools aim to replicate common conventional tasks such as removal and adding of plaster, correction of the alignment and determining trimlines (Fig. 2b). The software rectification process can be complicated for beginners, novice and infrequent users, and hence careful consideration should be given to the design user interface to increase the adoption of AM by the industry (Pallari et al. 2010).

Combining design of devices with computational analysis tools like finite element (FE) analysis and curvature analysis can further enhance the outcomes and comfort. FE analysis provides the assessment of the design and appropriate fit of the device ahead of manufacture. FE analysis can deliver stress distribution in the tissues of the human body and in components of the prosthesis or orthosis, determine the load transfer mechanism and identify biomechanical behaviours on the contact interface between the body and the prosthesis or orthosis (Wang et al. 2020). FE analysis can further optimize the fit by assessing the thickness of the material to predict the stiffness of the parameterized object, which may help facilitate successful outcomes for the user.

Once the design of a device has been analysed and is ready for printing, the file is exported in *.stl format to a printer software for manufacture. Software for 3D printers and slicers can be used to model supports, set printing modes and density, adjust slicer zones and filling levels. The printer settings, including the Andrew number (SLS), layer thickness and resolution (FDM), and the time to print, are crucial in determining the final quality of the device (Fig. 2c).

The above-mentioned processes emphasize the engineering and analysis skills needed for a clinician to perform successful design optimization through effective

AM. A future CAD environment containing a library of easily incorporated features would improve accessibility to technological solutions for clinicians without extensive training, leading to greater adoption of digital technologies, including AM. Once a device is made, it is essential to conduct clinical investigation of the AM solutions, as this provides important information on how well the devices perform during everyday use. With the overwhelming urgency to print P&O devices, it is vital to maintain robust and standardized research into the long-term impact and effectiveness of AM.

2.3 Prototyping and Final Product Fabrication

After identifying the critical factors for success and completing design optimization, it is important to prototype and verify the design with the user, especially in highly complex devices. Prototyping helps to communicate design ideas and allows the users to experience them and provide feedback. For example, a more complex residual limb shape may require a test socket to be printed and trialed with the user before the final device is delivered. This phase of the process enables the user and the clinician to verify the fit and function, while potentially addressing the cosmesis or aesthetics of the design. In addition, holding a physical object provides the user and the clinician the richness of spatial data missing from the modelled images. Final verification includes subjective and objective feedback and considers the view of the user and the clinician on areas like physical measurements, pressure, temperature and forces, to help reiterate the design. However, this may not always be possible with all highly complex devices, as the industry demands fast and efficient care with cost-effectiveness.

If the opportunity is available to verify the design through prototyping, it could enhance outcomes and reduce unnecessary costs further downstream. Prototyping can also be a platform to select appropriate materials that consider the essential features such as weight, heat and strength. Current limitations of materials and AM processes suggest that should a failure occur, it would be catastrophic, with breakage occurring between the layers from excessive horizontal shear forces or fusion errors during the fabrication. The materials for prototyping vary in cost and complexity. Inexpensive materials are helpful early in the process, especially if they are to be scrapped. Common materials used in AM for P&O devices are polyamide (PA11, PA12), Nylon, DuraForm (PA, GF, EX), polycarbonate, polylactic acid (PLA) and even silicone for prosthetics liners. New AM technologies that can combine materials during fabrication are also emerging. These technologies allow the design and fabrication of prosthetic sockets with heterogeneous material compositions. This unique manufacturing capability offers the possibility to design a structure with variable stiffness depending on the specific strength required in the different parts of the socket (Nguyen et al. 2018). Support can then be tailored to specific areas of requirement while others can have the flexibility and comfort for activities such as

sitting. It would be important to accurately determine these areas on the user during prototyping.

3 Benefits of a Digital Workflow in Prostheses and Orthotics

Value creation for AM of P&O devices can be summarized into three areas, namely, customization, cost-effectiveness and quality and time (Fig. 3). Each benefit compliments the other. For example, a highly complex device may require multiple iterations and many manufacturing hours with traditional methods, but with digital processes, the use of CAM and design can print complex structures in one print, using less material and saving many man hours, and many unnecessary steps such as repeat visits by the user for testing.

3.1 Cost-Effectiveness

AM technology has positioned itself to improve the cost-effectiveness, manufacturing time (Chen 2016), amount of waste and human resources needed to develop customized user-specific devices, compared to traditional manufacturing. Designs that would otherwise be prohibitively expensive or even impossible to manufacture using conventional methods (Rogers et al. 2007) can now be created with specific shapes and sizes to achieve highly customizable and versatile designs for

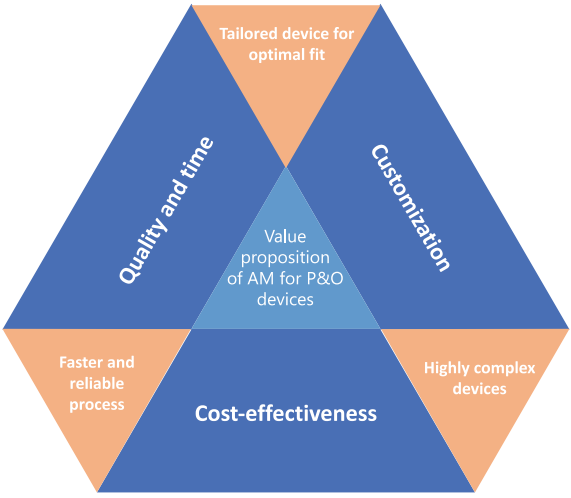

Fig. 3 AM considerations for P&O devices

various purposes and activities. AM makes it possible to tailor a device as per individual requirements through size, shape and topology optimization for a perfect fit. However, regardless of material or manufacturing process, high-quality parts remain expensive and can have a direct impact on cost (Rosen and Kim 2021).

The cost of manufacturing a part through AM remains stable irrespective of the number or nature of parts manufactured. The cost of AM is expected to rationalize over time with gradual increase in demand, generic low-cost printers, expiry of original technology patents and technology understanding among the industry. Although the equipment costs required to outfit a P&O workshop for AM are much lower than traditional equipment, such as a large oven for heating plastic and grinders for post-processing, high-quality SLS and FDM printers can still be expensive. The initial cost outlay in purchasing scanners, computers or 3D printers can cause apprehension over the return of investment (ROI). As such, the benefit of outsourcing has grown to be a viable option for many small start-ups or businesses wishing to pivot their service models. This option minimizes the risk of downtime for the clinician or department, allowing them to focus on their clinical service.

While a traditional device needs weeks to be manufactured and delivered, additive manufactured devices can be produced in a day or less based on their size, freeing up manpower and reducing costs. In addition, the conventional process from the first consultation to fitting and delivery is considerably reduced with a digital workflow. This savings in time can increase throughput and shorten delivery times, bringing care to the users sooner and improving clinical outcomes. Should businesses decide to pivot their service models, opportunities to upskill staff to take on new roles in patient care or administration exist, further adding value to the service. For example, manpower can be retrained in scanning or software rectification while still maintaining their technical skills through the fitting and adjustments that continue to be required.

3.2 Customization and Complexity

In AM, there is a freedom to introduce design solutions that would be difficult or impossible to implement using traditional manufacturing processes. As the cost is related to the volume of the part rather than its complexity, there is no cost penalty for a more sophisticated design (Rogers et al. 2007). Currently, AM is better suited to prototyping or producing small-scale items and highly complex jobs. P&O design is limited only by the limits of CAD software and the imagination to fabricate almost any shape. The ability to customize jobs to the individual ensures uniqueness in design and personalization for the user. This capability is evident in the development of 3D-printed cosmetic covers. These are anatomically shaped, and the surface can express the lifestyle and personality of the user. The aesthetic appeal increases self-esteem for the user and encourages its use. The benefits of topography optimization for complex jobs help to optimize interface interaction between device and skin to prevent skin breakdown. This benefit seems substantial (Pirjan and Petrosanu 2013).

The ability to rapid prototype and test designs with the user and reiterate those after receiving feedback ensures continual improvement and leads to improved outcomes. Being able to rapidly print smaller items has benefited many children requiring upper limb prostheses. The lower production cost enables the child to get frequent updates to parts of their limb prostheses as they grow. The developing nations are starting to use such services as the digital growth in rural areas improves. However, significant issues with durability and long-term outcomes remain.

3.3 Quality/Repeatability and Time

Modern AM technologies can achieve quality standards realized by traditional manufacturing processes, that is, repeatability and performed in less time. Quality is the result of data input and process output, so it is reasonable to expect that high-quality digital workflows and skills would produce high-quality additive manufactured devices. The digitalization process offers us a way to perform a high-quality check before its manufacture. Through visualization of the design and FE analysis, it is possible to quickly assess for errors and make improvements. With traditional manufacturing, the quality of the final product is only evaluated after finishing, which can be costly if there is a need to remanufacture. However, traditional methods do have their advantages during fabrication, e.g. it is easier to detect problems during the production and take corrective action, as opposed to AM, whereby a failure in the print requires the entire printing process to start again. The quality with AM can be demonstrated through material consistency to ensure replicable quality of strength, dimensions and thickness of material. This ensures repeatable outcomes and greater satisfaction.

The repeatability of AM processes is enhanced by capturing and storing all data of the digital process, which can be used to duplicate devices with minimal effort. Should the user require an exact repeat socket or one with only minor adjustments to improve the fit, the digitalization of the design enables such actions to be done with quick and subtle changes.

4 Challenges and Barriers to DfAM of P&O Devices

AM offers manufacturers a more time-efficient and cost-effective solution to build prostheses and orthoses with the required functionality, aesthetics and fit. Although especially useful for devices that are low in volume, or small in size, or incorporate complex geometries, several challenges continue to delay the large-scale adoption of AM (Pirjan and Petrosanu 2013) (Fig. 4). AM can be hampered by factors including non-guaranteed quality print the first time, limited choice of durable materials, lack of process capability and responsibility, and material properties data. A further challenge involves limitations in printer size for large-scale objects that are common to

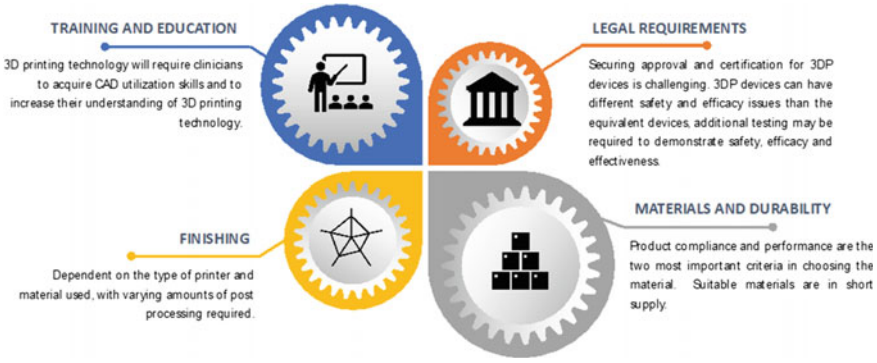

Fig. 4 Challenges and barriers to DfAM for P&O devices

the P&O industry, which can lead to an increase in production costs (Nguyen et al. 2018). It is not easy to apply AM to the manufacture of a prosthesis or orthosis with a considerable circumference or height due to the dimensions of current printers (Choo et al. 2020). Other associated costs that are also overlooked in the price of AM include the costs for support structures, machine utilisation rates, labour and print preparation, post-processing equipment, time, associated effort, machine maintenance and error failure (How much does 3D printing cost 3D Printing Price Calculator—Bitfab (Internet) 2020).

4.1 Finishing Quality and Weight

The quality of finishing with additive manufactured devices is dependent on the type of printer and material used, with varying amounts of post-processing required. The rise of low-cost printers and materials requires caution as it does not offer a guaranteed quality end product, and may cause secondary damage to users (Choo et al. 2020). Many devices are printed with support structures that require removal, or the device may have a staircase effect between the printed layers which will require sanding before it can be fitted to a user. The use of sandpaper, however, may lead to the appearance of holes, depending on the type of fill used for printing. These holes could be repaired with epoxy, but these additional steps add to the cost and time of production and may compromise the structural properties of the final product. Optimal orientation of printing can mitigate some of these post-processing and surface finish issues.

The need to develop a structurally sound connection for the adaptor which connects the componentry is another issue. Some creative designs have been developed to overcome these limitations, which integrate the connection in the printed object enabling it to mate with the adaptor. With average forces up to 1600lbf exerted

during walking, these innovative designs can withstand bending forces of approximately 4000lbf with a safety factor of three (Burhan and Crawford 2004) and seem suitable for many users.

The weight of printed devices may not be as light as traditionally manufactured composite devices in many cases. For example, a 3D-printed socket can weigh more than three times that of a carbon fibre socket (Sengeh and Herr 2013) as it aims to achieve the same strength-to-weight ratio. In this instance, users may opt for the lightest option, considering their residual limb strength is reduced following surgery.

4.2 Materials and Durability

The P&O industry is unique in its demand of material characteristics, and material manufacturers must constantly innovate and enhance the product and processing characteristics to add value such as weight and variable mechanical strength. Material manufacturers should collaborate with additive manufacturing companies and clinicians to understand the application demand in providing sustainable solutions. Multi-material components currently being developed are expected to improve product performance in terms of stiffness, functionality and environmental adaption, which are impossible to achieve through traditional or single-material AM processes (Wang et al. 2020). A major constraint of this technology is the combination of dissimilar materials with differences in thermal expansion and contraction and differing rates of heat release, which would not be a problem in traditional fabrication (Bandyopadhyay and Heer 2018). Also, it presents a significant challenge in ensuring the final material composition is compatible for medical use without compromising safety and compliance with regulations and testing standards.

Product compliance and performance are two main criteria that influence material selection to produce P&O devices. There is a need in the design for variability of stiffness and high strength-to-weight ratios. ABS materials possess good strength and durability in testing, but samples of ABS plastics have been reported to have variable mechanical properties based on print orientation. They are estimated to have between 10 and 73% of the strength of samples produced by injection moulding (Song et al. 2017; Dizon et al. 2018). Suitable materials are in short supply for such a specific industry, and questions remain over the long-term durability of the devices. Anisotropic behaviour induced by weak bonding between layers and structured porosity (Cox et al. 2015) imposed by the building direction may lead to early failure (Lee et al. 2007), putting users at risk. Another significant limitation to the introduction of this technology is the time taken to print devices in the z-dimension. Sockets can take up to 20 h to print. Manufacturers are looking for ways to decrease the time taken; however, increase in printing speed may decrease manufacturing accuracy and device strength and, in turn, compromise safety (Golovin et al. 2018). When designing, it is essential to consider realistic load expectations and manufacturing methods, which can be done with FE analysis to improve performance.

4.3 Legal Requirements

AM has rapidly progressed in the past few years, but unfortunately, the regulations have not kept pace with the innovations. In the healthcare industry, securing approval and certification for additive manufactured prosthetics can be challenging. The US Food and Drug Administration has been slow to approve AM for prosthetics and drugs, although, in 2016, they released a draft guidance for AM of medical devices. The FDA states that additive manufactured medical devices must meet the same regulations as their non-additive manufactured counterparts. Because additive manufactured devices can have different safety and efficacy issues compared to the equivalent devices, additional testing may be required to demonstrate safety, efficacy and effectiveness (Food and Drug Administration 2017). While FDA guidelines made many recommendations towards workflow and documentation for device tracking in the event of a part failure (Ahn et al. 2002), better understanding of the underlying principles behind device vulnerability can help to minimize those risks pre-emptively (Manero et al. 2019). However, with affordable 3D printers entering the market, devices can now be printed at home. With access to care restricted in many parts of the world, many charities have been formed to provide P&O services at a low cost, or even remotely. The accessibility and affordability have led to a growth in maker space design and DIY printing to generate more affordable devices. However, it also presents a challenge in ensuring the quality and safety of the final device. With devices requiring certain strength and flexibility to optimize performance, variations in the design and printing are potentially damaging to user outcomes should the devices fail.

Devices made for a specific patient are considered under the 'custom-made' definition in many established regulatory frameworks and are typically low risk to users since the numbers were few. However, as the number and complexity of custom-made devices grow, there is a need to ensure they are subject to the same high-level scrutiny as mass-produced devices. Moreover, should the device fail, there is a question of responsibility to be asked. Is the designer responsible or the manufacturer? These issues need further discussion as technology grows in the industry to minimize risk to users.

4.4 Training and Education

AM technology will require clinicians in related fields to acquire CAD skills and increase their understanding of AM (Choo et al. 2020). These skills are necessary to encourage adoption of technology and to enhance user outcomes. Without practice, clinicians struggle to navigate the maze of procedures in designing and producing an additive manufactured device (Binedell et al. 2020a). Perhaps due to a lack of skill sets, many clinicians do not believe additive manufactured devices fit well, perform better and last longer (Binedell et al. 2020a). With education institutes still lagging

in their efforts to train students with digital technologies and practical applications of those technologies, the effectiveness of such technologies in the field will remain low.

3D scanners have increased usability to provide a seamless transfer of data to a CAD system for further processing without training and advanced technical skills. However, cleaning the data and designing a P&O device take time and skill. Many software applications used in P&O design lack a simple flow of ideas that mimic the traditional workflow process, which clinicians are familiar with. Often training and retraining are required with constant updating of software licenses to ensure all features are available for the design. Most modifications made with CAD software follow similar guidelines and patterns, but few are pre-programmed into the software. Steps are often complicated, isolated and sequential. However, the artist inside the clinician moves backward and forward as they rectify the mould in a pattern that may be hard to replicate with algorithms. For example, when adding relief to bony prominences, the clinician will blend the relief with the rest of the mould, whereas AM may merely add the stipulated build up without considering its effect on the rest of the shape. Given the scenario: 1) how can we expect prosthetists and orthotists to use a CAD system with terminologies, user interface and operations designed for engineering product design applications?; (Global 3D Printing Materials Market 2020) can the time-effort efficiency be improved by developing a graphical user interface for prosthetics and orthotics industry clinicians? and Mulford et al. (2016) what steps could be automated to ease the burden placed on the design process by the existing CAD system?

The perception of AM from end users though has been encouraging. Most are inspired by the freedom of design and aesthetic advantages and are willing to try something new. It should not be unexpected that there is such interest in this technology. AM is appealing to users who may have suffered discomfort for many years or even decades with the same traditional designs. Unfortunately, too many clinicians remain doubtful of AM advantages, as they have spent many years perfecting their craft. They feel traditional manufacturing provides better outcomes than AM. An experienced clinician with the know-how, physical touch and hand skills can quickly identify the required amount of loading and relief during the assessment, casting and rectification processes. However, a clinician early in their career may find a digital workflow more appealing to achieve consistent results due to its accuracy and repeatability. Those starting in the profession or with minimal experience may be better placed to take the profession forward. Thinking outside the box and designing with freedom are required to meet the changing needs of users.

5 Design of a Forequarter Prosthesis (Case Study)

The following case study showcases how DfAM was used to create a customized and user-specific prosthesis. The user, a 60-year-old male, presented to the hospital clinic with a right forequarter amputation due to a malignant tumour. His current cosmetic prosthesis no longer meets his expectations due to its design and function.

5.1 Digital Design and Data Collection

Following a user-centric design (UCD) approach, the clinician conducted a thorough investigation of the user's requirements through interviews about his lifestyle, employment and social activities. An analysis of his current prosthesis, including its limitations and strengths, was also determined. The design characteristics for the new arm were discussed at length to align user and clinician expectations, ensuring an optimal outcome.

The iterative UCD and development methodology adopted for this case study involved the following:

1. Capturing residuum and contralateral arm geometry.
2. Designing different prosthetic elements from the captured geometry, e.g. socket, elbow, hand and lock.
3. Manufacturing the prosthetic elements and verifying the fit, user comfort and technical requirements.
4. Digital capturing and documenting the design and development process.
5. Administration of the Quebec User Evaluation of Satisfaction with Assistive Technology (QUEST) 2.0 survey to verify the design and determine user satisfaction (Binedell et al. 2020b).

The user analysis determined seven design criteria for the new prosthesis (Table 1).

5.2 Prototyping and Final Product

The digital data that was captured was used to design the prosthesis for the above criteria and with the correct morphology by firstly mirroring the sound contralateral limb shape. The first version of the socket prototype and interface was designed with a carved-out portion of the shoulder and upper arm (Fig. 5a). The user's feedback on the design was positive, but he had suggestions for improvement. It was not easy to wear the prosthesis with one hand. The size looked more prominent than his current arm even though it was identical in dimensions, and the holes used to make it cooler to wear, allowed his business shirts to sink through them, making it less aesthetic.

Table 1 Criteria for new prosthesis (Binedell et al. 2020b)

Item no	Criteria	Rationale
1	Self-suspending	To allow the user to hold and fix the strap around the body with one hand
2	Smooth surface texture	To prevent friction between device and shirt
3	Cooler	As Singapore has a hot climate, the user required a cooler interface between his residuum and the socket
4	Aesthetic	User requested for the arm to match sound side in overall size, shape and contour
5	Lightweight	Due to the difficulty of suspension for this level of amputation, the user required the device to be as light as possible and to enable long periods of use
6	Non-metallic	As the user was a frequent traveller, the device requirement was to be metal free to pass through airport security easily
7	Locking elbow	During business meetings, his current prosthetic arm would slip off the armrest, drawing attention to the device. Also, while driving, it would slide between the driver's seat and the car door, sometimes becoming stuck. A locking elbow would eliminate these problems

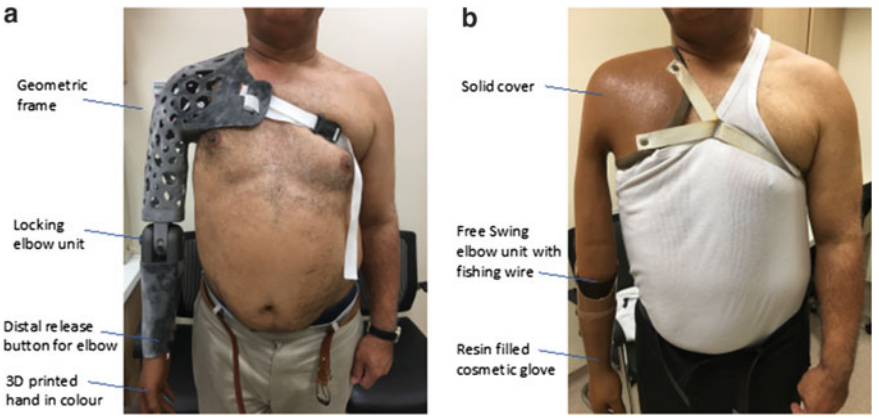

Fig. 5 First iteration of the prosthetic arm, design aimed at getting user feedback on form, fit and usability. 5b: Final design of the prosthetic arm with mesh-like structure (optimized for weight, strength and interface temperature) and functional elbow with options for free-hanging as well as locked in certain position. 5c: User's previous prosthetic arm (foam, solid, with a lack of a functional elbow and symmetry) for comparison

The design mitigation for these issues included making the arm smaller (shrinking the size to 90%), applying mesh on hollows to increase aesthetics under his shirt, and redesigning the strap slots for improved suspension.

The user was happier with the second version; however, further iterations were required, particularly around the neck region. The contact surfaces near the neck needed to be fileted for congruence with the residual limb. We also applied a mesh to the entire upper section of the limb to reduce overall weight. To facilitate easier wearing, mesh cut-outs were strategically located to provide the user with a grip when wearing the prosthesis using one hand. Suggestions were also made to move the release mechanism for elbow lock nearer to the wrist to reduce the need to abduct the contralateral arm to operate it.

The final version included a completed metal-free design, a mesh-like structure for a cooler fit and improved weight, a locking elbow at 90 degrees with a free swing in extension and a 3D-printed soft hand. However, the patient decided to use the silicone moulded glove from the hand geometry created instead of the 3D-printed hand as it was too tacky to slide through the sleeves of his shirt, making it hard to wear.

5.3 Benefits of AM

The benefits of AM in this case were threefold. Firstly, this was a large and highly complex device design that would take a large amount of time to produce and at a high cost if done traditionally. There was a need to balance the time required to pre-process, print and post-process the device. The time taken to fabricate the prosthesis with AM would be considerably less than traditional methods. For traditional methods, the labour would have been over 10 h to cast, rectify, manufacture, fit and deliver the prosthesis. Digital methods allowed for data capturing, geometry modifications, design, print and post-processing to be done faster, while accuracy of scanning and digital analysis helped to reduce the number of repeat visits during the fitting. This resulted in an overall saving of approximately 5 h. AM provided augmentation and optimization for the customized upper limb prosthesis while reducing human resource costs and time. The cost to produce this prosthesis was $1830, which is approximately 20% cheaper than traditional methods (Binedell et al. 2020b).

Secondly, the design freedom offered by AM accelerated the reconstruction process of the 3D anatomical limb, allowed for subtle variations in design between iterations and contributed to a very symmetrical look of the arm when worn under business shirts. Structural integrity of the locking mechanism and the mesh structures of the socket were tested using FE analysis. AM was then used to rapid prototype these parts for user feedback and reiteration. The final design of the prosthesis is a departure from the user's original design as it incorporates strategically placed mesh structures, resulting in a device that is cooler and more comfortable to wear. The added functions of a locking elbow provided freedom for the user to lock when driving or in business meetings, addressing a key requirement.

Thirdly, the material choice available for AM resolved the issue of being detected while passing through airport security, lowering his psychological stress. In deciding to use AM, specifically the Multi-Jet Fusion (MJF), the arm could be made completely metal free without sacrificing strength and shape. MJF printed parts have excellent mechanical and thermal properties and are less porous with smoother surfaces. Therefore, apart from the security clearance benefit, this smoother surface would allow the user to easily slide his business shirt over the prosthesis when getting dressed, improving his usability experience.

5.4 Validation

AM technologies have been around in the P&O industry since the 1980s, but the adoption rate has been slow due to its limitations. However, following the wide availability of desktop printers at affordable prices, many designs can now be found on social media. The success of AM in replicating many common objects including prostheses and orthoses is regularly showcased on the Internet. As media outlets report these stories, patients worldwide are inspired and often encouraged to try these 'new' technologies. Their expectations from these reports are that it will fit better, be more comfortable and more useable.

In our case study, the user had not considered 3D printing his new arm. Instead, he was looking to make a new arm the traditional way, with a few upgrades. After a detailed discussion about the user requirements, it was clear that AM provided the best chance of a successful outcome. By providing the user with our rationale, he became aware that AM would be the preferred method of manufacture to address all his requirements. Throughout the prototyping and iterations, the user had his expectations of the device easily surpassed, leading the user to request new options like the location of the release lock mechanism near the wrist. It may be common for users to alter their expectations based on the prototype design, and hence trialing with the user is critical to ensuring optimal outcomes.

We also found that having the right team members with the right skills aided in a successful outcome. With the CAD systems still very engineered focused, we needed an expert in CAD to assist with the design and printing as well as time to practice with the scanner and software. The clinician and engineer communication also needed to be clear to ensure the correct changes were made between iterations. It was a challenge to communicate the clinical need into a design problem that could be mitigated as there was a difference in the language terms used. Having clear definitions and a good working relationship will help to overcome such challenges in the future.

Finally, apart from the user's expectations about the process and product, there were issues regarding the durability of the device. Due to the moveable locking elbow section and it's controlling mechanism, the user was apprehensive about the long-term durability of the device. Again, this may have been due to his limited knowledge of the strength of materials or capabilities of AM, but it still needed to be addressed.

Over time, the user became confident in the strength of the arm and his satisfaction increased. The final satisfaction with the device was determined through the validated Quebec User Evaluation of Satisfaction with Assistive Technology questionnaire (Quest). Scores were higher or the same in all categories except durability, for reasons previously mentioned. Recording the outcomes of AM with validated instruments can help verify whether AM has met the user's expectations.

6 Value Analysis

To date, research has mainly focused on the potential of AM through case studies which describe specific aspects of AM. In this research, additive manufactured designs are regularly portrayed as superior to traditional designs. However, an important consideration is the value analysis of the technology (Fig. 6). AM technology has the potential to modify healthcare delivery profoundly, but it is crucial to consider its use in a sustainable and feasible way. By continually applying the AM value chain, one can reengineer the process to achieve the results desired by the user through better process management.

6.1 Integration of AM

Stakeholders such as hospitals, private or community-based healthcare service providers, and users generally understand the benefits and potential of AM. However, its true potential has not been delivered as promised during the early-stage development of these technologies. One significant reason is that AM has not been well integrated into the value chain. While AM is a next-generation healthcare-enabling

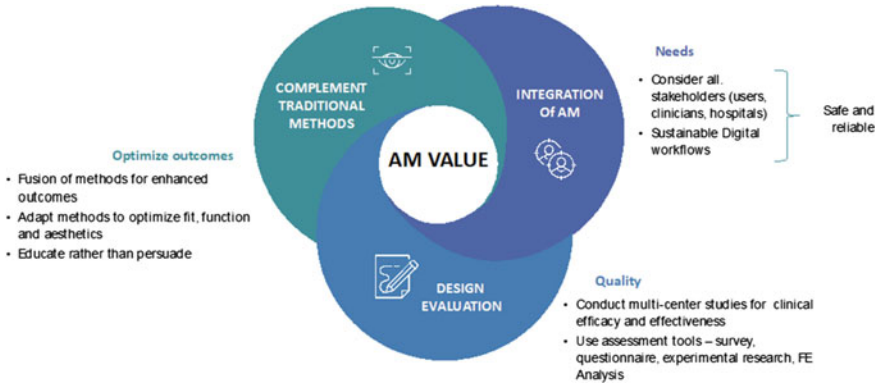

Fig. 6 Value chain of AM in P&O devices

concept, stakeholders must move into a partnership to provide comprehensive clinical care that helps develop P&O devices and value-based healthcare services. AM is an enabler in innovating the healthcare space in two dimensions: product innovation and process innovation. In both sub-spaces, design plays a significant role in understanding the downstream implications, the roles of multiple stakeholders and evolving industry regulations.

The value chain of AM in P&O devices considers the perspectives of the user, the clinician and the system in which they operate. Most users understand that digital workflow (design, development and manufacturing with AM technologies) is the next level of optimal care that is tailored for them by improving their function, fit and aesthetics. They may also benefit from the cleanliness and personal space associated with digital scanning over the traditional plaster techniques. They will, however, expect that the accuracy of the technology offers a greater fit with enhanced comfort. Although AM is limited in the types of materials and colours offered, the end user may be willing to spend more on an additive manufactured device if it meets or exceeds their expectations.

For the clinician, the use of a digital workflow potentially allows for enhanced efficiencies of work processes. However, for AM to be adopted into their current operations, it should be seen to add value to the users they take care of. For example, many of the clinicians are highly skilled in casting, cast rectification and producing devices that fit well, providing user satisfaction. If AM merely replicates what can be done traditionally, takes a similar amount of effort and the result resembles a similar looking item, there may appear little value to adopt AM and the user themselves may feel it lacks a next-generational wow factor. Therefore, when considering DfAM for P&O services, it is necessary to evaluate the needs AM is trying to address to improve user outcomes rather than replace what is currently available.

The benefits mentioned in Sect. 3 may at least persuade some to adopt AM. The amount of time the clinician has with each user varies, so a process that improves efficiencies will be welcomed for those clinicians with limited time. These efficiencies cannot materialize in larger clinics if the clinic has only one scanner for several staff members. It could lead to frustration and a rejection of the technology based on its availability and not capability. Likewise, for private software companies offering a license-based subscription, one license may not be sufficient for a group of staff in a clinic that has shifted towards digital workflow processes. However, the extra costs for more licenses may not be feasible. Thus, the development of high-quality open-source software tools or charge per-use licenses could exponentially increase the adoption of digital workflow and improve access and adoption for the clinician.

A safe and reliable product is important for the user, the clinician and the healthcare system to avoid safety-related litigations or negative publicity. An additive manufactured device must ensure user safety. If possible, the product must pass specific safety standards, and be of high quality. A hospital system will prioritize patient safety above all, and any switch to new technologies would be made easier with the assurance of product and process safety.

6.2 Design Evaluation

The use of AM appears promising as the technology rapidly advances; however, it is critical to analyse the value such technologies offer. The provision of prostheses or orthoses is only a small part of the treatment plan. Successful outcomes also include appropriate assessment, prescription, fitting, adjustments and training by qualified prosthetists/orthotists or adequately trained healthcare professionals. Unfortunately, little research has been conducted validating the technology for its larger impact. Most research is currently focused on the limited assessment of the functionality, providing evidence that an AM device is somewhat as functional as the traditional one (Diment et al. 2017). Comparing kinematics is helpful, but it does not demonstrate the clinical efficacy or effectiveness of such designs. Thus, multi-centre level efficiency and effectiveness studies are warranted to instill confidence in AM technologies for wider implementations. It is essential to validate the long-term implications of the additive manufactured device to ensure the best user value (Diment et al. 2017).

Several methods, such as questionnaires and experimental research, can determine the device's functionality, effectiveness and value. Often lacking though is the design evaluation and validation of the user's acceptance, use, function and durability (Kate et al. 2017). Some of the subjective questionnaires that could be considered for validation include The Quebec User Evaluation of Satisfaction with Assistive Technology questionnaire (QUEST), which evaluates the user's satisfaction with the device and service provided; The Prosthesis Evaluation Questionnaire (PEQ), utilizing some of the subscales on fit, function, aesthetics and The Orthotic Prosthetics Users Survey (OPUS) with five modules including the measurement of satisfaction with devices and services. Experimental studies can also be conducted to determine compliance. The use of activity monitors, temperature sensors, pressure sensors and FE analysis can all be used in various ways to assess the usage, fit and durability of the devices. However, it is important to be selective in the validation methods used to minimize discomfort to the user and to achieve time efficiency.

6.3 Complementing Traditional Methods

AM is a process that provides a faster, cleaner and more cost-effective care for one part of the treatment plan. While it cannot replace clinicians and traditional methods, AM can aim to complement the existing traditional methods, especially for complex cases where current design and manufacturing solutions are sub-optimal or fail to meet the functional requirements. By fusing AM with traditional practice, its use and capabilities will increase, and the end users will benefit. Often traditional and AM methods are viewed as a dichotomy, however that is not correct. Clinicians and users need to understand the advantages of using AM to complement traditional methods and decide on the most appropriate pathway together. The adoption of AM technology must be achieved through education, rather than persuasion alone.

7 Conclusion

Studies clearly show that clinical, technological (on both design and manufacturing) and financial barriers need to be overcome before the AM technology can be adopted for full-scale implementation in a service system for the P&O industry (Chen 2016). While the industry does not use only one manufacturing method, AM offers design opportunities to break down barriers and provides alternatives to current traditional approaches. With barriers lowered, opportunities increase for users to receive optimally fitted and functional devices that will lead to greater outcomes.

AM has shown the potential to outperform traditional manufacturing for complex tasks and small specific tasks in both design and cost-effectiveness. Greater adoption of the technology is dependent on material advancement, digital expertise, the development of easy-to-use software and increased communication and collaboration with industry experts. By addressing the requirements of the user, the clinician and the system, AM may prove to be valuable in creating sustainable and feasible solutions. AM will transform the industry eventually, but an integration of AM with traditional practice may be the most appropriate method to take currently as the P&O industry transitions into digital design and workflows.

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Chapter 6
Muscle Health and Lower Back Pain: Architype Towards Simulation-Driven Product Design in Healthcare

Zartasha Mustansar and Saadia Talay

1 Lower Back Pain and Muscle Health

Low back pain (LBP) is considered one of the most common problems in the modern era causing enormous social, psychological, and economic burden (Rubin 2007; Volinn 1976). Lower back pain can arise from a wide range of conditions including pathologies of the lumbar and sacral spines. The most common spinal tissues involved in producing low back pain are the intervertebral disc, facet joints, nerve roots, and musculature. Disc herniation and dislocation cause an abnormal force distribution which disturbs spinal stability. There must be a relationship between muscle activation patterns and the physics of intervertebral disc dynamics towards improved mechanical stability of the lumbar spine. This forms the basis of this chapter.

There is a demanding need to understand spine problems and their dynamics as a combination of several factors can contribute to LBP. These include bony stress causing disc degeneration (Chepurin et al. 2019) as well as weak musculature. The aim of this chapter is to examine weak musculature as a possible cause of low back pain. A significant correlation between the two would direct healthcare providers to inspect LBP patients for muscle weakness and produce a focused prognosis.

Biomechanics examines forces, pressure points, inertial impact, and momentum to identify the leading cause of backaches. Excitation loads and specially the motion on lumbar spine can result due to manufacturing activities such as lifting objects. This can cause spinal instability leading to lower back pain.

LBP is defined as pain that lasts for at least one day (with/without pain referred into one or both lower limbs) in the area on the posterior aspect of the body from the lower margin of the 12th rib to the lower gluteal folds (Hoy et al. 2010). This means that LBP is usually referred to as pain in lumbosacral region of the spine. Let's

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look on how can we explain this. This explanation has been taken and described from Tiffany Gendal work (Günther et al. 2011). A lumbar vertebrae L4–L5 can be assumed as an inverted pendulum with a single degree of freedom model. The pivot of which represents the most problematic lumbar joint, L4–L5 (Fig. 1).

It is used because of its simple yet accurate representation of the human spine in both flexion and extension. Figure 1 shows the model in its most simple state. Here, the spine is represented by the link between the mass and pivot joint, whereas the flexors and extensors are represented by the spring and damper systems (Günther and Wagner 2016).

To represent this by a mathematical equation, a central equation can be derived from a basic differential equation as shown:

$$f(t) = m\ddot{\theta} + (c_e + c_f)\dot{\theta} + (k_e + k_f)\theta + \mu_e[\theta(t - \tau e) + \dot{\theta}(t - \mu_e)] + \mu$$
$$= \mu_f\left[\theta(t - \tau_f) + \theta(\dot{t} - \tau_f)\right] \quad (1)$$

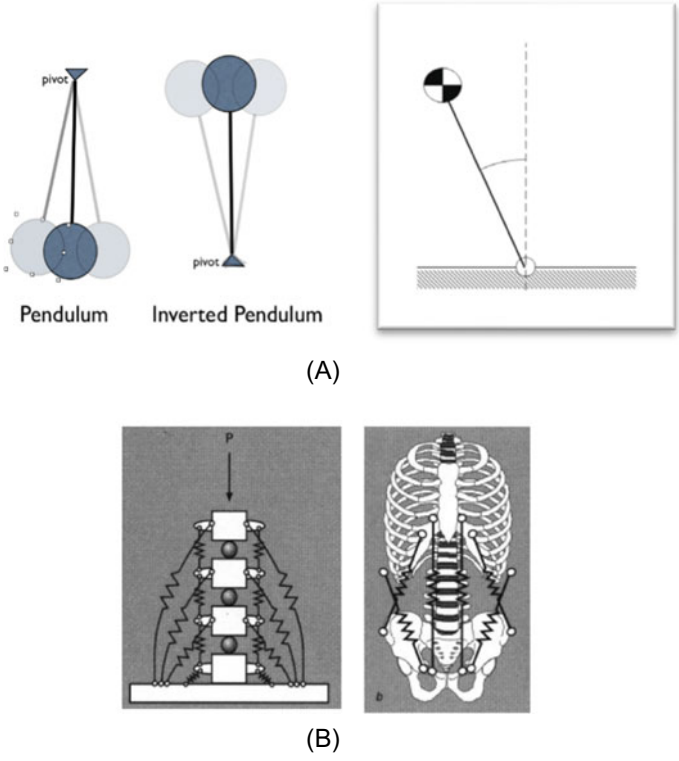

Fig. 1 **a** DOF inverted Pendulum (Vukobratović et al. 1990); **b** springs and dampers representation (Vukobratović et al. 1990)

The coefficients c_e and c_f represent damping forces pertaining to the extensor and flexor muscles, respectively. The coefficients k_e and k_f represent the spring forces of the extensor and flexor muscles, respectively. Reflex delays in the equation are represented by gains μ_f for the flexors and μ_e for the extensor muscles. The time delay in both the flexor and extensor muscles is represented by τ. Mass of body above the L4–L5 joint is represented by m. Variables $\dot{\theta}$, $\ddot{\theta}$, and θ represent velocity, acceleration, and position, respectively (Günther and Wagner 2016).

If we replace the damping coefficients with a resulting damping coefficient and similarly for stiffness coefficients, as well as natural frequencies calculated from frequencies of the muscles of flexors and extensors; following equations can be obtained:

$$C_r = c_e + c_f \tag{2}$$

$$K_r = K_e + K_f \tag{3}$$

$$\omega_r = \omega_e + \omega_f \tag{4}$$

The relationship among the natural frequency, stiffness coefficient, and damping coefficient can therefore be expressed as following:

$$K_R / m = \omega_R^2 \tag{5}$$

The flexor and extensor trunk muscles allow motion in the spine. They bend it forward and backward with respect to the L4–L5 joint. The flexor and extensor muscles are represented as elastic bands, in Fig. 1 shown as set of springs and dampers. While the muscle reflex delays provide modulations to feedback gains. Dynamic equations, usually which determine forces, moments, velocities, and accelerations of the spine are integrated with spinal stability indices. Stability index is an important functional parameter. This index determines how robust the lumbar spine is against perturbations while doing any kind of work. This may include, pushing, pulling, and lifting objects. Spine dynamics play an important role in the stability of the spine and subsequently, good spinal health as well. The important aspect here to mention is how a computational biomechanist makes sure that the indices are within the range and within functional curve. Biomechanics deals with motion of objects and position, velocity, and acceleration play an important role to determine the dynamics of the spine. Physiological limits to these factors can be introduced by research into spine physiology and biomechanics. The best way to do this to take into account muscle which is serving as an actuator in the body machinery. Stability is directly associated with my muscle actuation pattern and COM line. Using integrating reflex delays of the muscle and the dynamic equations it is possible to check how stable a spine is by using biomechanics (Fig. 2). This figure shows, that by changing the center of mass (COM) and altering the pendulum model, i.e., double

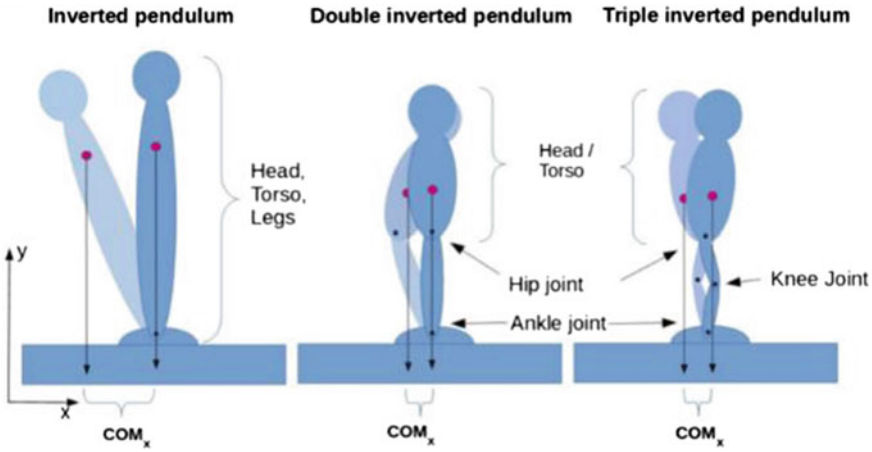

Fig. 2 Representation of different models for approximating the upright position based on the inverted pendulum with mechanically inert joints to represent the physiological properties of the muscles. Left: Inverted Pendulum with one free joint; center: double inverted pendulum (DIP) with two free joints (ankle and hip); right: triple inverted pendulum (TIP) with three free joints (ankle, knee, and hip) (Günther et al. 2011; Günther and Wagner 2016)

inverted, triple inverted, and free can yield to absolutely changed stability posture and weight transfer capability.

When a spine is healthy, it is able to transfer weight correctly. Not only this, it can better handle bending moments of the head, trunk, and pelvis safely as well. The question here is to understand that how surrounding trunk muscles, helps the spine allows physiologic motions between the head, trunk, and pelvis. This is because of an optimal muscle index. In addition to this, spine and trunk muscles play a great role to protect the spine cord from experiencing damaging forces (White and Panjabi 1990). Any condition that causes the spine to be considered clinically unstable also reduces the spine's capability to remain biomechanically stable. Clinical instability is a serious concern and it refer to as "the loss of the ability of the spine under physiological loads to maintain its pattern of displacement so that there is no initial or additional neurological deficit, no major deformity, and no incapacitating pain" (White and Panjabi 1990). To address this, we build a case study with two major hip muscles to demonstrate role of muscle, in the spine health.

2 Muscles, Muscle Indices, and Their Linkage to Motion

Here, only two major muscles are going to be discussed to support our theory of muscle role for lumbar spine health; the gluteus maximus and the gluteus Medius. The gluteus maximus is the largest muscle in the body and is the most superficial out of the muscles of that region (Snell 2012; Amabile et al. 2017). It has a broad

origin and therefore, it is connected to multiple areas of the posterior pelvic region. The origins include the posterior gluteal line of the ilium and the rough area of the bone, including the crest, immediately above and behind it; from the aponeurosis of erector spinae; the dorsal surface of the lower part of the sacrum and the side of the coccyx; the sacrotuberous ligament; and the fascia (gluteal aponeurosis) which covers gluteus medius. There may be additional slips from the lumbar aponeurosis or ischial tuberosity. Acting from its distal attachment, it may prevent the forward momentum of the trunk from producing flexion at the supporting hip during bipedal gait. However, it acts with the hamstrings in raising the trunk after stooping, by rotating the pelvis backwards on the head of the femur (Favier et al. 2021).

The gluteus maximus along with the gluteus medius are the two primary hip abductors and they play an important role in stabilizing the pelvis on the femur during gait. The anterior portions of both of these contribute to the forward contralateral rotation of the pelvis (Semciw et al. 2013). The gluteus medius completely covers the gluteus minimus. They lie inferior to the anterior part of the iliac crest in a slight depression under the gluteus maximus (Favier et al. 2021). Paralysis of these muscles have serious effects on the patient's ability to tilt the pelvis during gait (Snell 2012).

Apart from this, we need to understand how muscle mass index is associated with motion mechanics. Muscle mass index has long been used as a useful index to evaluate the risks of developing functional impairments. However, there is evidence not only this, but other indexes (e.g., muscle strength-based indexes) may play a great role too. Thus, we wanted to design a study to understand how a greater muscle mass and smaller muscle mass contribute to the spine stability and motion. Greater muscle mass can generally produce greater muscle strength. However, whether higher muscle mass is associated with higher muscle quality (muscle strength relative to muscle mass) remains unknown. Furthermore, the nature of this relationship, and how their interaction determines the presence of functional impairments are also unknown.

The spine as far we understand is a complicated system, consisting of numerous degrees of freedom and complicated, nonlinear viscoelastic dynamics. The spine also features changing stiffness created by the various trunk muscles. By using the physiological background, assumptions can be made to make a simplified, yet accurate representation of the spine. Figure 3 shows a mechanistic diagram of lumbar spine.

Muscle composition on lumbar spine is another factor which cannot be overlooked while designing therapies and devices for lower back pain. Usually, older adults who exhibit evidence of poor trunk muscle composition, i.e., higher levels of fat infiltration appear to have a greater risk of reduced mobility over time. This is more noticeable in those persons with a history of at least moderate back pain severity.

Importantly, the association between lower levels of trunk muscle attenuation and lower functional capacity is completely independent of thigh muscle composition [reference].

This finding has important implications for rehabilitation efforts to improve mobility-related function in older adults because current efforts have largely focused on lower extremity muscles.

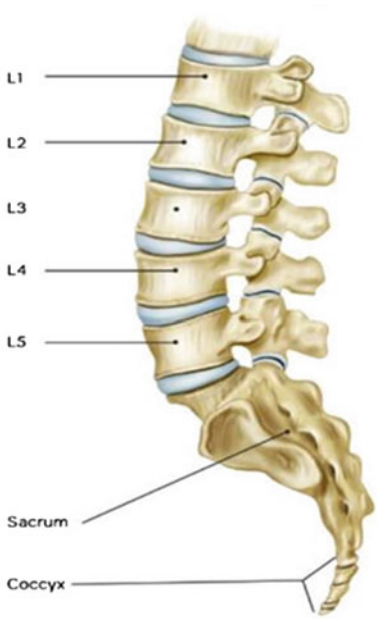

Fig. 3 Lumbar spine structure (Degenerative Disc Disease (DDD) 2016)

3 Posture Mechanics, Disability, and Motion

A good posture creates an equilibrium position that minimizes abnormal spinal stresses. Normally, the backbones are shaped in an 'S' with three natural curves. In the standing posture, we must balance our bodyweight on both legs and in sitting posture we must keep our back supported. If we don't do this, we introduce the risks associated with back pain. There are two types of the risks associated with back pain, modifiable, and non-modifiable. Weak abdominal muscles and short hip flexor tip may cause back sprain.

Aging is associated with decrease in muscle mass, muscle strength, and muscle power. All of these parameters constitute the muscle quality. Muscle quality is still a debatable topic. However, with muscle strength declining at a higher rate than muscle mass suggests functional incapacities. Figure 4 shows a synergy of this concept.

One of the factors in nonspecific chronic low back pain is instability of pelvis, sacroiliac joint, and lower spine. A number of muscles are involved in stabilizing the pelvis, the sacroiliac joint, and the lower back (lumbar spine). Among them is the gluteus maximus, and the gluteus medius (Snell 2012). The forces generated by gluteus maximus act directly on sacroiliac joint and indirectly on the lumbar spine through the thoracolumbar facia. Any alteration in the muscle mass/function would affect the balance of forces on the sacroiliac joint and the lumbar spine and could lead to dysfunction/pain in the lower back (Barba-Artigas et al. 2012) (Fig. 5).

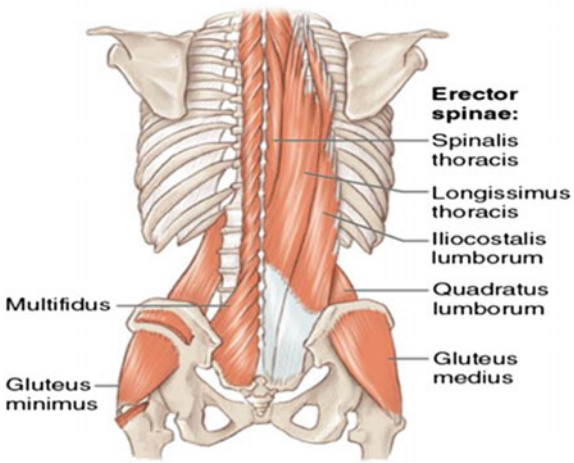

Fig. 4 Lumbar spine anatomy (Integraadmin 2019)

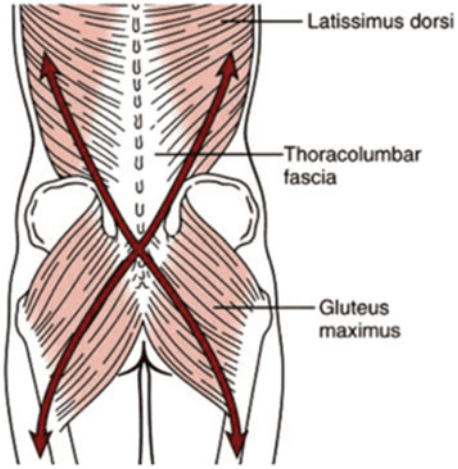

Fig. 5 Lumbar spine, the gluteus maximus, and the thoracolumbar fascia (The Anatomy of the Glutes and their role in lower back pain)

4 Computational Biomechanics and Natural Force Computation

Computational models can be used to study the effects of physiological and anatomical changes on the human body. Favier et al. (2021) created an open-source musculoskeletal model with detailed representations of the lumbar spine and lower limbs. The model was used to generate joint reaction forces between the lumbar vertebrae in different postures. The forces were then validated against EMG recordings and previous literature.

Clinical studies point biomedical engineers towards potential problems that need to be studied. A study conducted in 2016 by Amabile et al. reported that there exists a

statistically significant negative correlation between the cross-sectional area (CSA) of the gluteus maximus and lower back pain as reported in Sect. 3 specially in women between the ages of 40 and 69 (Amabile et al. 2017). Jeong et al. noted that including gluteus strengthening exercises in a regimen along with lumbar segmental stabilization exercises was more effective in treating lower back pain than just lumbar segmental stabilization exercises alone (Jeong et al. 2015). Skorupska et al. confirmed in a study that 50% of lower back-related leg pain had a smaller volume of the gluteus maximus (Skorupska et al. 2016).

A study has correlated lower back pain (LBP) with gluteus medius strength concluding that the muscle is weaker in people with non-specific LBP compared to control subjects (Cooper et al. 2015).

5 Case Study—Lumbar Spine Forces

The goal of this study was to provide a proof of concept of what we have been describing in the sections above. Moreover, this study is designed to test whether there was a relation between the muscle strengths of the lower extremities and the joint reaction forces (JRF) in the lumbar spine during a dynamic movement to pave a way towards simulation driven assistive devices for backaches. Since lower back pain is one of the major causes of low work performance, it became the most important aspect to stabilize work performance to-date.

An existing example model of the cross-trainer model was used (with permissions from Anybody Tech Platform using a trial version) to perform the analysis. The cross-trainer model is most similar to a walking model. The strength of the muscles was varied by varying the strength index, which affected the physiological cross-sectional area (PCSA) factor of the muscle fibers. The PCSA factor determines the maximum force output at optimum fiber length of the muscle. In the AnyBody Modeling system, the PCSA factor is calculated using the following formula:

$$\text{PCSA factor} = \text{Specific Strength} \times \text{Strength Index of the Leg} \tag{6}$$

where the specific strength is 90 N/cm2 as is the default in the software (Fig. 6).

A simple model of the muscles was used on the lumbar spine, which include the lumbar extensors and flexors, as the three-hill muscle model is computationally complex and requires finer controls. The lumbar discs were set to nonlinear stiffness and the lumbar ligaments were activated. Simple muscles were used in both the left and right legs. The strength indexes chosen were 1, 5, and 10, which are, respectively, the minimum, median, and maximum possible values. The analysis was run for only 1 s due to computational and time limitations.

For each strength index, the mediolateral, proximodistal, and anteroposterior joint reaction forces at the interface of each lumbar vertebra were computed using the

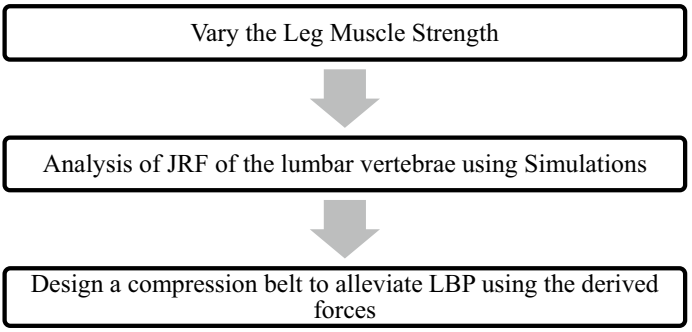

Fig. 6 Methodology

simulation platform plotted against time. The interfaces of the simulation are as follows:

a. Sacrum–pelvis,
b. L5–sacrus,
c. L4–L5,
d. L3–L4,
e. L2–L3, and
f. L1–L2.

Moreover, the plots of the sacrum–pelvis axial and lateral moments and the gluteus maximus, gluteus medius, and gluteus minimus activity were also computed against time which is described in Sect. 7. The quantification of these forces, in the inter-segment lumbar vertebra is very important parameter, to understand why we need assistive devices based on simulation driven data. This data will be used as a standard to develop friendly assistive technologies for treating backaches (Fig. 7).

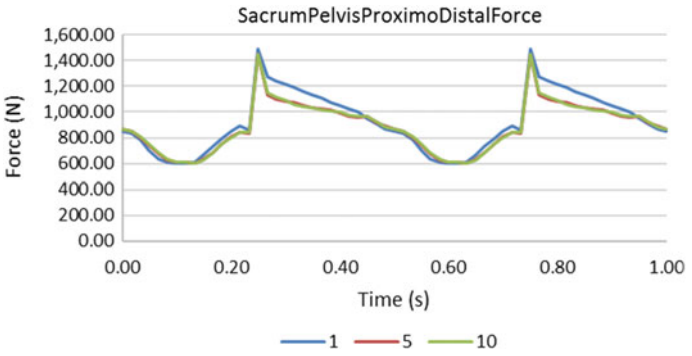

Fig. 7 Sacrum–Pelvis proximodistal force

6 Results

The plots in the following figures show time on the x axis, and joint reaction forces on the y axis. The title of the plot is represented on the y axis, while the x axis represents time. Figures 8, 9, 10, 11, and 12 show the interfaces as mentioned in Sect. 6 from a to f.

The results show that the overall proximodistal joint reaction force at each interface is the most at the minimum muscle strength index of 1. As the strength index is increased to 5, the overall joint reaction forces decrease. However, no significant change is observed between the JRF at the strength index of 5 and the strength index of the maximum possible value of 10.

To ensure that the resultant values are valid, they were compared against a previous study which quantified the inter-segmental spine joint reaction forces during common workplace physical demands (Cooper et al. 2015). The range of the JRFs is similar and therefore the results can be considered valid.

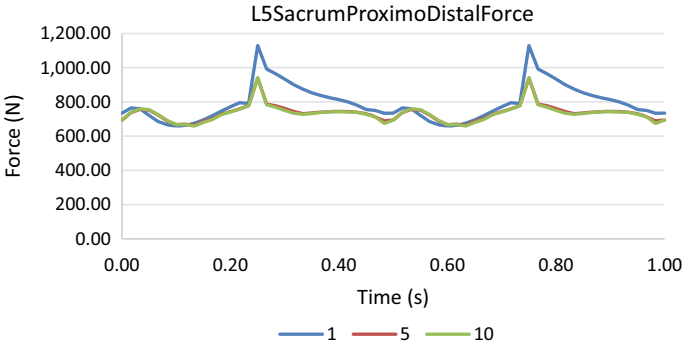

Fig. 8 L5–Sacrum proximodistal force

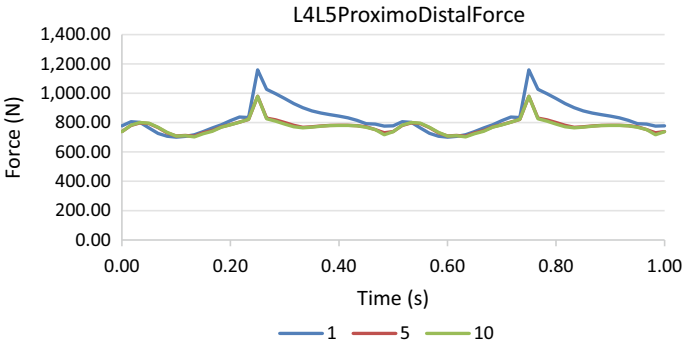

Fig. 9 L4–L5 proximodistal force

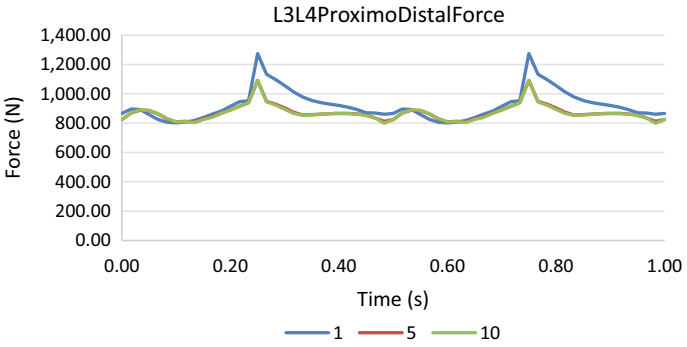

Fig. 10 L3–L4 proximodistal force

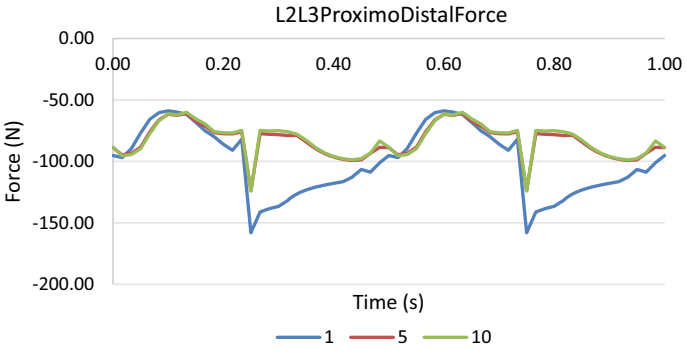

Fig. 11 L2–L3 proximodistal force

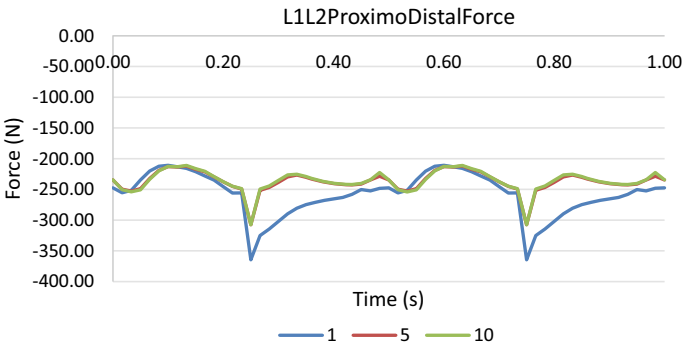

Fig. 12 L1–L2 proximodistal force

The JRF varies as the model moves since the acceleration of each vertebra varies according to its co-ordinates at each time step. As the strength of the leg muscles is increased, lower inter-segmental spine joint reaction forces are observed. This indicates lower compressive forces and lower stresses on the intervertebral discs. Increasing the strength of the leg muscles decreases the inter-segmental spine joint reaction forces to a certain limit after which any further increase in strength causes a negligible decrease in the JRF. This principally means that there is a need to incorporate muscle strength indices as a functional parameter for spine dynamics prior to designing any assistive devices for LBP. The JRF alone with muscle indices can't make muscle, strong or weak. Sometimes a quite weak muscle musculature could contribute to the same. For example, decreased back extensor muscle endurance is another important factor in chronic LBP. Muscle weakness is definitely a major reason but associated factors, due to posture mechanics in daily life including hip adductor muscles, size of the lumbar lordosis, pelvic tilt, and foot arch may contribute as well.

Besides this, it is important to understand that the back is considerably much complicated machine system than simple arm or leg systems, with various muscles and joints between vertebrae, all having mechanical advantages less than 1. Back muscles, therefore, exert very large forces, which are borne by the spinal column. Moreover, intervertebral discs crushed by mere exertion are very common due to factors like weight, or underlying health conditions. Muscle mass, and its physiological cross-sectional area therefore is the iota of back mechanics in various postures.

Computational models have the limitations of approximations and therefore are not completely anatomically accurate. Moreover, due to computational limitations, the model could not be run for a longer time. A longer simulation often yields more accurate results and sometimes produces interesting insights. This model also did not account for variation in muscle mass due to the physiological state of the person which occurs naturally.

7 Conclusion

Image-based modeling using finite elements has the ability to robustly generate meshes for topologies of arbitrary complexity, such as human spine. For this specific work, we have not run a numerical simulation (Finite Element Method) in this specific study, which could serve as a valuable addition to this work in future.

However, the relationship of muscle indices with JRF is a significant step before image-based modeling could be taken up for stress quantification in LBP. The JRF indices, indicates a strong correlation for maintenance of spine dynamics. To further study this phenomenon, dynamic finite element analysis can be performed to examine the concentration of stresses on the lumbar vertebrae as the strength of the leg muscles is varied. This would provide us with more explicit results showing the effects of variation of the strength of the leg muscles on the lower spine.

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Chapter 7
Foot Biomechanics with Emphasis on the Plantar Pressure Sensing: A Review

Gunarajulu Renganathan, Yuichi Kurita, Saša Ćuković, and Swagata Das

1 Introduction

Plantar pressure (PP) sensing technology has become an important tool for gait analysis in both clinical and research settings. The sensor technology, which can measure static and dynamic pressure, has been critical in studying the effects of pressure on the foot. A wide range of pressure sensing systems are now available on the market, with research always striving to improve and create new systems to satisfy the rising expectations of a vast user base. The nature of the pressure sensors employed in commercially available systems varies slightly, and each has benefits and limitations in their application. However, these sensors have one thing in common: they generate electrical signals that are proportionate to the vertical pressures applied on the various sensors when the plantar surface of the foot makes contact with a supporting surface. Capacitive, piezoelectric, piezoresistive, and resistive sensors are the most often used pressure sensors (Wafai et al. 2015).

In this review chapter, our focus is to report state-of-the-art research and technologies about foot orthoses and monitoring. We give special emphasis on the research that accentuate PP measurement for the assessment of patients, runners, and elderly. This review will begin with summarizing the existing methods for detecting foot PP, as well as the benefits and drawbacks of a variety of commercial pressure sensors utilized in published studies. Following that, the discussion will focus on the development of a novel pressure sensor with much improved performance characteristics. Finally, possibilities proposed by researchers for measuring foot PP utilizing an in-shoe device will be discussed.

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1.1 Human Foot and Plantar Pressure

Our feet endure the body's weight and respond to different ailments that may not be as easily discernible by observing the rest of the body. In addition to illnesses, the careful analysis of the behaviour and motions of our feet may help us understand how our body reacts in settings like sports, exercise, overload, and growth, thus, enabling us to prevent injury and maintain healthy locomotion. Foot monitoring and Orthoses have been applied to the field of healthcare in every stage of human life including analysis of growing children (Cousins et al. 2012), investigation of the effects of backpack load in school going children (Pau et al. 2015), probing athletic activity in adults (Yang et al. 2020), and prevention as well as aftercare of ailments such as diabetic ulcer (Ulbrecht et al. 2014), Cerebral Palsy (CP) (Meyns et al. 2020), arthritis (Eerdekens et al. 2020) and stroke (Dean and Kautz 2015). PP is the pressure applied on the bottom skin of the human foot during any specific activity. The PP is evidently affected by changes in the musculoskeletal health of the lower limb. Foot/Ankle orthoses for healthcare:

- Improving gait in children with CP
- Treating plantar fasciitis pain
- Post-stroke gait stability

1.2 Human Foot and Plantar Pressure

PP is useful in various applications as listed below:

- Evaluation of the various characteristics of the pathological feet
- Prediction and monitoring diabetic neuropathy and ulceration
- Measuring the foot-associated consequences of arthritis
- Training and monitoring adults with Chronic Ankle Instability (CAI)
- Examining the control and biomechanics of lower limb in runners with Patellofemoral Pain Syndrome (PFPS)
- Examining the effects of plantar fasciitis
- Walking, running, jogging and stair-climbing kinematics related to different types of surfaces and running behaviour
- Influence of body characteristics and backpack loading on children's growth
- Activity monitoring and fall prediction in elderly

Out of the above, we consider the first four applications to review recent publications that have introduced novel techniques and made significant observations in the associated data.

1.3 Inclusion, Exclusion Criteria and Prisma Chart

The search keywords for this review are foot 'and' biomechanics, foot 'and' biomechanics 'and' pressure, foot loading, foot pressure, foot 'and' pressure, foot biomechanics, plantar loading and PP. We covered the following databases for an extensive search: Semantic Scholar, IEEE, PubMed and Microsoft Academic. The period of publication considered was from 2011 to 2020. As mentioned in the Prisma Chart (Fig. 1), research publications are screened carefully to include 98 pieces to ensure the insertion of different categories of research as structured in this review chapter. The Prisma Chart also depicts the various exclusion criteria followed during the scrutiny. The finally included research pieces were further reduced to 53.

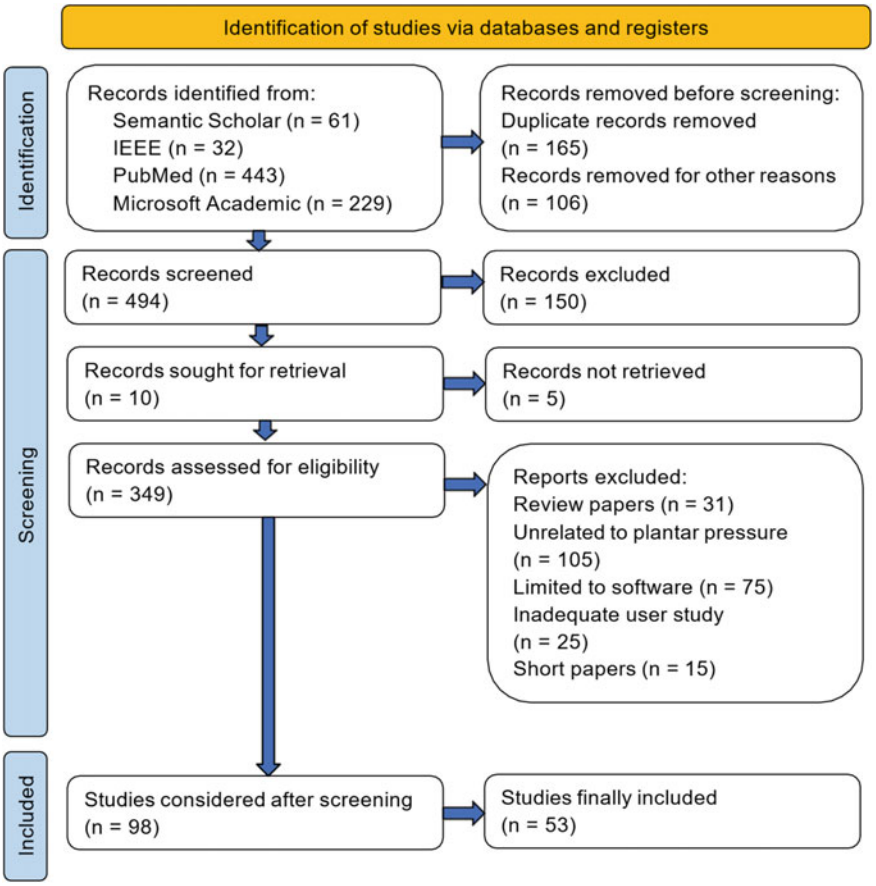

Fig. 1 Prisma flowchart showing selection of research works for this review

2 State-of-The-Art Review

PP measurement has been implemented through different types of transducers. Capacitive sensors comprise of two electrically conducting plates separated by an insulating elastic layer. When a force is applied, the distance between the plates changes, resulting in a voltage fluctuation. The most commonly used sensor types are Force-Sensitive Resistors (FSRs). They are comprised of a conductive polymer such that, when a force is applied, the material's resistance diminishes as the applied pressure increases. Optical fibre-based sensing includes Polymer Optical Fibre (POF), Optical Fibre Grating (FBG) pressure sensors and Optical pedobarographs. The optoelectronic sensors comprise of a transmitter (laser or light-emitting diode LED) and a receiver (photodiode) between a silicon structure. When a force is applied, it causes a deformation which is proportional to the sensor's output voltage. Piezoresistive and piezoelectric sensors utilize the piezoelectric effect. The variation in the applied pressure is converted into an electric energy. For piezoelectric sensors, when the material is stretched, the electrical resistance is changed. Textile sensors are also gaining popularity. These are thin and sensitive to pressure with conductive links used for manufacturing. However, these sensors have limitations of being non-linear and exhibiting hysteresis.

There are several types of PP monitoring systems, however, they may be divided into three major categories: Platform with pressure sensing systems, Insoles, and optical measurement systems. The categorization of these systems are illustrated in Fig. 2 and described in this section accordingly.

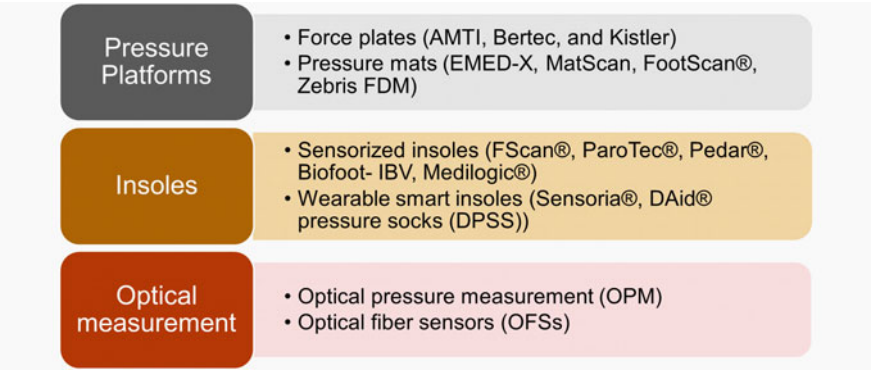

Fig. 2 Categorization of plantar pressure measurement systems

2.1 Platforms with Pressure Sensing

In order to analyse the kinetics and kinematics of the human movements and to record the subject's footprint, force and/or pressure measuring transducers are used. These platforms-based systems are commonly considered as the gold standard in PP measurement and holds the advantages of measurement with high precision and spatial resolution. These systems are broadly categorized into two forms: 1. Force plates, 2. Pressure platforms (Instrumented mats). Both force plates and pressure platforms are very reliable and accurate because these devices are sensitive (sensitivity up to 1 μN) and provide high-frequency data (sampling frequency of 200 Hz). These devices may be used for both static and dynamic situations, such as measuring balance, posture and gait (Crea et al. 2014).

Force plates. The widely used force plates for foot biomechanics research are AMTI, Bertec and Kistler force plate. A brief description has been provided below.

AMTI (AMTI, Watertown, MA, USA). The force components along the axes and moment components around the axes are measured concurrently by the AMTI Biomechanics platform. Strain gauges mounted to specialized load cells near the platform's four corners are used to measure the forces and moments.

Bertec (FP4060-10, Bertec Corporation, USA). The force plates in Bertec's product range are created particularly for gait, balance, sports and other static and dynamic studies. These force plates are ideally suited for both static and dynamic applications due to the excellent strain gauge technology, creative design and high-quality manufacture. Each force plate has a number of strain gauged load sensors as well as a signal conditioning digital pre-amplifier. Bertec force plates are available in a number of sizes and load levels to meet a variety of application requirements. The 4550, 4060 and 4080 series force plates are created for clinical and research gait assessment, whereas the 6090, 9090 and 6012 series force plates are ideal for sports and other dynamic biomechanics, ergonomics and industrial research.

Kistler (Kistler, Winterthur, Switzerland). Kistler force plate was designed specifically for gait and balance studies. The type 9260AA is equipped with a built-in charge amplifier that is compatible with all current motion analysis systems. The force plate is suitable for monitoring slow and medium-fast activities where precision of the Centre of Pressure (COP) is essential or accessibility is required. This multi-component force plate type 9260AA has some excellent features which include COP accuracy, availability in different sizes, mountable, flexible, integrated with mobile applications and easy installation.

Pressure mats. In this section, we compare different types of pressure mats as shown in Table 1. The most widely used instrumented mats are TekScan MatScan®, Emed-X 400®, Footscan® (RSscan International, Belgium) and Zebris FDM (Zebris Medical GmbH, Isny im Allga¨u, Germany).

Table 1 Comparison of most widely used force platforms for foot pressure measurements (Razak et al. 2012)

Specifications	Emed-X®	MatScan	Footscan®
Dimension (mm)	700 × 403 × 15.5 (18)	508 × 499 (Height—0.57 cm)	2096 × 472 × 18
No of sensors	6080	2288	12,288
Resolution (sensors/cm^2)	1 or 4	1.4 or 9.2	NA
Frequency (Hz)	100 or 400	40	200
Pressure range	10 1270 kPa	862 kPa	0–200 N/cm^2

Emed-X 400®. This is a dynamic barefoot PP platform (Novel GmbH, Munich, Germany), a 700 × 403 mm platform with 6080 capacitance transducer sensors (4 sensors/cm^2) sampling at a frequency of 100 Hz (Buldt et al. 2018a, b).

TekScan MatScan®. The TekScan MatScan® pressure mat model type 3150 (Tek-Scan Inc, South Boston, USA) is a thin (5 mm) floor mat with 2288 resistive sensors (1.4 sensors/cm^2) and a sampling frequency of 40 Hz. (Cousins et al. 2012, 2013; Butterworth et al. 2015).

Footscan® (RSscan International, Belgium). This is a dynamic pressure measurement system, used to record the Peak pressure, COP coordinates, velocity and progression angle. The hardware part includes 0.5 m plate with 4 sensors/cm^2 with a sampling frequency of 500 Hz (Chiu et al. 2013). The scientific Footscan® software associated with the instrumented mat divides the foot into 10 zonal masks: Hallux (T1). Toes 2–5 (T2), first to fifth metatarsals (M1–M5), Midfoot (MF), Medial Heel (MH) and Lateral Heel (LH). The clinically most relevant estimated parameters are Peak Pressure (PP, kPa), Contact Time (CT, % of stance time), Contact Area (CA, cm2) and Pressure–Time Integral (PTI, kPa). Hence, a total of 40 parameters are evaluated for the four different loading variables under the 10 zones (Pau et al. 2015; Willems et al. 2012; Naemi et al. 2012; Yan et al. 2013).

Zebris FDM (Zebris Medical GmbH, Isnyim Allga¨u, Germany). PP data can be collected by using an FDM 1.5 capacitive pressure distribution platform (Zebris Medical GmbH, Isny im Allga¨u, Germany) with a resolution of 1.4 sensors/cm^2 and a sampling frequency of 100 Hz. On the peak pressure footprint, nine anatomical subareas are determined. For each subarea, peak pressure pmax and relative pressure time integrals are computed (Bates et al. 2013; Squadrone et al. 2015).

2.2 Insoles

Pressure-sensitive insoles tend to give the optimum trade-off in terms of gait analysis when maximum mobility is desired or monitoring of pressures at the foot–shoe interface is required.

Sensorized insoles. Insoles can measure PP within shoe and can provide us the features similar to the platform-based systems as depicted in Table 2. When it comes to pressure-sensitive insoles, there are two primary considerations: (1) the sensor technology utilized, and (2) the actual information that can be derived. These sensorized insoles have been designed and commercialized using a multitude of sensing methods. FSRs are used in the F-Scan® system (Tekscan®, South Boston, MA, USA); piezoresistive sensors are used in the ParoTec® system (Paromed®, Neubeuern, Germany); and integrated capacitive sensors are used in the Pedar® system (Novel® GmbH, Munich, Germany); Biofoot-IBV in-shoe system (Valencia, Spain); resistive sensors are used in the Medilogic® system.

F-Scan® system. The F-Scan In-Shoe System was used to quantify PP and foot COP in various anatomical areas of the foot. The sampling frequency of these insoles can be varied between 50 and 100 Hz. These sensors are cut to fit inside ordinary shoes and affixed. Each insole sensor was allowed to warm up within the shoe before being calibrated using the manufacturer's indicated clinical calibration procedure (calibration considering each subject's body weight). The Tekscan system has been reported to be reliable when calibrated using this approach. A strap was used to secure the cuff unit to the participant's leg, and a 9.25 m cable was used to connect it to the computer (Rome et al. 2011; Ledoux et al. 2013).

Table 2 Comparison of most widely used insoles for foot pressure measurement (Price et al. 2016)

Insole features	Pedar	Tekscan	Medilogic
Sensor model	PedarX	Fscan 3000E	SohleFlex Sport
Pressure sensor technology	Capacitive	Resistive	Resistive
Insole thickness (mm)	2.2	0.2	1.6
Sampling rate (Hz)	100	169	300
Pressure range (kPa)	20 600	345 862	6 640
Sensor density	0.57 0.78 per cm^2	3.9 per cm^2	0.79 per cm^2

ParoTec system. The system comprised of two insoles and a belt-mounted data collection box with a sampling rate of 250 Hz. Sixteen microsensors are placed within a confined hydrocell in each insole (using effect size to quantify PP asymmetry of gait of nondisabled adults and patients with hemiparesis).

Pedar System. The in-shoe pedar system measures in-shoe pressure in a reliable, valid and precise manner. The pedar insoles are around 2 mm thick and are made up of 99 capacitive pressure sensors organized in a grid pattern. PP data can be captured at a rate of 50 Hz. Prior to the start of the experiment, all of the insoles are calibrated with the trublu calibration device (Novel GmbH, Munich, Germany). These insoles can be placed on top of the shoe insert. The pressure insoles are zeroed before to the first walking trail of each condition, as per the manufacturer's instructions (Sacco et al. 2014; Koldenhoven et al. 2016; Chapman et al. 2013; Bus et al. 2011; Waaijman et al. 2012; Ribeiro et al. 2011; Arts and Bus 2011).

Biofoot 2001. The Biofoot-IBV in-shoe system (Valencia, Spain) is made up of 64 sensors with a thickness of 0.5 mm and a diameter of 5 mm that have already been validated and used to evaluate sports tasks (García-Pérez et al. 2013).

SohleFlex Sport Medilogic. This insole were of resistive sensor type which can be customized based on the need and have a sensor density of about 0.79 per cm2 with 1.6 mm thickness and a maximum sampling rate of 300 Hz. The measurement range were between 6 and 640 kPa. These insoles are calibrated using polybaric characteristics as per the instructions provided by the manufacturer (Price et al. 2016).

Wearable smart insoles. Wearable smart insoles are textile-based solution with sensor embedded in it. These insole-like wearable device addresses the existing challenges with gait laboratory, video and IMU, and enables real-time gait monitoring. This technology resembles an insole and is capable of monitoring both inertial and pressure data from both feet. A typical example of a wearable insole is the Smart Insole system that consists of a low-cost sensing insole and application software for data storage and display on both a smartphone and a PC. An array of sensors, an ultra-low power Microcontroller Unit (MCU) and Bluetooth Low Energy (BLE) wireless transmission module, a channel multiplexer (MUX), a Li-battery and a micro-USB connection module comprise the insole. The data recorded on the Secure Digital (SD) card will be used to analyse lifestyle and health behaviours in order to gain a better understanding of them and to develop effective intervention options to enhance individual freedom. Smart Insole can specifically measure step counts, step pace, swing duration and COP changing velocity, among other things, to infer the walking balance state and possible fall risk in real life. Instead of participating in a specialized gait laboratory, individuals may track and evaluate their gait in their regular lives by utilizing Smart Insole (Lin et al. 2016). There are two smart socks commercially available for biomedical and sports applications. They are Sensoria® and DAid® Pressure Sock System (DPSS).

Sensoria®. Sensoria fitness e-textile socks, when compared to the gold standard stabilometric platforms, are shown to be a low-cost option for evaluating changes in the COP signal. The data transfer has been via Bluetooth and the sensors over the socks are magnetically connected each other. These socks are deployed with Bluetooth-enabled anklet. The associated application allows the user to define individual goals for any statistic that he or she wishes to monitor. The anklet is removable, and the socks include unique textile sensors. This allows the socks to evaluate parameters such as cadence, foot landing forces, impact forces, step count, speed, calories and distance.

DPSS®. DAid Pressure Socks contains an array of piezoresistive pressure sensors, knitted together with electro-conductive lines. They are communicated via electronic devices for data acquisition and transmission from sensors to a computer. The system has the following advantages: it is transportable, lightweight, does not cause discomfort when walking or running and provides exact temporal locomotion data; hence, it may be utilized as a practical tool in medical and sporting applications (Dragulinescu et al. 2020).

2.3 Optical Measurement

Based on silicone technology, there are two major type of pressure sensors: optical fibre pressure sensors and optical pressure sensors.

Optical Pressure Measurement (OPM). This is a novel non-contact pressure measurement method that employs a unique material. On the surface of the model, a pressure sensitive coating with the function of a pressure sensor is sprayed, which may ignite fluorescence under the excitation light of a specified transition length. Because the pressure field is related to the fluorescence intensity field, the pressure distribution on the model's surface may be determined using computer image processing and a high-resolution digital CCD camera. Finally, image processing techniques such as segmentation are required for further categorization and identification of the images acquired using the OPM-based foot three-dimensional (3D) scanner.

Optical Fibre Sensors (OFSs). A non-invasive e-Health architecture has been developed that includes OFSs integrated into a shoe-sole for continuous remote monitoring of foot PP during gait to improve the life quality of physically impaired citizens and increase the mobility of elderly citizens (Domingues et al. 2019).

2.4 *Novel Approaches to PP Measurement and Orthoses Design*

The most important stage in the success of a medical device is its design and development. A medical device that is poorly specified and developed will not be able to meet regulatory requirements and reach the market. Or, even if it passes compliance, it will fail to offer the specified functionality and advantages based on market demands, resulting in lower market acceptance compared to well-designed alternatives.

Design Input development and approval, which comprises device design and manufacturing procedures to be carried out in the production phase, is the first step from which Design Control begins. It is an ongoing process to build a useful product for a user, and therefore for the improved product, it considers revolutionary changes from usage patterns as well as evaluating unsuccessful products. The Waterfall model for Design Control implementation is detailed in Fig. 3.

Waterfall Model for Design Control

1. Needs: The requirements are determined in the perspective of the market demand, and the gadget is created to meet that need. The medical device design is completed and sent to production for manufacture after a sequence of evaluations. There is a need for input at every stage of this procedure.
2. Design Input: This is a step-by-step procedure. When a company decides to meet a specific need, it reviews and tests the acceptability of Design Input generated by the need. The iterative process of translating requirements into device design begins at that moment.
3. Design Process: These Design Inputs are transformed into Design Outputs by translating the requirements into high-level specifications (which are Design Output).

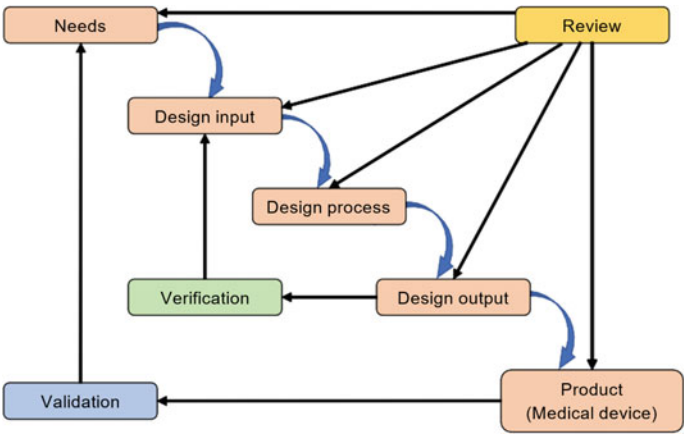

Fig. 3 Design control can be implemented using the Waterfall model (Food 1997)

4. Design Output: The verification procedure validates whether or not the specifications meet the criteria. And the outcome becomes the input for revising the requirements, and so on until the Design Output matches the Design Input.
5. Product (Medical Device): When the final design is complete, it is sent to the manufacturing plant for mass production.

Design Control Regulations require the creation of a Design History File (DHF), which depicts the connections and interactions between all Design Controls and aids in the tracking of all changes during the product development process (Food 1997). The design approaches for different pressure sensing technologies are detailed in Table 3.

2.4.1 Flexible PolyDiMethylSiloxane (PDMS) Capacitive Pressure Sensor for PP Measurement (Lei et al. 2014)

Product Feasibility/Market Requirement. Most pressure sensors on the market today lack the flexibility to fit into curved interfaces. To answer that specific demand and practicality, a product designed with sensor flexibility to increase measurement accuracy and sensor durability utilizing micro-fabrication technology was developed. The flexible sensor has numerous silicon chips linked by two layers of polyimide film and a resistive metal-based sensor for high sensitivity.

Design Plan. A flexible PDMS capacitive pressure sensor for measuring PP in biomechanical applications have been created. Because of its high dielectric constant and adjustable elasticity, was chosen as the dielectric layer material. To study the stiffness under varied PDMS, pre-polymer and curing agent were chosen under different mixing ratios, PDMS characterization was performed. Within our pressure area of interest, PDMS in a 16:1 mixing ratio was chosen because it exhibits the most linear stress–strain relationship with the best elasticity. Since the sensor was intended to detect PP, it can also measure pressures up to 945 kPa. Furthermore, flexible printed circuit film was used as the sensor substrate to minimize measurement disturbance to the curved surface and to reserve electronic circuit integration. Due to the sensor's compactness and flexibility, it has the potential to build a shoe-integrated sensor system for long-distance data gathering for gait analysis.

Design Input Requirement Specification. There were four layers in the capacitive pressure sensor: a bottom layer, a dielectric layer, an upper layer and a bump layer. The lower and top layers were made of flexible printed circuit film to create a flexible substrate that was also compatible with the peripheral electronic circuit for future development. The electrodes were placed on the top and bottom surfaces of the dielectric layer, which was constructed of PDMS material. To give four independent capacitance measurements, four electrodes on the bottom layer and one common electrode on the upper layer were constructed. For uniform pressure distribution, the bump layer created a point contact between the applied force and the sensor. The sensor's operation is based on measuring the capacitance change to determine the

Table 3 Design Approaches for different Pressure sensing categories Competitive Analysis. Abbreviations used: PP Measurement (PPM), Ground Reaction Force (GRF), Ankle Foot Orthosis (AFO), Plantar Fasciitis (PF), Pressure Sensitive Conductive rubber (PSCR)

System	Application	Technology/ Fabrication	Portability	Usability	Wireless	Low Cost	IMUs	Analysis/ Methods	Accuracy claimed	References
Flexible	PPM	Flexible Sensor–Micro fabrication	Yes	No	No	No	No	Gait Analysis for long distance-based approaches	Yes	Lei et al. (2012)
Insole + Force Platform	PPM and Accelerationof foot	3D Printed instrumented insole	Yes	No	Yes	No	No	Static and Dynamic PPM and GRF	Yes	Stoggl and Martiner. (2017)
Orthosis	Comfortand NovelAFO Design	3D Printing	No	No	No	No	No	Comparative analysis with prefabricated insoles	Yes	Rui et al. (2019)
Optical	Non-invasive PPM	Optic fibre sensor network	No	No	Yes	No	No	Accuracy and reliability of the system	Yes	Domingues et al. (2019)
Insole	Remote Monitoring and eHealth applications	3D Printed instru mented insole	Yes	No	Yes	Yes	No	Static and dynamic PPM and GRF	No	Leal-Junior et al. (2019)

(continued)

Table 3 (continued)

System	Application	Technology/ Fabrication	Portability	Usability	Wireless	Low Cost	IMUs	Analysis/ Methods	Accuracy claimed	References
Wearable Socks	GAIT analysis and PPM	Textile and wearable	Yes	Yes	Yes	Yes	Yes	Quantification of pressure analysis, steps, balance and inertial measurement. Reliability and usability competitive analysis of exiting methods	Yes	Lin et al. (2016)
Insole	PPM	PSCR sensors	Yes	Yes	Yes	Yes	No	monitor PP during natural walking	Yes	Saito et al. (2011)

applied pressure. Capacitances are reported as zero when no pressure is applied to the sensor. The dielectric layer's distance is decreased when pressure is applied. Capacitance values rise throughout four independent measurements. Because dielectric layer deformation may not be homogeneous, four independent observations might enhance pressure accuracy estimation.

Design Output High-Level Design. The PDMS was created by completely combining a certain weight ratio of PDMS pre-polymer and curing agent. By degassing in a vacuum chamber, the PDMS mixture was ready. As a result, photolithography was used to create the electrodes on the polyimide film, which had a pattern of upper and lower electrodes with a diameter of 6 mm. By controlling the spinning speed, a 30 mm thick dielectric PDMS layer was spin-coated on the bottom layer. For adhesion between the top and lower layers, a small coating of PDMS was spin-coated on the upper layer.

A PolyMethylMethAcrylate (PMMA) mould was manufactured using micromachining equipment, which was used to form a PMDS spherical bump layer. The bump's diameter and height were 6 and 3 mm, respectively. Surface plasma treatment was used to bind each layer of the sensor. According to the manufacturer's instructions, the standard mixing ratio of PDMS pre-polymer and curing agent in the PDMS process is 10.1. Different mixing ratios, on the other hand, can produce varying degrees of elasticity. In this example, the mixing ratios for individual layers were different dependent on their purpose. Because the dielectric layer in the pressure measurement was a compressive layer, flexibility can increase the sensor's sensitivity.

Design Verification. Adjusting the mixing ratio of the PDMS pre-polymer and curing agent can be used to control the elasticity of the PDMS. Material testing was carried out to describe the stiffness of the PDMS material at five different mixing ratios of the PDMS pre-polymer and curing agent, namely 12:1, 16:1, 20:1, 24:1 and 28:1. Tuneable elasticity might improve sensitivity and expand the range of force detection. The variation in capacitance values may be used to directly reflect the applied pressure. PDMS is a highly elastic polymer with a strong non-linear stress–strain relationship. The stiffness of PDMS was determined by varying the mixing ratios of the PDMS pre-polymer and the curing agent. Within our pressure area of interest, PDMS in a 16.1 mixing ratio was chosen because it has the most linear stress–strain relationship with the best elasticity.

The sensor can monitor pressures up to 945 kPa and can measure the majority of PPs. The applied force under the sensor region was used to compute the pressure. The sensor's total capacitance was calculated by averaging the capacitances produced by the four sensing components. Pressure ranges up to 945 kPa were recorded, and also the capacitance values ranging from 0.95 to 2.69 pF.

Design Validation Strategy. The sensor can monitor pressures up to 945 *kPa* and can measure the majority of PPs. Furthermore, flexible printed circuit film was used as the sensor substrate to minimize measurement disturbance to the curved surface and to reserve electronic circuit integration. Because the sensor is small and flexible, it may be incorporated into a shoe for long-distance data gathering for gait analysis.

2.4.2 Customized 3D Printed Orthosis (Rui et al. 2019)

Product Feasibility/Market Requirement. Plantar fasciitis is not effectively treated with conventional ankle–foot orthoses (AFOs). As a result, customized 3D printed ankle–foot orthoses are advised for successful treatment for a variety of anklefoot disorders.

Design Plan. AFOs are biomechanically designed devices that are used to prevent and cure illnesses of the feet and lower limbs. 3D printed AFOs have a superior effect on increasing comfort and altering foot biomechanics in plantar fasciitis sufferers. The Footscan® 7-gait system is the second-generation device developed for the biomechanical analysis.

Design Input Requirement Specification. 3D printed AFOs are made additively with computer assisted design and production. Body arch X1 printer is used to obtain, create and print patient pictures made of Ethylene–Vinyl Acetate (EVA).

Design Output High-Level Design. Footscan® is made up of resistance sensors that record the dynamic pressure of the foot. The system includes a connection with computer for data acquisition.

Design Verification. General design of the study are planned to conduct as randomized and controlled design study. The study's goal is to evaluate the effects of personalized 3D printed AFOs on biomechanics and comfort in the plantar foot in patients with plantar fasciitis to those of standard prefabricated insoles.

Design Validation Strategy. Statistical program is used to compare the mean and significance between the test conditions. Study participants are selected based on the inclusion and exclusion criteria of sex, age and metabolic condition, respectively. Software are divided into different coverage areas for analysing the PP data using the Footscan® system. Compared to prefabricated AFO, the efficiency of customised 3D printing AFO enhances patient comfort and is beneficial in the treatment of plantar fasciitis.

2.4.3 Insole Optical Fibre Sensor (Domingues et al. 2019)

Product Feasibility/Market Requirement. To improve the utility of mobile device technology in medical and health practise, researchers created a non-invasive optical fibre with sensor architecture adaptable to a shoe sole for remote PP monitoring, which can be integrated into an IoT e-Health solution to monitor people's well-being.

Design Plan. The optical fibre sensing network with FBG sensors, the interrogator system, and the wireless mobile connection comprise the remote sensing system. FBG sensors are responsible for the data sensing, interrogator system is responsible for analysis of data and the wireless gateway is responsible for the data process and

wireless transmission to the decision centres. Cork is utilized for the insole because of its superior properties like as heat isolation and sensor integration.

Design Input Requirement Specification. The suggested system comprises of an optical fibre sensor network combined with a wireless transceiver to provide effective and ubiquitous patient monitoring.

Design Output High-Level Design. The architecture's sensing mechanism is based on Fiber Bragg Grating (FBG) technology. This sensor device is embedded in the optical fibre core, and it takes use of the benefits inherent in OFSs such as electromagnetic interference and intrinsic electric safety. The sensing network is linked to an interrogation system, which is in charge of acquiring the sensed modulated signal. Both are linked through a secure body network to a mobile gateway responsible for collecting and analysing all the sensor's data and capable of connecting to the cloud.

Design Verification. To calibrate the FBG sensing network in the insole and to improve measurement accuracy using the suggested sensing architecture.

Design Validation Strategy. The study's goal is to show the sensor network's accuracy and reliability in monitoring foot PP distribution during walking. The calibration and measurement obtained with the monitoring system demonstrated the purpose of the study through designed architecture.

2.4.4 3D Printed Insole (Leal-Junior et al. 2019)

Product Feasibility/ Market Requirement. To improve the quality of life in healthcare sector, a low-cost sensor system with 3D-printed instrumented insoles for static and dynamic assessment of PP and Ground Reaction Force (GRF) was created.

Design Plan. A wearable gadget for clinical evaluation and remote health monitoring is a 3D-printed insole. For balance and gait analysis, the gadget is made up of POF sensors and 5 FBGs embedded in Cyclic Transparent Optical Polymer (CYTOP) fibre. The 3D-printed insole is composed of Thermoplastic PolyUrethane (TPU), a flexible material ideal for insole manufacture, and the sensors are made of silica optical fibre, which is lightweight, electrically isolated and electromagnetic field immune.

Design Input Requirement Specification. 3D-printed insole with a single POF and pressure sensors to cover the pressure spots on the foot. To acquire the answer from each sensor, the multiplexing approach is utilised.

Design Output High-Level Design. Fifteen intensity variation-based sensors are multiplexed in a single POF utilizing a time-domain multiplexing method based on side-coupling between the light sources and POF lateral portions in a 3D printed footbed. The GRF and PP distribution of individuals are monitored at home while

conducting their everyday activities in 3D-printed insoles, and the data are transferred to the clinician through gateway for offline processing and supplied to the Clinician via cloud for further analysis.

Design Verification. Insoles are classified to suit static, dynamic and gait conditions. Through force and area, the pressure sensor in the 3D printed insole delivers consistent pressure to each detecting zone. To verify the reliability of both static and dynamic measurement of 3D printed insole.

Design Validation Strategy. The study's goal is to evaluate the performance of a 3D printed insole in both static and dynamic conditions to that of a commercial force platform. Statistical program is implemented to compare the mean and significance between the test conditions. Study participants are selected based on the body mass such weight and height. It is feasible to monitor PP and GRF using a 3D printed insole, and there is a strong correlation between the insole and the force platform on GRF measurements and the assessment of bidirectional displacement of the centre of pressure.

2.4.5 Wearables Socks (Lin et al. 2016)

Product Feasibility/ Market Requirement. In gait study and analysis, a smart insole was created to address the problem of efficient gait tracking in real life.

Design Plan. A smart insole is a wearable sensor device that has a 3-axis accelerometer, a 3-axis gyroscope and a 3-axis magnetometer to collect gait parameters in motion. A graphical user interface is being developed to show sensor data directly through Bluetooth interface. Smart insole designed to collect inertial and pressure data from both feet, as well as PP and IMU data through wireless technology.

Design Input Requirement Specification and Method. Smart insoles are made up of sensory insoles and application software that runs on both a smartphone and a computer to store and visualise the data. Step count, step tempo, swing time and centre of pressure were measured by the smart insole.

Design Output High-Level Design. An array of sensors, an ultra-low power MCU and BLE wireless transmission module, a channel multiplexer (MUX), a Li battery and a micro-Universal Serial Bus (USB) connection comprise the smart insole. The smart insole is shown with three important subsystems: 1. a low-cost sensor array with 48 pressure sensors, a 3-axis accelerometer, a 3-axis gyroscope and a 3-axis magnetometer; 2. a data acquisition and transmission subsystem with an MCU and a Bluetooth module; and 3. a visualization and Graphic User Interface (GUI) subsystem. The Hardware Design consists of 1. The textile pressure sensor array is used to obtain the high-solution pressure map from feet; 2. The accelerometer and gyroscope are inertial sensors which measure the movement information of the subject; 3. Microcontroller unit and Bluetooth are implemented in a single device; 4. Bluetooth low

energy; 5. Battery and Micro-USB Connector; 6. Package and Ergonomic Design. Software is implemented with multi-threading technology.

Design Verification. To verify the reliability and usability in real life for gait monitoring through competitive analysis of exiting methods.

Design Validation Strategy. The study's goal is to analyse and verify the Smart insole by collecting gait data for quantitative and longitudinal analysis. Pressure analysis, steps, balance and inertial measurement are examples of quantitative studies. Study conducted in four real-life scenes includes hallway walking, slope walking, ascending stairs and descending stairs. The device offers complete gait parameters acquisition, and it is comfortable to wear, convenient to use and cost-effective. Statistical program is implemented to compare the mean and significance between the test conditions. Study participants are selected based on the body mass such weight and height.

2.4.6 PP Measurement in Relation to Ailments

In this section, we categorize the selected research works according to different types of deformities and ailments associated with growth and aging.

Arthritis. Arthritis is an irreversible ailment affecting the body joints and muscles with numbness and pain particularly at older age. The knee and hip joints of the lower and the wrist joint of the upper extremity are commonly affected. People with arthritis have decreased postural stability and the healthcare requirement of such patients can be effectively estimated by monitoring their foot biomechanical features. Marten et al. have used a GRF measurement approach to partition the shear forces in 3-foot segments of patients with aberrant gait. The study showed significantly reduced posterior force on the rearfoot segment for the patients when compared to non-aberrant gait group. A certified fact from this research is that osteoarthritic deformities in the foot may cause anterior shift of the ankle GRF causing decreased posterior forces (Eerdekens et al. 2020). Gout is a more complex form of arthritis causing sudden joint inflammation that can also affect the foot function. The effects of gout on foot PP have been studied in Rome et al. (2011) by including 25 patients with a history of gout. Chronic gout signalled significantly lowered peak PP in the hallux. Both studies indicated slower gait in patients. Owing to the importance of foot measurement in relation to arthritis, researchers have specifically evaluated sensing modules for people affected by arthritis. TekScan MatScan has been declared useful and reliable in assessing postural stability of older people (60–80 years) with Rheumatoid Arthritis (Brenton-Rule et al. 2012).

CAI. Recurring ankle sprains when not addressed correctly may result in CAI with altered gait mechanics in worst cases. There is less research that consider the computation of foot biomechanics related to CAI. Here, we cite three selected studies that have reported different consequences of CAI on foot pressure. A study comprising 17 CAI patients indicated the presence of significantly increased peak PP and pressure–time integral for the lateral anterior foot. In addition, the 100 ms period of pre-initial

contact of the CAI group showed reduced anterior tibialis RMS areas and significantly increased medial gastrocnemius, gluteus medius and peroneus longus RMS areas compared to the matched healthy group (Koldenhoven et al. 2016). Another study has shown that CAI patients show increase in vertical GRF during early stance and between terminal stance and pre-swing stages of gait (Jun Son et al. 2019). The effect of a balance training regime was identified by observing the changes in COP of CAI patients. The COP position of the intervention group showed a shift from more anterior to being less anterior, whereas the control group showed no significant changes in their COP position (Mettler et al. 2015).

Diabetes. Diabetes is the highest reported and studied ailment in relation to PP measurement. PP monitoring has proved to be an effective tool in prevention and monitoring of progression of the ailment-related adversity.

Therapeutic footwear. Customized designs are recommended to diabetic patients to reduce in-shoe pressures. One such intervention is rocker shoe which was evaluated in Chapman et al. (2013). 12 different designs of rocker shoes were tested in 24 diabetic participants and PP measurements were recorded. The main goal being offloading of the diabetic foot, a 20° rocker angle and a 95° apex angle at 60% shoe length position were suggested optimum. In-shoe PP analysis was once again proved to be an effective tool to achieve guided footwear design in order to reduce foot pressure in neuropathic patients (Ulbrecht et al. 2014; Bus et al. 2011). As for the evaluation of custom-made therapeutic footwear, a study provided the optimum recommendation of 12 midgait steps per foot to obtain reliable in-shoe PP distribution data for assessment (Arts and Bus 2011).

Barefoot PP predictors for diabetic neuropathy. Rise in plantar foot pressures increase the risk of ulceration in diabetic patients. Therefore, establishing a relationship between factors affecting the PP distribution and the risk level of diabetic ulceration provides a hope for better diagnosis and treatment approach. Barn et al. determined the significant contribution of local deformity in increasing barefoot dynamic PP (Barn et al. 2015). An extensive clinical trial involving 1522 subjects revealed that most ulcer occurrences were reported in the hallux, combined metatarsals and the heels. The ulcer risk elevation in relation with PP was however observed only under the metatarsal head regions (Ledoux et al. 2013).

Characterizing diabetic foot biomechanics. The differential effects of foot sole sensory on PP distribution during standing and walking conditions were reported in Li and Zhang (2013). The foot sole tactile feedback control was reported more significant in case of standing posture when compared to gait, which, in turn associates to feedforward control.

2.4.7 Foot Postures and Deformity

Per cavus and pes planus. Foot deformities develop with growth discrepancies in several individuals. The shape of the human foot may vary while standing and walking and the related data is used for clinical assessment. This is commonly called foot posture, that are of normal (pes rectus), flat (pes planus) and high arch (pes cavus) types. Asymptomatic healthy adults show a relationship between their foot structure and functionality (Mootanah et al. 2013). In terms of PP, forefoot pressure substantially differs between planus and cavus foot postures. The peak pressures at the fourth and fifth MetaTarsoPhalangeal Joints (MTPJ) in the planus foot were reported highest (Buldt et al. 2018b). In addition, per cavus foot shows a reduced total surface contact under the first toe compared to pes rectus (Fernández-Seguín et al. 2014). When compared to planus, the cavus feet exhibits a slightly higher peak PP in the lateral heel. The foot posture also affects gait kinematics. The cavus feet shows reduced motion during initial gait contact and midstance. On the other hand, the planus feet show reduced midfoot Range of Motion (ROM) during pre-swing phase (Buldt et al. 2015). Another work that studied several foot biomechanical parameters for the 3-foot postures reported significant differences of foot structure (arch height index and malleolar valgus index). Planus feet displayed significantly different COP excursion indices compared to the other two postures. COP is an important parameter associated with the instantaneous ground reaction force acting on the plantar surface of the foot. COP represents the centroid of the active pressure sensors for each sample, thus, representing the spatial distribution of PP over time. COP progression is the series of coordinates in the COP as it passes from the posterior to the anterior foot. COP progression has shown promising potential in assessing foot function dynamics. Repeatability of COP characteristics in similar foot postures and different COP characteristics in different foot posture groups have been reported by recent studies. Planus and rectus foot show differences in the medial shift of the medial–lateral force index during terminal stance of gait. Therefore, differences in COP have been indicated as an effect of foot posture, especially on the propulsive phases of gait (Buldt et al. 2018a).

Hallux valgus. Hallux valgus represents the deformity in which the joint connecting the big toe and the foot (MTPJ) is affected by pain, inflammation and functional disability accompanied by lateral deviation. The effect of hallux valgus on various parameters associated to PP were studied separately. A significant negative correlation was reported between the hallux valgus angle and the peak pressure, contact time, maximal force, force–time integral and contact area of the hallux region. In addition, a significant positive correlation was reported between the hallux valgus angle and the peak pressure, maximal force, force–time integral and contact area of the fifth metatarsal head and also between the subluxation of the sesamoids and the contact time and peak pressure of the third to fifth toes. In conclusion, the plantar load tends to shift from the medial towards the lateral side of the foot, as the hallux valgus angle increases (Koller et al. 2014). Another work has indicated the presence

of a lower COP excursion index and a higher modified arch index in hallux valgus patients, thus affecting the foot arch structure and pronation (Galica et al. 2013).

Plantar Fasciitis (PF). Plantar Fasciitis (PF), also known as jogger's heel, police foot and tennis foot, is a common musculoskeletal foot ailment as a result of tendon or fascia inflammation. PF is common among runners and has significant effects on the PP distribution as reported in recent studies. In this section, we report two papers that studied the effects of PF on gait and running and two papers that assess the effectiveness of ankle–foot orthoses on PF treatment. A study recruited 45 recreational runners with PF (both symptomatic and with PF history, now asymptomatic) and 60 without PF and verified that PF does not affect the PP distribution patterns while running which indicates that the plantar load remains unaffected by PF (Ribeiro et al. 2011). However, another study indicates that PF results significantly different gait kinematic and kinetics in individuals with PF as compared to without PF. PF affected individuals show a higher peak First Metatarsal Phalangeal Joint (FMPJ) dorsiflexion and total rearfoot eversion. In addition, compensatory movements were indicated by decreased propulsive GRF and increased medial forefoot plantar flexion during initial gait contact (Chang et al. 2014). Rocker shoes and FOs have been commonly used to reduce PF-related pain and discomfort. Research has shown significant improvement in PF foot when the two are combined as compared to individual usage. The visual Analogue Scale (VAS) pain score for combination of rocker shoes and FOs, only rocker shoes and only FOs was reported as 9.7, 30.9 and 29.5, respectively. The rocker sole effectively redistributes the PP to mid-foot which is in turn reduced by the FO. Therefore, a significant reduction in the medial heel PP is achieved (Fong et al. 1077). Another study has proved the efficiency of customized 3D printed over prefabricated AFOs for improving PF comfort (Rui et al. 2019).

3 Discussion

Limitations and prospective improvements for proposed PP sensing modules and orthoses are reported in this section.

3.1 Mechanical Properties

Force plates used in research facilities are often embedded into the surface and can be detected only by small gaps in the flooring where the plates are positioned, but they can alternatively be entirely buried beneath a larger piece of flooring material. Pressure mats, on the other hand, are generally put on top of the flooring, creating a distinct visible target and a little rise in surface height (Sandhu et al. 2020; Sinclair et al. 2014). Advantages of the PP sensing systems are easy to use, stationary and flat. However, these platforms also have some limitations such as lack of portability, high

weight, these platforms are affected by the targeting effect which significantly alters the human gait (Crea et al. 2014). Optical measurement sensors have advantages of anti-radiation, anti-electromagnetic interference, simple technology. This helps in boosting the non-invasive pressure measurement. However, optical measurement-based pressure sensors are still in the development stage. Wearable systems also have disadvantages such as handmade and highly complicated fabrication technology.

3.2 Sensing

Despite the fact that all of insole methods have demonstrated their usefulness in gait analysis applications, certain drawbacks have been identified, such as, unwanted sensor fluctuations and deformation in contact surface. Owing to heat within the shoe, there may be drift in the output if load is applied over a longer period of time. Moreover, such systems demand subject-specific calibration. Optical measurement sensors have advantages of high sensitivity, high precision and wide measurement range. PDMS capacitive pressure sensors provide the advantage of being highly sensitive to small spikes in pressure on the surface due to which these have been utilized as artificial skin in robotic applications.

3.3 End-User Comfort

In the existing market, most of the pressure sensors lack flexibility to fit in to curved interfaces. In-soles are flexible, portable and are applicable and suitable for indoor and outdoor monitoring. However, they are only useful for situations that do not need highly accurate measurements. Optical measurement sensors, on the other hand, are portable and small-sized and can still give accurate measurements. PDMS material was selected as the dielectric layer of the PDMS capacitive pressure sensor because of its advantages of high dielectric constant and tuneable elasticity. Because of the miniaturization and flexibility of the sensor, it has the potential to develop shoe-integrated sensor system for long-distance data collection for gait analysis. In case of orthoses, 3D printed designs have the advantage of increased comfort due to customized design tailored to user's needs. 3D printed insoles also provide high portability, customizable design and can be fabricated with different sizes, and sensor positions to improve assessment. PP measurement using wearable socks has shown advantages of being lightweight, thin and comfortable to wear.

3.4 Power Consumption and Cost

Modernized in-soles have optimized circuit designs and communication channels to achieve minimal power consumption and reduced cost compared to platform-based systems. 3D printed insoles mentioned in Leal-Junior et al. (2019) also provide low-cost feasibility with low power consumption and wireless connection. Compared to platform-based systems, insoles show promising cost-effectiveness due to the minimized sensor array size and material requirements. However, this comes with a trade-off between the cost and data acquisition efficiency.

3.5 Algorithm

In-sole sensing may be user-friendly but needs user-specific calibration that may increase the set-up time. Similarly, a disadvantage of the PSCR technique is that all sensors must be calibrated before gait measurements begin, because degradation of the PSCR occurs over time. To avoid this laborious procedure, the pressure sensor should be replaced by a less susceptible sensor to enable longer use. The measurement range was limited to the area near the mobile personal computer, because the maximum transmission distance was approximately 10 m.

3.6 Future Possible Research Directions

Foot lesions in individuals with diabetes is a major concern in the field of medicine. This is because of disruption in glucose metabolism and alterations in the peripheral blood flow. This often results in the development of trophic ulcers and, in certain circumstances, the necessity of limb amputation. In order to address this particular problem in a timely manner, plantar pressure measurement has high potential of empowering researchers and entrepreneurs working in this field. However, the issues that need to be addressed in this area include lack of easy to use and comfort footwear, absence of standardization of PP measurement modules, especially for diabetic neuropathic patients.

The potential research direction that could address the above-mentioned issues would be as follows:

- Development of technical specifications for the design of shoe types.
- Sufficient investigation of the anthropometric data of the foot to facilitate customization.
- Defining the parameters for the shoe design.
- Development of testing prototypes for patients with diabetic neuropathy.

The specific design should provide uniformity of the load across the surface of the foot and allow offloading for patients with complexities. It should be ensured that the research takes care of the design approaches mentioned in this review while developing the sensors/ shoe for addressing their research problem. Moreover, the design must be meet the requirements of the application. The requirements may vary according to resolution, comfort, ease of donning/doffing, ease in data acquisition, portability, longevity, hours of usage and so on. Therefore, the researchers must define their application requirements prior to approaching the selection of PP measurement sensor. Recent advances in technology also facilitates us with AI-powered smart algorithms that can be integrated with PP measurement to help us prevent injuries and detect gait irregularities.

3.7 Design Standard Requirement

ISO 9999:2016 defines a categorization and nomenclature for assistive items, particularly those manufactured or widely available for people with disabilities. This WHO standard and its specification requirement should be taken into consideration for developing Assistive devices especially therapeutic footwear for foot complexities. These design requirements provide description and its intended use for the development process; development of assistive devices for heel, toe, and foot protection and also for sports shoe and in-shoe layers.

4 Conclusion

In this book chapter, we review the latest technologies reported for the measurement of PP and the orthoses used to support such measurement. PP measurement has been proved useful in predicting and analysing the progression of various ailments and deformities such as diabetes, arthritis, CAI, PF, hallux valgus and pes planus. Recent advancement in various PP measurement techniques has made it possible to implement data acquisition through portable, flexible and wearable modules applicable for individuals with any pathological condition. From this literature review, it can be observed that the extent of developing new innovations addressing plantar pressure measurement has significantly increased. Most technologies contribute towards new research and clinical possibilities. These systems have addressed issues such as portability, reliability and cost-effectiveness. In-shoe measurement devices are specifically beneficial for therapy and diagnostics. However, due to the lack of standard practices in clinical settings, applications are developed to a limited extent. The design approaches discussed in this review might be helpful for upcoming researchers in selecting application-specific product design and architecture with possibility of acceptance in the commercial zone.

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Chapter 8
Prosthetic Socket Designs in Rehabilitation and Improving Healthcare to the Transtibial Amputee: Challenges and Opportunities

Akshay Kumar and Vinita

1 Introduction

The prosthetic prescription depends on factors like cognitive ability, muscle strength, neurological status, cardiovascular condition that affect the gait. The increased energy expenditure is required for them to walk with prosthesis, and the energy expenditure increases with the level of amputation higher (Bastas 2020). An accurate and comfortable prosthetic socket fit for prosthetic users is the burning challenge since the beginning of the prosthetic socket and device development. It acts as a mechanical coupling between the human residual stump and the prosthetic limb. Prosthetic socket is worn over the residual stump and transfers loads to the surface in static and dynamic conditions. The snug fit of a socket over the stump turns out into a stable connection and generates limited/reduced friction and shear stress. The prosthetic clinician faces a lot of challenges to create feasible interface between residual limb and the socket. Studies suggest that prosthetic socket remains the priority for prosthetic users because the physiological condition of residual stumps are not deemed to tolerate forces and moments applied by the socket. The overall quality of life might deteriorate due to an ill-fitting prosthetic socket. This will promote unnecessary pressure, shear forces, and irritation over the surface of residual limb and patients may feel pain and suffer tissue damage/abrasion. Further, it will impact the individual's activities of daily living (ADL) and community involvement (Safari and Meier 2015a).

Despite the considerable advancement in prosthetic socket designs, function and biomechanical implications, the rate of rejection of prosthesis is worrying. The skin issues occur in 63–82% of the lower leg amputees and the rate of rejection vary

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25–57%. However, socket shape and materials used in its fabrication, suspension technique that holds the stump within the socket are important factors of satisfaction (Paterno et al. 2018).

The functional comfort of prostheses depends on many interrelated factors including socket design, materials, and suspension methods, etc. The socket transfer loads under both static and dynamic conditions during various phases of gait with minimal piston between limb and prosthesis. To achieve optimal comfort and function, and to prevent it from loose-fitting that may lead to injury, skin problem or rejection of prosthesis. Pressure distribution within the socket too is a vital criterion (Stevens et al. 2019).

Besides, other prosthetic components like socket adaptors, pylon, knee joint, foot, etc., may increase discomfort and energy cost if assembled inappropriately. Faulty assembling of components can affect muscle function and produce pathological gait. Prosthetic feet also play an important role in stability, permitting sufficient knee flexion moment during early stance and later on, permitting forward progression of the contralateral limb in the late stance. Dynamic and carbon fibre foot causes less energy expenditure and improved gait and minimizes the pressure and shear forces on the residual limb. Therefore, the coordination of prosthetic components is essential also to limit the interaction between the residual limb and prosthetic socket (Paterno et al. 2018).

Studies are evident that the volume fluctuation of residual limb occurs due to pressure and shear stress between the stump and prosthetic socket. Blood occlusion, volume loss, and skin breakdown are the effects of shear stress and pressure applied to the soft tissue of the stump. It is very common among amputees to have skin problems like cysts, blisters, dermatitis, edema, and skin itching attributed to ill-socket-fit and discomfort. Therefore, to gain control over mobility, stability, and load transmission, the socket should be designed properly (Golbranson et al. 1988; Bennett et al. 1979). Trauma is a leading cause of amputation, As per a report in 2017; about 57.7 million people need prosthetic intervention. Falls, road accidents, transportation injuries, and mechanical forces are the main causes of amputation. East Asia and South Asia have the highest prevalence of traumatic amputation and are followed by Western Europe, North Africa, and the Middle East, high-income North America and Eastern Europe. Nearly, 75,850 prosthetists are required worldwide to rehabilitate people with traumatic amputation (McDonald et al. 2021). Amputation prevalence estimates and patterns can inform prosthetic service provision, education, and planning. Amputee rehabilitation is a serious challenge, particularly in developing countries where the availability of prosthetic professionals is only one per million as compared to developed countries with 5–10 prosthetic clinicians per million population (Kumar and Vinita 2021). In an online survey study conducted by Turner and McGregor (2020) about the perceived effect of socket fit on lower limb rehabilitation among user amputees and clinicians, it is found that 48% of amputees and 67.7% of clinicians considered socket fit as an important factor in achieving daily tasks and improved quality of life (Turner and McGregor 2020).

The chapter explains the transtibial socket designs available for the transtibial user amputee and their impact on amputees rehabilitation and healthcare benefits. It

focuses on the associated factors that affect socket comfort and explains the challenges and opportunities in socket design to improve the user experience in the future.

2 Socket Biomechanics

The main concern of any prosthesis is to achieve a comfortable gait and function. Prosthetic satisfaction is subjective and hard to define. However, technological innovations improved the gait and quality of functioning (Pirouzi et al. 2014). The understanding of biomechanics and the evolution of materials brought changes in socket designs. The focus was prioritized at the end of World War II and since then many improvements took place (Sewell et al. 2000). The concept of socket biomechanics arises due to discomfort to a user despite wearing prostheses of modern technologies. The stump–socket interaction causes discomfort and tissue damage. The fixation of biomechanical principles to the prosthetic socket can minimize the stump–socket shear stress along with socket design and fabrication (Rajtukova et al. 2014). Transtibial amputees may develop deep tissue injury (DTI) and prosthetic socket and design are the most discussed components (Graser et al. 2020). The residual limb skin and underlying tissues are intolerable to shear stress, pressure, physical stress, and slippage experienced due to prosthetic sockets. To reduce the residual limb skin problems many improvements have been achieved/developed in the sockets and their accessories. Interferential pressure distribution between the prosthetic socket and residual limb is an important factor in socket fit and design. A large number/variety of transducers have been used nowadays to measure the stump–socket interface pressure. It requires appropriate measurement techniques, like placement within the socket, data collection, and controlling approach. Generally, used transducers are pneumatic sensors, fluid-filled sensors, printed circuit sheet sensors, beam strain gauge, and diaphragm deflection strain gauge, which are applied according to the modus operandi. The placement of the transducers is not much difficult and it can be fitted between the skin and the socket or positioned within or through the socket and/or liner. However, the thin sensors are ideal to be fitted between skin and socket. The slippage of the socket happens due to the loose fit of the prosthetic socket and the low friction between the residual limb and the socket. Friction between the residual stump and the socket produces shear action and may contribute to tissue damage and at the same time, the shear forces produced due to friction suspend the prosthesis in the swing phase of the gait cycle. It will be of importance to understand the parameters of tolerance and adaptation depends on. An appropriate coefficient of friction is needed to sustain the loads, prevent slippage and apply effective prosthetic control. The direction, distribution, and duration of the loads to the residual limb are also responsible for the damage to the skin. Besides, ischemia, sweating, pain, skin temperature, etc., are other negative results of the prolonged and improper external forces (Mak et al. 2001).

The feature of sensing tools to measure the pressure and shear stress is of substantial significance in the development of prosthetic socket design. In the past 50 years, prosthetic socket fit and comfort have been improved due to development of force transducers, which can measure the residual stump/interface pressure effect and distribution during and after socket design. Transducers make it possible to measure and collect the quantitative data, and do their statistical analysis. It was not possible before its development, and a high skill and experience were required to check the pressure under static conditions, based on the change in the skin color with the help of clear check socket and stick corset. The strain gauge, piezoresistive, capacitive, and optical sensors are used to measure the pressures (Al-Fakih et al. 2016).

Tissue breakdown may occur often in the deep tissues. The common DTI injuries are direct deformation that disrupts the coherence of skeletal muscle if high load is applied longer. Ischemia caused due to blood flow restriction through collapsed blood vessels restricts the oxygen and nutrient supply. The oxidative stress immediately after load release is ischemic reperfusion. Obstruction in the lymphatic vessel due to load may lead toxic cell environment in the lymph node (Graser et al. 2020). To design a comfortable socket and to achieve efficient gait patterns, the sound knowledge /understanding of the residual limb anatomy, tissue responses to the external loads and movement biomechanics is also important to achieve efficient gait patterns. The understanding of biomechanical advancements needs for their incorporation into the clinical practice. New designs of sockets and materials development are still the need of the hour to improve its functioning. Additionally, prosthetic interface stresses understanding can enhance socket design and its adjustments (Mak et al. 2001).

3 Socket Designs

The socket design and fit are essential in the successful rehabilitation of an amputee because the residual stump cannot bear the weight in the way the foot does (James et al. 2021).

The objective of the socket is to transfer body weight and loads under both dynamic and static states with minimal piston between the limb and the prosthetic socket. The comfort and function of transtibial prosthesis largely depend on the socket design and pressure distribution within the socket. The other factors that affect prosthetic success are socket and interface materials, suspension, and the prosthetic foot. Unsatisfactory fitting of the socket and prosthesis may cause skin breakdown, soft tissue damage, and prosthetic rejection (Stevens et al. 2019). When targeting the comfort, load transfer, and smooth static and dynamic gait function, the transtibial socket design mechanism has traversed the following socket development/design.

1. Patellar tendon bearing (PTB) Design
2. Total surface bearing (TSB) Design
3. Hydrostatic (HS) Design
4. Vacuum-assisted suction Socket (VASS) Design (Safari and Meier 2015a)

4 PTB Socket Design

The Patellar Tendon Bearing socket originated in the 1950s. The socket design concept was to identify the pressure-sensitive and pressure tolerant areas in the residual stump. It utilizes the pressure and pain threshold of the underlying tissues of the residual limb (James et al. 2021). Though the Total Surface Bearing (TSB) socket has the biomechanical advantage of even weight distribution over the greater surface area and even weight distribution, PTB sockets are still in vogue globally (Al Shuaili et al. 2019).

PTB sockets are also known as Specific Weight Bearing Sockets because of their characteristics to transfer the load through specific pressure-tolerant areas of the residual limb. The PTB socket design follows the theory of selective loading and total contact. Selective loading theory follows the pressure tolerant and sensitive area in the residual stump. The major tolerant areas are the patella tendon, tibial medial flare, and shaft of the fibula, remaining pretibial muscle, popliteal area, and gastrocnemius muscle belly. The areas that are considered sensitive are tibial tuberosity, the crest of the tibia, fibula, and its distal end, head of the fibula, peroneal nerve, hamstring tendons and patella.

PTB socket exists triangular in shape due to selective loading application. However, the theory of total contact follows to fully encapsulate the residual stump within the socket. Total contact refers to that all the parts of the residual stumps are not involved in bodyweight loading, but socket contact to the residual limb (AustPAR—Transtibial Sockets 2021). In the PTB design, the loads are shared over pressure-tolerant areas of the residual stump. The prominent weight-bearing areas are patella tendon (PT), anterior muscular compartment, the medial flare of the tibia, anteromedial and anterolateral tibia, the mid-shank of the fibula, and popliteal area in the posterior side, while commonly load sensitive areas are tibial tuberosity, fibula head, mid-shaft of the tibia, anterior distal cut ends of tibia and fibula, and anterior tibia crest where load relief is needed in socket modifications. The pressure-tolerant and pressure-sensitive areas have been identified qualitatively and have been used as principle for PTB socket modifications for long back. The PTB sockets are all-time popular design and have shown satisfactory outcomes in majority of the cases. The socket proximally extends up to the femoral adductor tubercle in the medial and lateral aspects/side, stabilizing the knee and distributing the load. The PT is enclosed partially and covers the distal one-third of the patella on the anterior side. In the posterior side to achieve comfortable knee flexion and reduce the pressure over the hamstring tendon, the socket flares out in the proximal area. Polyethylene foam of 5–6 mm thickness is used to line the socket that minimizes the interface forces between the residual limb and the socket. The socket and suspension are interrelated to achieve functional outcomes and comfort. Pistoning, rotation, and translational moments between socket and residual limb can be reduced through appropriate suspension. The widely used suspension methods are supracondylar cuff with or without waist belt, supracondylar-suprapatellar (SCSP), Supracondylar (SC), Cuff suspension, figure-8 supracondylar strap, articulated supracondylar wedge, and

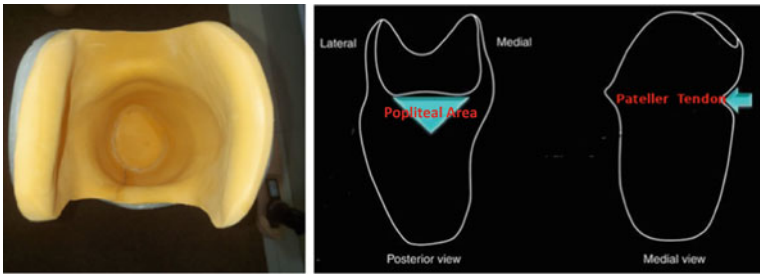

Fig. 1 **a** Patella Tendon Bearing (PTB) Socket **b** Major loading areas in PTB Socket (Lee et al. 2013)

rubber sleeve. However, PTB suspension methods/systems and socket designs turn out into intensive pressure on the tolerant regions that results in skin damage and injuries. This socket design may not be suitable for residual stump with sensitive skin and bony prominences (Al-Fakih et al. 2016).

In general, the inner soft liner is made to chase the pressure of socket to the residual limb soft tissues. It improves the amputee's comfort and safety by acting as cushioning between socket and residual limb and assist in molding the accurate shape of the socket. Liners help in smooth load transfer of load to the ground. Wool or cotton socks of different thicknesses were used earlier as an interface between socket and stump. However, presently softer and resistant to compression materials like P-lite, silicone, urethane, etc., are used. It helps in maintaining stump volume fluctuations, perspiration, and protects from shear forces and provides additional comfort. Additionally, it provides suspension of prosthesis on the residual limb (Klute et al. 2010) (Fig. 1).

5 TSB Socket Design

TSB socket design increases the contact area between residual limb and prosthetic socket to produce constant pressure over the residual limb to minimize the pressure per unit area. Therefore, peak pressures are less than in case of PTB sockets. TSB sockets were first described by Staats et al. in 1987 with a concept to develop total contact in-between socket and residual stump (Steer et al. 2020). In this design, forces are uniformly applied over the residual stump to avoid peak pressure in any specific region as occurs in PTB. It is designed differently to compress the soft tissues up to tolerance level according to their texture and the bony areas are secured firmly in the residual stump. The Pe-lite, Surlyn, or silicone materials can be used for the soft suction liner of the TSB socket. As the silicone liner tends to snugly fit the residual stump, it improves the pressure distribution on the residual stump and suspension of the overall prosthesis. The application of silicone liners reduces skin damage due to

uniform pressure distribution. The considerable suspension systems used is pin-lock at the distal end of silicone liner (uses Dermo liner, TEC liner, Alpha liner (3, 6, and 9 mm), elastomeric gel liner, and ICEX system), seal-in circumferential liners (uses seal-In X5 liner, polyurethane liner, and neoprene sleeve) that create vacuum at the socket and socket with magnetic lock system. The TSB socket indicates notable edge and acceptance over PTB/previous sockets in suspension due to silicone liner adherence on the residual stump, even pressure distribution, cosmetic appearance, decreased pistoning, improved skin condition, increased activity levels and function. Silicone liners increase the pressure seal during sitting, bending, and athletic activities. A prefabricated silicone liner, the Icelandic Roll-On Silicone Socket (ICEROSS) with silicone cone available in six sizes are rolled over the residual stump to provide total contact with the stump. The disadvantages observed in the TSB socket designs after implication are increased perspiration, skin itching, volume fluctuations during daily use, bulkiness around the knee and proximal region of the socket, and difficulty in donning and doffing and milking phenomenon (Hachisuka et al. 1998). The use of vacuum assist TSB socket maintains the volume of the residual limb and secures a comfortable walk throughout the day. However, without vacuum assist, it may reduce the stump volume up to 6.5% with regular use in the day and may cause pistoning and irritation to the residual stump (Board et al. 2001). The precision casting procedure followed to get the TSB socket provided a specified method of modification must be carried out to get the result. There is no need for build-up and relief over the sensitive and tolerant areas if measurements are taken carefully (Staats and Lundt 1987). If the effectiveness and comfort between TSB and PTB are compared, the conclusive results in a study done favors the TSB socket. In the study, it is observed that cadence, intact side-step length and walking velocity increased using the TSB socket. TSB socket helps in better sound limb forward than before as better load acceptance creates better proprioception by the TSB socket (Yiğiter et al. 2002).

TSB socket is appropriate for a transtibial amputee, provided residual limb is mature and the amputee can don and doff the prosthesis independently and easily. Nevertheless, it can be avoided to the amputee having very long stump, bony prominences at the distal end of residual limb, and difficulty in donning and doffing of the socket (Hachisuka et al. 1998) (Fig. 2).

6 Hydrostatic Socket (HS) Design

With the launch of Dundee Socket, the use of hydrostatic theory in socket production was demonstrated by Murdoch in 1965. He applied the fluid as a medium to apply equal pressure around the residual limb during casting to reduce manual skill in socket fabrication. Conceptually, the hydrostatic socket design is an improved and advanced version of the TSB socket design that consolidates the residual stump into one mass. Hydrostatic refers to the properties of fluids under pressure or the fluids under equilibrium. It is also known as quasi-hydrostatic design as the hydrostatic

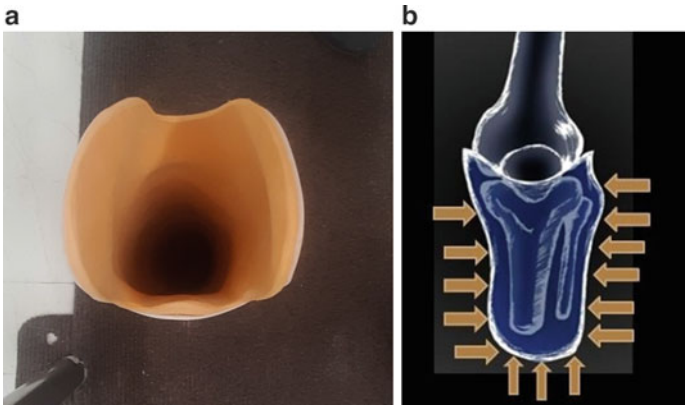

Fig. 2 **a** Total Surface Bearing (TSB) Socket. **b** TSB Loading Mechanism (Transtibial—Socket Finder 2021)

implies a closed system. Hydrostatic socket design integrates sound fluid mechanism in combination with advanced material technology. A liner with gel flow characteristics is generally used to maintain the uniform pressure on the residual stump regardless of minor volume changes. To achieve uniform fit, the socket design aims to create a compression chamber following specific principle of fluid mechanics. The socket includes a vacuum pump or valve that creates a condition of hypobaric cushion and suspension between residual limb and the liner. It also uses a silicone suspension sleeve. The mechanical principle is to achieve hydrostatic fit through Pascal's law of fluids that defines that confined fluid in the residual limb transmits externally applied forces uniformly in all the directions and resultant forces act perpendicular to the container's surface. A uniform and safe redistribution of forces can be achieved following Pascal's law of fluids and Rogers and Wilson's curve. To contain the residual limb fluid, proximal seal is created by the silicone suction, anatomic knee unit and pressure chamber. On the posterior side, the trim lines are defined by insertion of flexors tendons. The socket design improves the range of motion because of lower proximal trim lines with respect to PTB and TSB socket designs. The proximal seal of the condyles is the pre-condition for a hydrostatic fit. Therefore, to achieve the hydrostatic fit, essential components are silicone suction suspension sleeve and pull shock or pin mechanism to set the seal on proximal condyles for fluid containment and appropriate tissue elongation. The cast taken under vacuum or Iceross's ICEX system is used to achieve a true hydrostatic design that provides optimal, consistent, and reproducible fit (T. KJ. 1999; Laing et al. 2011) (Fig. 3).

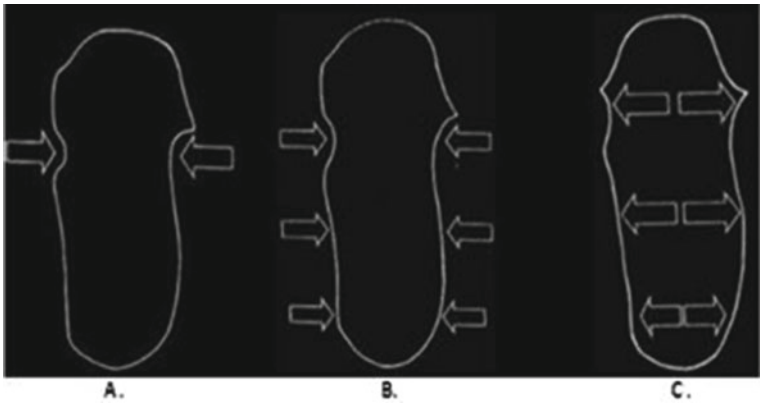

Fig. 3 Comparision of pressure mechanism of PTB (A), TSB (B), and HSD (C) (Bearing and TT Socket 2021)

7 Vacuum-Assisted Suction Socket (VASS) Design

The residual limb volume reduction caused by acting compressive forces during the daily weight-bearing activities on the limb results in an ill-fitting prosthesis or vice versa. The axial movement of the limb relative to the socket, skin breakdown or damage, injuries, discomfort, and activity limitation are the consequences of failure in controlling residual limb volume fluctuation, either due to lack of appropriate socket design or layering of socks on residual limb. The new design of the prosthetic socket is based on the evacuation of space through air expulsion between the prosthetic socket and the liner through a unidirectional valve, generating a negative pressure between the socket and the liner that covers the residual limb (Samitier et al. 2016). The VASS is a residual limb volume management and moisture evacuation system. The attachment of an external pump at a constant high vacuum can produce fluids into the residual limb during non-weight-bearing and gained residual limb volume after walking may result in a more consistent and accurate fit and eliminating the requirement of supplementary socks. There are several studies to support the functionality of vacuum-assisted sockets for maintaining the residual limb volume constant and ease contact between prosthetic sockets and residual limbs. Vacuum-assisted socket systems have shown greater fit and comfort than the previous non-vacuum socket designs (Klute et al. 2011).

The mechanism of VASS system is to minimize the pressure and shear stress on the residual limb, maintain residual limb volume throughout the activities, and increase proprioception and suspension without limiting vascular flow. To develop a VASS system, a cushion liner is required to place over residual limb, suspension sleeve is required to create a seal between the residual limb and the prosthesis and, most important, the vacuum pump that is placed distal to the prosthetic socket, which evacuates the air from the socket unidirectionally. Two types of vacuum pumps are used: Mechanical and Electric Vacuum Pumps. The mechanical pump can be

integrated into the prosthetic foot or can be separated. Usually, it expels air from the socket during each step by compressing the vacuum pump. While the electric pump is a separate component that maintains the desired socket pressure and the pump activates when the pressure inside the socket falls, it starts evacuating air out of the socket. The electric pump is more advantageous in turning when the patient gets up and walks, immediately. However, mechanical pump requires some time and steps to expel air. The electric pump needs to be charged every night to function properly but the mechanical one does not require such a charge (Bock O, Research C). Reduced pistoning, increased proprioception, socket comfort, improved prosthesis control, smoother gait, and healthy soft-tissue of the residual limb are the major clinical advantages of vacuum-assisted socket system (Fig. 4).

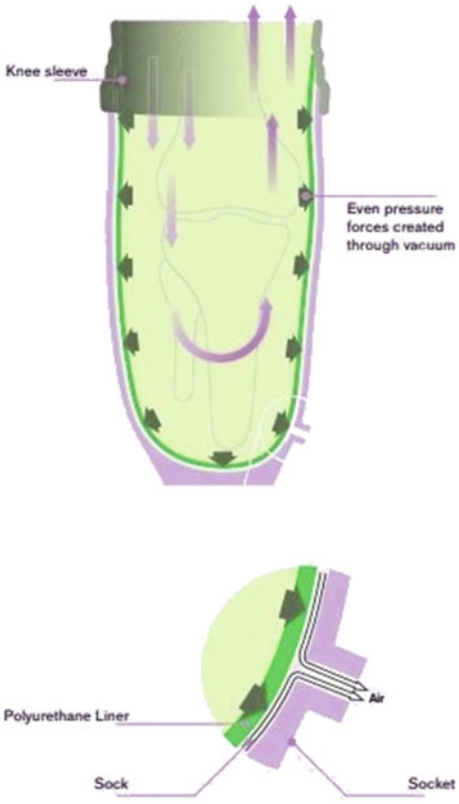

Fig. 4 Mechanism of VASS design (Information for Practitioners Harmony System)

8 Other Socket Designs

The Socket-less Socket™ ICON BK™ is now available for Transtibial and Symes users. This is a dynamic socket design. It works on the principle that our body shape is dynamic and changes its shape and size during sitting, standing and walking. The manufacturers of this socket believe that it conforms to every move. Its open frame and conformable material allow the residual limb skin to breathe and flex. It claims real-time user adjustability ensuring socket fit the way users want. The socket can be customized according to the need of the users including suspension, contouring, and fit. The Infinite Socket™ TT-S is the other design that claims to be the thinnest and lightest dual-wall adjustable socket in the prosthetic industry. It has posterior adjustment facility for compressive volume management. It offers selected areas of flexibility and rigidity for better comfort (Sockets and Access Prosthetics 2021).

The Range of motion, Comfort, & Rotational control (RCR) transtibial socket is designed by a Prosthetist-cum-Prosthesis user, Dale Perkins, who was not satisfied with the existing socket designs. In this socket design, the patellar bar pressure is removed. The socket follows the total surface bearing principle and it increases Range of Motion (ROM), de-rotates the residual limb within the socket and improves comfort to the user. This socket design is recommended with suction lock for a better outcome. The liner durability increases due to no pressure over the patellar bar (Technology and is a top priority at Louisville Prosthetics 2021).

Another manually adjustable transtibial socket design is RevoFit Socket, commercially available with Boa system that can be adjusted through the encircled band through a lacing system. The sockets are divided into struts. Besides, many sockets are tested and used using inflatable sensors, socks, pads, or air bladders to control the residual limb volume fluctuations (Paterno et al. 2018) (Table 1).

9 Factors Affecting Socket Designs

Some other factors that ease the socket fitting and reduce the forces acting on the residual limb interface are advanced prosthetic feet, ankle adaptors, vertical shock-absorbing pylons (VSAPs), and transverse rotation adaptor or turnbuckle/rotator. Generally, rotators are placed at the socket base or between the foot and the socket adaptor; it allows micro-rotation of the prosthetic components in the transverse plane with respect to each other. The variable stiffness rotators control the prosthetic system stiffness and reduce the shear stress on the residual stump interface. Vertical shock-absorbing pylons (VSAPs) reduce the impact of ground reaction forces (GRF) to the socket and residual limb. It absorbs/arrests the cyclic load applied on the residual limb tissues. These devices can further reduce energy expenditure, minimize the metabolic cost, and enhance the activity level of the patients (Paterno et al. 2018).

Alignment is another important factor that impacts socket comfort (Talaty and Esquenazi 2013). The static and dynamic alignment determines the gait efficiency

Table 1 Comparision of transtibial socket designs (Laing et al. 2011; Samitier et al. 2016; Table 8, Summary of Findings Included Systematic Reviews—Elevated Vacuum Suspension Systems for Adults with Amputation: A Review of Clinical Effectiveness 2021)

Socket Design	Features	Functionality	Challenges	improvement/Advancement
PTB	• Patella tendon and popliteal area bear substantial amount of load	• Accomodate various stump shape Better cosmesis compared to plug fit and thigh lacer	• Excessive shrinkage of stump and edema at end of stump Skill is required to fabricate	• Various materials and suspension methods were applied in socket fabrication Better suspension with condyler indentation
TSB	• All portion of the stump carry the amputee weight • No relief is included over pressure-intolerant areas	• "Round peg" in a round hole • No areas of relief to allow potential fluid retention • Pressure is distributed over larger area, therefore potentially lower peak pressures • Greater range of knee flexion • Less traumatisation of the skin • Lighter than a PTB • Assumptions towards better proprioception & security due to a more secure fit and less pistoning	• Loss in stump volume • High risk of skin irritation • Difficult donning/doffing • Increased perspiration, itching and odor	• Even pressure distribution on the stump compared to PTB design • Increased intact step length • Increased cadence • Reduced step width • More normal weight acceptance • Reduced socket volume, which should lead to reduced pistoning and better pressure distribution • Faster functional mobility (stairs and inclines)
HSD	• Apply uniform pressure over the residual limb • Pascal's principle of fluid dynamics • Socket is used with silicon or urethane liners	• Increased range of motion (ROM) • Reduced popliteal wall	• Can cause thrombing or cramping • Pulling sensation over the distal stump	• Easy Implimantation • Better suspension compared to TSB

(continued)

Table 1 (continued)

Socket Design	Features	Functionality	Challenges	improvement/Advancement
VASS	• Utilizes unidirectional valve to actively extract air from the socket • It creates negative pressure between socket and liner	• Improved balance, gait and transfer compared to other socket design • Increased proprioception • Accelerate healing of wound in the stump	• Time taking donning and doffing • Limit knee range of motion (ROM) • Wrong socket don can cause blister	• Gain in residual limb volume • Less pistoning compared to the TSB socket • Less residual volume fluctuation • Axial movement of the liner and tibia in relation to the socket was smaller in the VAS socket compared to TSB

and comfort. The translational and rotational optimization of components in different planes minimizes the forces acting on the residual limb interface. Increased energy consumption during activities results due to the wrong alignment and it changes kinematic parameters (Andres and Stimmel 1990; Schmalz et al. 2002).

The mechanical advantage of prosthetic feet adds on the comfort and further minimizes the forces acting on the residual limb during the entire phase of gait. The prime function of a prosthetic foot is to mimic the anatomical foot and provide a base of support in the initial stance (Stevens et al. 2018). Adequate knee flexion and forward progression of the contralateral limb may reduce energy consumption during walking. Presently, more advanced versions of the foot like dynamic foot, energy-storing carbon fiber foot, hydraulic foot, and microprocessor-controlled foot add ease in daily activities and greatly impact residual limb interface pressure (Cherelle et al. 2014).

The suspension method impacts hugely on the socket comfort. The suspension system reduces the relative vertical movement/pistoning between residual limb and the socket and prevents skin damage and improves the gait (Gholizadeh et al. 2014). The suspension which is being used since twentieth century is elastic suspension or harness. Though, not much effective it is frequently used (Ali et al. 2012). Other suspension systems are sub-atmospheric suspension that creates negative pressure inside the socket to give better proprioception and comfort, roll-on silicone, and elastomeric liners with pin lock or without pin lock. Magnetic lock with silicone liners is a recent development that adds quality to older patients. The adhesion properties of roll-on silicone liners act as an artificial muscle and protect the residual limb skin from abrasion and distribute the load (Kapp 1999).

The performance of the socket varies greatly on the materials used in fabrication to obtain optimal comfort and function (Ma et al. 2015). The outer socket is generally made up of thermostable or thermoplastic polymers and the most commonly used type are high and low-density polyethylene (PE) and polypropylene (PP). PP is preferred in socket fabrication due to its lightweight, high tensile strength, stiffness, and hardness

along with characteristics of deformation under heat to get the desired adjustment in the socket post-fabrication (Quintero-Quiroz and Pérez 2019). To achieve stability and strength of the socket, composite materials are used like unsaturated polyester resins, epoxy, vinyl ester, and glass fabrics (Arun and Kanagaraj 2016). Glass fiber significantly increases mechanical properties such as strength, stiffness, hardness, and dimensional stability of polymeric compounds. However, carbon fiber enhances the mechanical properties of thermoplastic composites, adds stiffness and high resistance to the material, and reduces the weight of the reinforced material (Scholz et al. 2011). The inner socket or interfaces have been developed from shock-absorbing foams to provide cushioning in the residual limbs. Urethane is widely used in the prosthetic industry for cushioning with varying densities. The latex, polyurethane, and polyethylene cushioning foams such as plastazote and pelite have characteristics to recover to their original position and support the compression loads (Ambrosio et al. 1996). The liners are made from silicone gels and silicone thermoplastic elastomers (TPE) with additives. It allows liquid extension under load due to crosslinked polysiloxane networks, with high polydimethylsiloxane (PDMS)-free fluid content. The viscoelastic property of the silicone allows the flow of high pressures to the low-pressure surface under load and improves the suspension. More than 15 types of silicone are available commercially, but silicone gels are the softest and appropriate for cushioning at the bony end. Nevertheless, resistance to compression, shear, traction and stiffness lower than silicone elastomer (Ambrosio et al. 1996; Sanders et al. 2004).

10 Challenges

As discussed above, the factors that influence the transtibial socket comfort and performance are residual limb volume fluctuation, residual limb interface pressure, and shear stress and temperature rise inside the socket. These are the main cause of prosthesis rejection in more than 50% of cases. The residual limb volume fluctuation causes the relative movement or pistoning between socket and residual limb leading to skin breakdown. In the early stage of prosthetic fitment, it is critical and dissatisfies the prosthetic user. Each residual stump undergoes volume changes ranging from severe to mild as per stump condition. Three to five percent volume changes are enough to cause discomfort (Board et al. 2001). The appropriate material development and socket design can intercept the volume fluctuation and adjust accordingly. The use of various sensors and suspension systems may play an important role. The inbuilt mechanism development to measure and optimize shear stress on the residual limb system during prosthesis on may improve the user's activity outcome and satisfaction (Paterno et al. 2018). As the type and condition of the amputation varies distinctly among the users, greater effort is needed to evaluate the force distribution on different socket designs and residual limbs (Sanders et al. 2011). Maintaining residual limb temperature is another challenge to a clinician and is important for acceptance of

prosthetic device. Merely, an increase of 1–2 degrees is enough to create discomfort (Peery et al. 2005).

The silicone liners tend to increase the residual limb temperature, though they evenly distribute the pressure around the stump. The increased temperature causes perspiration and invites fungal and bacterial infections. Some commercially available liners claim temperature maintenance; one such is Endolite silicare breathe liner that uses breathable fabrics to release perspiration outside and the other is Ohio Willow Woods SmartTemp® Liner that absorbs the extra heat generated and maintains the temperature. However, much more await in the area of material development to overcome the current challenges (Gupta et al. 2020).

Some other factors that are challenging in socket satisfaction and compromise mobility are the selection of appropriate suspension that prevents pistoning, rotation, and translation of residual limb. In the low- and middle-income countries, limited access to prosthesis and its design and quality, post-fitment complications and paying capacity and poor quality of life are the prime barriers and need to be addressed with established linkages with the developed countries (Shaw et al. 2018). Other critical gaps include the absence of an organized and trained professional workforce in low- and middle-income countries relative to developed countries. As per standard norms, per million populations, 5–10 prosthetists and orthotists are needed. But, in low- and middle-income countries, it is just one, impacting the standard service delivery. Hence, a comprehensive strategy is needed to fulfill the global professional requirements (Kumar and Vinita 2021).

Mostly, the prosthetic sockets are fabricated manually by clinicians (Prosthetists). But, in low- and middle-income countries the training facilities are not well developed to train the professionals in quality socket fabrication and fitting. A uniform and centralized socket production to better serve end-users may be an ideal option and computer-aided designing and computer-aided manufacturing (CAD/CAM) systems may play an important role. In CAD/CAM system the residual limb is scanned and software-based modification can be done that can be manufactured automatically into a socket or positive model, provided the clinicians have sufficient exposure to and expertise in CAD/CAM (Andrysek 2010; Wyss et al. 2015).

11 Discussion

The advancement in socket design has been improved biomechanically to control forces and pistoning on the residual limb interface. Besides, prosthetic component selection, alignment and suspension approach may also affect the prosthesis stability and comfort. In a cross-over trial done by Yiğiter et al. (2002),the pistoning was reduced greatly in the TSB socket in comparison with the PTB. It was found to be 4 mm in TSB and 16 mm in PTB. Besides, the step length difference between the amputated and contralateral sides was less in the TSB socket (Yiğiter et al. 2002). Board et al. (2001),while comparing the TSB socket with sleeve suspension and VASS socket, reported that the latter one encountered less pistoning and increased

gait (step length, stance duration) symmetry (Board et al. 2001). No differences were found in stride length, walking speed, swing symmetry, and stride length symmetry in VASS socket compared to the TSB socket with pin lock and HS Icex sockets (Selles et al. 2005). The less volume fluctuation and reduced pistoning in VASS socket compared to TSB might be attributed to lower positive pressure during stance and higher negative pressure during swing (Beil et al. 2002).

In a study, Board et al. (2001) found the axial rotation of liner and tibia in relation to socket was greater in TSB socket compared to in VASS but, distal tissue elongation was not different between the two suspension systems. VASS socket gained the volume by 3.7% and the TSB socket lost the volume by 6.5% in the same study. The reports support the above findings of investigations on different prosthetic componentry, alignment, pressure measurement, and sensor placement. The outcome indicates that VASS socket system has better comfort than TSB socket and PTB socket. In the PTB design, the highest pressure was applied to the popliteal area followed by the patellar tendon and anterior-distal tibia region. But, in TSB socket pressure depends on the liner used. The high pressure in seal-In liners appeared to be in middle of the residual limb due to seals around the outer surface of the liner. Pin-lock liners show high pressure on the proximal area of the residual limb. The interface pressure also depends on the thickness of the liners (Safari and Meier 2015b).

12 Conclusions

The advancement in prosthetic sockets is a continuous process and it has been improved and addressed drastically in last 50 years. The advancement must be aimed to reduce the impact of force generation on residual limb, control volume changes, and maintain normal body temperature. The osseointegration process is an alternative to eliminate the socket technology and to transfer the bodyweight through bone and prosthetic skeleton. However, till date, it is not widely accepted and practised due to its complications like infection, soft-tissue complication, device breakage, peri-prosthetic bone fracture, and implant loosening. The data quantification and visualization of the interaction between residual limb and socket may guide the prosthetic clinicians to reach maximal success and satisfaction.

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Chapter 9
Design and Development of Antibacterial Metal Implants

Ke Yang, Ling Ren, and Yachuan Yu

1 Introduction

Metal materials have been widely used in clinical medicines due to their incomparable excellent comprehensive mechanical properties (strength, shaping, toughness, hardness, fatigue, wear, torsion, etc.), good corrosion resistance, easy processing, stable production process, and high reliability of application. Metals are the preferred materials for hard tissue repairs and interventional treatments, where the implants are subjected to high loads. They are widely used in the manufacturing of various medical devices and surgical instruments in the medical field of orthopedics, dentistry, interventional stent, and so on. Internal fixation system for bone fracture, artificial joint, artificial vertebral body, skull repair stent and mesh, dental implant, and cardiovascular stent are typical high-end products, with many different types and specifications. Therefore, both the improvement of the performance of existing medical metal materials and the development of new medical metal materials have important practical significance for further improving the level of performance of metal medical devices, expanding the medical functions, enhancing the market competitiveness of the related products, and finally benefiting the majority of patients.

Among the medical metal materials, stainless steel, titanium and its alloy, and cobalt-based alloy are the widely employed. With the continuous progress and development of medical technology and the general life quality improvement of the public, the application and development of medical metal materials are severely challenged in the face of the development and clinical acceptance of other types of medical materials including polymers, ceramics, and composites. In the past 20 years, the research and development of medical metal materials have been continuously

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performed aiming at further improving the strength, toughness, corrosion resistance, wear resistance, biocompatibility, mechanical compatibility, and even biological activity of medical metal materials. The development of new medical metal materials and related surface modification technologies (Romanò et al. 2019), such as high-nitrogen nickel-free stainless steel (Yang and Ren 2010), low modulus titanium alloy (Niinomi et al. 2012), antibacterial metal (Ren et al. 2012a), biodegradable metal (Witte 2010), biofunctionalized metal (Zhang et al. 2021), surface bioactive coating, wear-resistant coating and drug coating, and so on, has brought new opportunities for the development and application of metal medical devices. Medical metal materials are developing toward the direction of better biocompatibility, better comprehensive performance, and specific biological activities such as antibacterial, osteogenic (Ren et al. 2015), angiogenic (Liu et al. 2020), anticoagulant (Ren et al. 2012b), etc., which are expected to continue maintaining the important position in the future clinical application of biomedical materials.

2 Implant-Related Infections

Bacterial infection associated with medical devices or implants has always been an important clinical issue in the medical field. Taking the orthopedic clinic as an example, even under the premise of strict aseptic operation and systemic preventive anti-inflammatory treatment, the incidence of infection after the first total hip arthroplasty is still 0.5–3.0%. Infection is one of the main causes of revision after total knee arthroplasty. The infection rate of prosthetic replacement with massive bone defects after tumor resection is between 5–35% and 2–30% of external fixation cases which has postoperative infection (Shirai et al. 2011). Statistics showed that about half of the 2 million cases of nosocomial infection in the United States are related to implants (Darouiche 2004), and the treatment and control of implant-related infection in the United Kingdom costs about 7–11 million pounds every year (Flock and Brennan 1999).

Once implant-related infection occurs, it may cause local tissue damage, systemic spread of pathogens and implant failure, and may also lead to serious diseases and complications, such as osteomyelitis and sepsis, and even amputation in severe cases (Hall-Stoodley et al. 2004). Moreover, this kind of infection may occur repeatedly and is difficult to control. Usually, the implants have to be completely removed, and long-term anti-infection treatment and reoperation after infection control have brought many serious problems to the patients: increasing the length of hospital stay and cost, the risk of reoperation, and even amputation or death.

Therefore, the active prevention of implant infection is particularly important. At present, the main preventive measures are to improve the cleanliness of the operation environment, control the possible pollution during the operation, and apply the prophylactic antibiotics during the operation period. However, there has not been a fundamental breakthrough in reducing the infection rate since the application

of antibiotics more than 50 years ago. In addition, with the increase of antibiotic-resistant strains, the problem of implant-related infection is becoming more and more serious. Thus, the development of new strategies for the prevention and treatment of infection caused by implants has obvious social and economic values in reducing medical and health expenses and ensuring the health of patients.

3 Innovative Research on Medical Antibacterial Metals

If the problem of bacterial infection caused by implants is resolved directly from the perspective of metal implant materials, it will effectively reduce the risk of bacterial infection, and avoid the antibiotics abuse and consequent drug resistance issues. Other side effects of antibiotics can also be reduced by the systemic intervention, and the effective prevention of infection around implants can thus be achieved. Therefore, the development of new medical metal materials with antibacterial function has become a new strategy to reduce or completely solve the infection problem caused by implants, which has important clinical application values.

Bacterial adhesion and then formation of bacterial biofilm are the initial cause of implant infection (Mack et al. 2000). Bacterial biofilm refers to the place where bacterial communities settle and propagate in the aqueous environment (Weir et al. 2008), and its formation mainly includes four processes: bacterial adhesion, aggregation and growth, extracellular matrix formation, and cell abscission and diffusion from the biofilm (Valappil et al. 2007). Mature bacterial biofilms can produce extracellular polymers (EPSs), which help bacteria to capture nutrients from the surrounding environment (VanHoudt and Michiels 2005). With the expansion and reproduction of bacteria, the biofilm can release free bacteria under suitable conditions. Biofilms contain polysaccharides, proteins, nucleic acids, lipids, and other substances (Sutherland 2001), which can maintain the structural integrity of the biofilms and provide an ideal place for bacteria to live free from autoimmune defense mechanisms and antimicrobial agents. Therefore, bacterial biofilms have strong resistance to antimicrobial agents (Shirai et al. 2011). In addition, the bacteria in the membrane are relatively lacking nutrients, the bacteria are in a state of starvation, growing slowly, and most of them are in a stationary phase, and are not sensitive to antibiotics, which leads to the enhancement of bacterial resistance (Bjarnsholt et al. 2007).

Therefore, in order to inhibit the formation of bacterial biofilm, the research and development of new medical metal materials with antibacterial function is one of the most effective ways to effectively reduce the occurrence of this kind of infection. The basic idea of this research is to add some amount of the antibacterial metal element into the existing medical metal materials. On the premise of not reducing the original properties and meeting the bio-safety, the material is endowed with strong antibacterial function, making it difficult to form a bacterial biofilm on the surface, thus fundamentally avoiding or greatly reducing the occurrence of bacterial infection (Hetrick and Schoenfisch 2006).

The use of copper (Cu) ions for sterilization has a long history. It has been more than 200 years since Schulthess used copper sulfate to control the wheat black disease in 1761. In 1885, Millardet, a French man, successfully developed the famous Bordeaux solution containing Cu ions, which had the function of sterilization, and solved the crisis of diseases and pests of Bordeaux grape in successive years. Subsequently, many kinds of bactericides containing Cu ions appeared one after another, which created an era of application of Cu ions in sterilization. Cu is a common alloying element in steel and other alloys. The strength and uniform corrosion resistance of the steel can be improved by adding appropriate amount of Cu, and the cold deformation processability of the steel can be improved, which provides conditions for the development of new Cu-bearing medical metal materials with antibacterial function through alloying.

On the other hand, Cu is also an indispensable micronutrient in human body, which is very important for the formation of connective tissue, nervous system, cardiovascular system, and the bone development as well. Cu is also involved in the metabolism of iron and energy, consuming molecular oxygen and acting as a reducing agent in many enzyme reactions. The Cu content in human body is about 100–150 mg, and the normal value of serum copper is 100–120 μg/dl, which is the second essential trace element in human body. The World Health Organization recommends that adults should take 0.03 mg of Cu per kilogram of body weight per day. Cu is mainly excreted through bile, which contains low molecular and high molecular weight copper-binding compounds. The former is mostly in liver and bile juice, while the latter is mostly in gallbladder bile, a small amount being excreted through intestinal wall and excreted through urine in a trace amount (Harris 2003). Copper deficiency in human body can lead to anemia, osteoporosis, coronary heart disease, and other diseases (Shim and Harris 2003). The above physiological characteristics of Cu make Cu-bearing metal materials have the basis of bio-safety as the bone implant materials.

In recent years, using the strong and broad-spectrum bactericidal ability of Cu ions, a series of new medical Cu-bearing antibacterial metal materials have been developed, including antibacterial stainless steels (304-Cu (Zhang et al. 2013), 316L-Cu (Zhuang et al. 2019), 317L-Cu (Ren et al. 2012a)), antibacterial titanium alloys (Ti-Cu (Liu et al. 2016a, 2018), Ti6Al4V-Cu (Ma et al. 2015), Ti15Zr-Cu (Kolawole et al. 2020)), antibacterial cobalt-based alloys (CoCrMo-Cu (Wang et al. 2014), L605-Cu (Jin et al. 2018)), and antibacterial magnesium alloys (Mg-Cu Liu et al. 2016b; Li et al. 2016)), almost covering the main medical metal materials in clinical application. Up to now, there is no application of the metal medical devices with antibacterial function in the world. The research and development of medical antibacterial metal materials has laid a material foundation for the innovation and development of metal medical devices, having attractive clinical application prospects.

In order to solve the problem of bacterial infection related to implants in orthopedics, dentistry, and other fields, a large number of systematic and in-depth studies have been made on medical Cu-bearing antibacterial metal materials, including fabrication and processing of materials, structure and performance characterization, antibacterial performances, bio-safety, anti-infection in animals, etc., which has laid a research

basis and is providing various scientific evidences for clinical application of the materials. Figure 1 shows that (Ren et al. 2012a), after co-culturing with the common clinical infectious bacteria (*E. coli* and *S. aureus*) for different times, dense bacterial biofilm gradually formed on the surface of the ordinary 317L stainless steel, while only sparse bacteria adhered on the surface of 317L-Cu stainless steel, indicating that the Cu-bearing stainless steel could significantly reduce the risk of bacterial

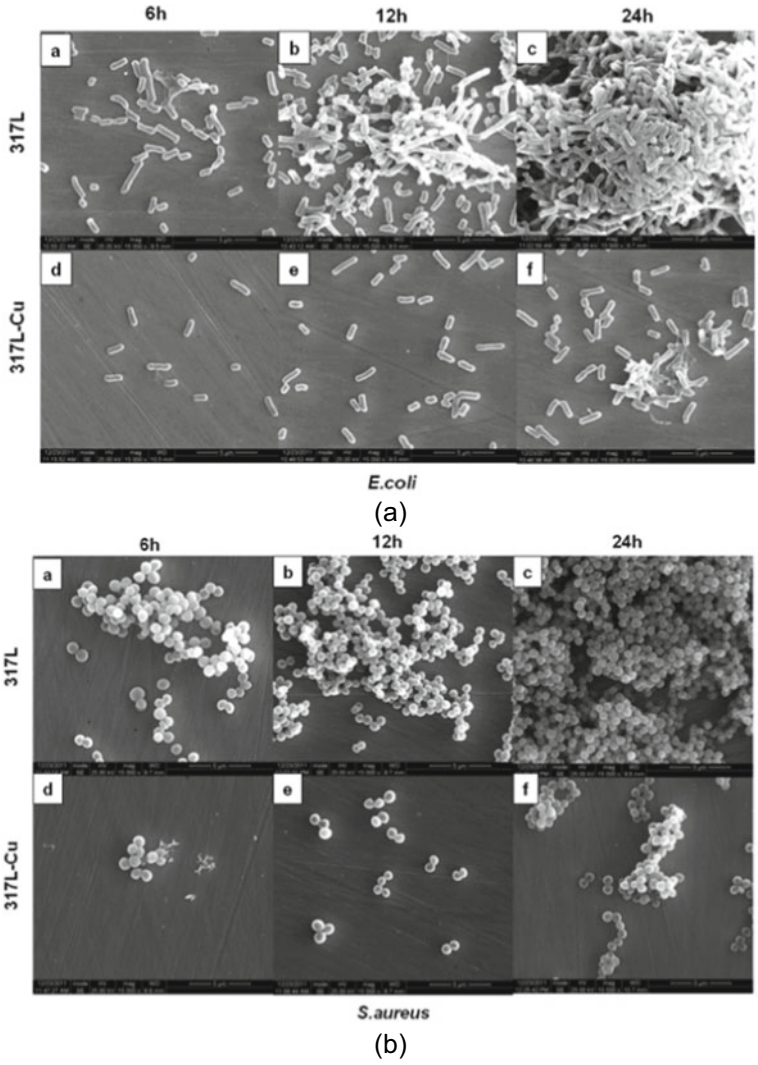


Fig. 1 Scanning electron microscope photos of bacterial biofilm formation on surfaces of 317L stainless steel and 317L-Cu stainless steel after co-cultured in *E. coli* **a** and *S. aureus* **b** suspensions for different times (Ren et al. 2012a)

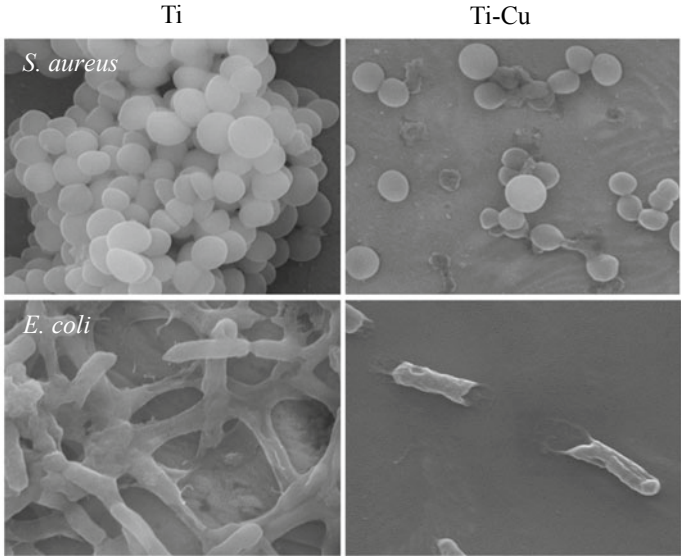


Fig. 2 Scanning electron microscope photos of bacterial biofilm formation on surfaces of pure Ti and Ti-5Cu alloy after co-cultured in *S. aureus* and *E. coli* suspensions for 24 h, respectively (Liu et al. 2018)

infection. Figure 2 shows that (Liu et al. 2018), after co-culturing with *E. coli* and *S. aureus* suspensions for 24 h, bacterial biofilm was formed on the surface of pure Ti, and the bacteria were connected by a large number of extracellular matrix. However, only a few bacteria adhered to the surface of Ti-Cu alloy, and some bacteria had died, showing strong antibacterial function. Figure 3 shows that Ti-Cu alloy also had strong killing effect on anaerobic bacteria (Liu et al. 2016a). After 24 h of co-culture with two kinds of anaerobic bacteria (*S. mutans* and *P. gingivalis*) which have been prone to oral diseases, the apparent morphology of bacteria on Ti-Cu surface has changed significantly, showing cell deformation and shrinkage, cell wall/cell membrane damage, separation between cytoplasm and wall, cytoplasmic loss, and so on, and thus resulting in death of bacteria. The bacteria on the surface of pure Ti were normal and good.

From the view point of bio-safety, after soaking 317L-Cu antibacterial stainless steel in normal saline for different times, the amount of Cu dissolved from the sample was measured to be about 5 × 10–6 mg/cm2. For a 317L-Cu antibacterial stainless steel bone plate with size of 40 mm × 10 mm × 2 mm, the daily Cu dissolution should be about 5 × 10–6 mg, much lower than the 2–3 mg Cu intake recommended by the World Health Organization for adults (IPCS 1998). Therefore, the boil safety of the Cu-bearing stainless steel can be preliminarily judged. The results showed that the addition of Cu had little effect on the mechanical properties and uniform corrosion resistance of 304, 317L and other antibacterial stainless steels. Therefore, the release of metal elements from the Cu-bearing stainless steel in physiological environment

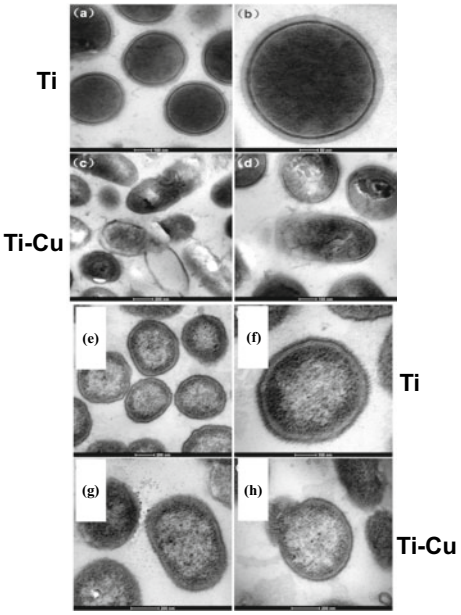


Fig. 3 Transmission electron microscope photos of bacterial biofilm formation on surfaces of pure Ti and Ti-5Cu alloy after co-cultured in *S. mutans* and *P. gingivalis* suspensions for 24 h, respectively (Liu et al. 2016a). **a**–**d** pure Ti surface; **e**–**h** Ti-Cu alloy surface

should be equivalent to that of the same kind of ordinary medical stainless steel, so they should have the same bio-safety. In addition, the cytotoxic test results showed that the cytotoxicities of 304-Cu antibacterial stainless steel to L929 cells (mouse fibroblasts), and MG63 cells (human osteosarcoma cells), KB cells (human oral epithelial cancer cells) were the same as those of pure titanium and 304 stainless steel, meeting the requirement of cytotoxicity to surgical implants.

Through establishment of the infectious animal implantation model, the anti-infection effect and related mechanism of medical Cu-bearing metal in animals were studied (Zhuang et al. 2019, 2021; Liu et al. 2018), and the results showed that the Cu-bearing metal implants could greatly reduce or completely inhibit the infection. For example, 316L-Cu antibacterial stainless steel and ordinary 316L stainless steel were used to manufacture bone screws, which were soaked in different concentrations of *S. aureus* suspensions for 6 min and implanted into the lateral epicondyle of femur in rats. The anti-infection effect of antibacterial stainless steel in animals was studied by imaging, histological, and microbiological methods (Zhuang et al. 2019). After treatment of stainless steel screws with low-concentration bacterial suspension (LB, 1 × 105 CFU/ml), the 316L stainless steel group showed typical implant-related infection. The typical "double line sign" of periosteum and mottled shadow of infection focus were found on the imaging (Fig. 4). Periosteal thickening and a large number of inflammatory cells infiltration could be seen on the tissue section. The bacterial biofilm formed on the screw surface was observed by scanning electron microscope. However, there was no obvious sign of infection in 316L-Cu stainless steel group. When using high-concentration bacterial suspension (HB,

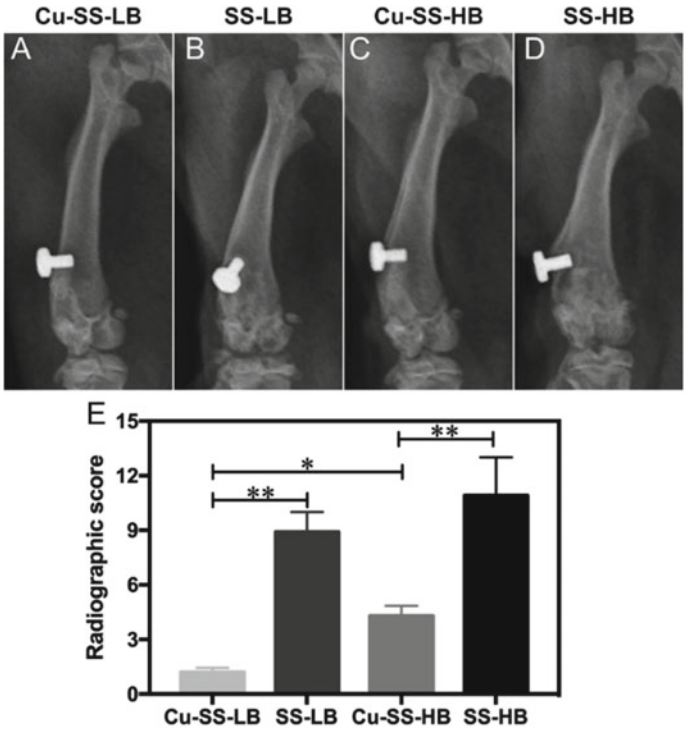


Fig. 4 X-ray photographs and imaging scores (Zhuang et al. 2019): **a** there was no obvious sign of infection in the low bacterial concentration of Cu-bearing stainless steel group (Cu-SS-LB); **b** in the low bacterial concentration of ordinary stainless steel group (SS-LB), there were obvious signs of infection: periosteum thickening and lifting, local mottled shadow, a small amount of dead bone formation and joint cavity spreading; **c** in the high bacterial concentration of Cu-bearing stainless steel group (Cu-SS-HB), mild infection was found, with only periosteal thickening and swelling; **d** in addition to periosteal thickening and lifting, local mottling, a small amount of dead bone formation, and joint cavity spreading, the narrow joint space could also be seen in the high bacterial concentration of ordinary stainless steel (SS-HB) group, indicating the middle-late stage of infectious arthritis. **e** Imaging scores of four groups, $*p < 0.05$; $**p < 0.01$

1 × 107 CFU/ml) to treat stainless steel screws, in addition to the above signs of infection, obvious dead bone formation could be seen on X-ray photograph of 316L stainless steel group, and more bacterial biofilm formation could be observed under scanning electron microscope. But the 316L-Cu stainless steel group showed only mild infection, with periosteal irritation and a small amount of inflammatory cells infiltration. These results indicate that 316L-Cu stainless steel could effectively prevent the implant-related infection. When the amount of bacteria was increased, the possibility or degree of infection could also be reduced to a great extent. In addition, there was no significant difference in the Cu content in many important organs of the animals implanted with Cu-bearing antibacterial stainless steel compared with implantation with the ordinary stainless steel, and there was no change in each organ

tissue, which proved the bio-safety of medical Cu-bearing antibacterial stainless steel in animals.

4 Application Prospect of Medical Antibacterial Metals

Large number of related researches has shown the material basis for clinical applications of medical antibacterial metals. Through the cooperation between The Institute of Metal Research, Chinese Academy of Sciences, and Suzhou Silvan Medical Devices Co. Ltd., a variety of antibacterial metal medical implant products have been developed, including fracture fixation system (plate, pin, screw, and intramedullary nail), spinal fixation system (rod, screw, etc.), stem of artificial hip joint, artificial knee joint, dental implant, orthodontic system (bracket, arch wire, mini-implant, etc.), anastomotic staple, antibacterial metal powder for 3D printing of various material series, as well as antibacterial stainless steel surgical instruments, as shown in Fig. 5. Among these novel metals, the strength of antibacterial titanium alloys (Ti6Al4V-5Cu, Ti-5Cu) is higher than that of the corresponding materials (Ti6Al4V, pure Ti) by 20%. This is due to the dispersed precipitation of Ti2Cu phases in the Cu-bearing titanium alloys and the improvement of processing procedures, which significantly improves the strength of the materials, but the ductility of the materials remains unchanged. The biological properties of antibacterial stainless steel (316L-Cu) and antibacterial titanium alloys (Ti6Al4V-5Cu, Ti-5Cu) have been inspected, all meeting the requirements of relevant standards for metal implants. An industrial trial production of antibacterial titanium alloys (Ti6Al4V-5Cu, Ti-5Cu) has been completed, which can provide the necessary raw materials for the development of metal products with antibacterial functions.

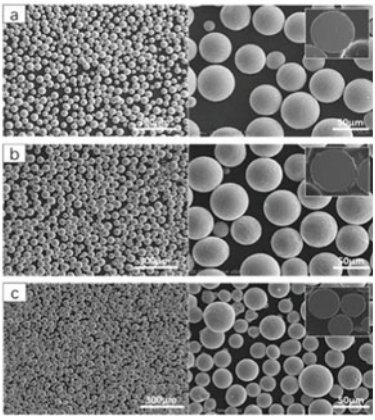
Suzhou Silvan Medical Devices Co. Ltd. has developed a series of new bone fracture fixation products made of antibacterial titanium alloy (Ti6Al4V-5Cu). In addition to their excellent antibacterial properties, the mechanical bearing capacity of the products has been greatly improved due to the increase of the strength of the material itself, and therefore the biomechanical safety of the products has been further improved. The results of biomechanical test showed that the tensile strength of the Ti6Al4V-5Cu bone needle was increased by 25%, the maximum torsional strength of the screw was increased by 89%, the torsion strength of the hollow screw was increased by 62%, the static bending load of the plate was increased by 67–89%, and the maximum loading force of the four-point dynamic bending cycle of the plate was increased by 41–91%, in comparison with the Ti6Al4V competitive products. The above results should be attributed to the strengthening effect of Cu in the antibacterial titanium alloy and the refinement effect of the microstructure. This indicates that the Cu-bearing antibacterial titanium alloy has the advantages of reducing bacterial infection and improving mechanical safety, which has a broad clinical application prospect.

Antibacterial titanium alloy bone plates

Antibacterial titanium alloy bone pins

Antibacterial titanium alloy bone fixation screws

Antibacterial titanium alloy hip joint stems



a: Ti6Al4V-Cu, b: Ti-Cu, c: CoCrWMo-Cu

Antibacterial metal powders for 3D printing

Fig. 5 A variety of antibacterial metal medical implants and powders for 3D printing

5 Opportunities and Challenges

Metal medical devices are widely used in orthopedics, dentistry, interventional stent, and other clinical medicines. Taking China as an example, it is estimated that the number of orthopedic patients in China each year reaches more than 16 million, of which more than 80% need surgical treatment (about 13 million patients). If 2% of them are infected, the infection cases will be around 260,000. The number is huge, and the suffering and economic burden will be immeasurable. Oral cavity is an open environment, thus the incidence of infection will be higher. The application scenes mentioned above have brought great opportunities for both the research of medical antibacterial metals and the development and application of new metal medical devices with anti-infection function. From the comparisons between antibacterial metals and their corresponding metals for implants shown in Table 1, it is believed that the anti-infective devices made of Cu-bearing metals must have high market competitiveness.

However, there are still many challenges to be faced in order to promote the development and application of antibacterial metal medical devices. First, the particularity of the relevant industry is that the development and application of medical devices are regulated. The products need to be registered, inspected, and approved for listing in different countries, maybe more complicated for those with antibacterial function. Generally, they need a long period of time and large investment in funds. The second is that both basic and applied researches with multi-levels on the medical antibacterial metal materials need to be systematically and deeply conducted, so as to make them further understood and developed, and to provide more scientific basis for their future clinical applications. There should be other challenges or problems need to be overcome for different countries.

Table 1 Comparisons between Cu-bearing metals and their corresponding metals for implants

Materials	Composition	Functionality	Bacterial resistance	Application	Clinical status
316L	FeCrNiMo	None	None	Orthopedics, stent, etc.	Clinical practice
316L-Cu	FeCrNiMo-Cu	Multifunction*	Broad spectrum	Orthopedics, stent, etc.	In registration
Ti	Pure Ti	None	None	Dentistry, etc.	Clinical practice
Ti-Cu	Ti-5Cu	Multifunction*	Broad spectrum	Dentistry, etc.	In registration
Ti6Al4V	Ti6Al4V	None	None	Orthopedics, dentistry, etc.	Clinical practice
Ti6Al4V-Cu	Ti6Al4V-5Cu	Multifunction*	Broad spectrum	Orthopedics, dentistry, etc.	In registration

*Antibacterial, osteogenic, angiogenic, etc.

6 Concluding Remark

The development of antibacterial medical materials is a new strategy to effectively solve the problem of infection caused by implants. The study and application of antibacterial metal materials has made an important contribution to this aspect.

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Chapter 10
Integration of Virtual Reality and Augmented Reality in Physical Rehabilitation: A State-of-the-Art Review

Vaidehi Patil, Jyotindra Narayan, Kamalpreet Sandhu, and Santosha K. Dwivedy

Abbreviations

VR	Virtual Reality
AR	Augmented Reality
MR	Mixed Reality
ER	Extended Reality
UAVs	Unmanned Aerial Vehicles
HMD	Head Mounted Display
TKA	Total Knee Arthroplasty
VRE	VR Exposure
PTSD	Post-Traumatic Stress Disorder
PD	Parkinson's Disease
MS	Multiple Sclerosis
CT	Conventional Therapy
VRT	Virtual Reality Therapy
ART	Augmented Reality Therapy
BBT	Box & Block Test
FIM	Functional Independence Measures
FMA	Fugl-Meyer Assessment
BPM	Balance Performance Monitor

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MBI	Modified Barthel Index
BBS	Berg Balance Scale
FOG	Freezing of Gait
ADL	Activity of Daily Living
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
UE	Upper Extremity
LE	Lower Extremity
MOCAP	Motion Capture
CAVE	Cave Automatic Virtual Environment
LCD	Liquid Crystal Display
LMC	Leap Motion Controller
MRI	Magnetic Resonance Imaging
GUI	Graphic User Interface
CVC	Central Venous Catheters
RGB-D	Red Green Blue-Depth
SD	Standard Deviation
VRG	Virtual Reality Group
CG	Control Group
MAL-QOM	Motor Activity Log-Quality of Movement
MEP	Motor Evoked Potential
PPT	Purdue Pegboard Test
CSQ	Client Satisfaction Questionnaire
B-Stage	Brunnstrom Stage
MMT	Manual Muscle Testing
NHPT	Nine Hole Peg Test
FSS	Fatigue Severity Scale (FSS)
MSIS	Multiple Sclerosis Impact Scale
ROM	Range of Motion
JTT	Jebsen-Taylor Hand Function Test
SIS	Stroke Impact Scale
BPO	Body-Powered Orthosis
PPD	Pneumatic-Powered Device
SOT	Sensory Organization Test
PDQ	Parkinson's Disease Questionnaire
FES	Fall Efficacy Scale
TUG	Timed Up and Go
FAC	Functional Ambulation Category
FRT	Functional Reach Test
ARISE	Augmented Reality for gait Impairments after Stroke
VRRS	Virtual Reality Rehabilitation System
VRRT	Virtual Reality Reflection Therapy

1 Introduction

Digital technologies, nowadays, are used substantially in several industrial and healthcare applications to display and approach environments which are physically inaccessible. Such technologies are based on the effective real-virtual interactions for the users. Virtual reality (VR) creates a simulated environment using digital technology, where the users are "immersed" in the experience and are able to interact with 3D scenarios. VR systems are commonly characterized by a headgear apparatus which exploits senses of vision and hearing; however, few advanced VR systems include haptic feedback technology to provide the impression of touch by employing forces, motions, or vibrations (Rizzo and Galen Buckwalter 1997; Riva 1997). These systems involve high computational power and intelligent sensors to position the subject's eyes within the surrounding such that the graphics react relatively to the user's movements. Meanwhile, Augmented Reality (AR), another form of digital technology, relates the virtual data to the actual world by overlaying simulated objects or sights produced through the computer to the actual scenario (Liu et al. 2017). This regulates the location and orientation of a camera using sensors and related algorithms. Graphics are rendered by superimposing simulated images over a subject's view from the real scenario. Milgram and Kishino (1994) define Mixed Reality (MR) as the merger of real and virtual elements where users are allowed to interact with both the elements through a single display screen. MR interfaces enhance the functionality of actual world instead of switching it entirely using the combined features of both AR and VR. On the other hand, the extended reality (XR) amalgamates the features of different digital technologies to improve the real and un-real experiences, collectively. It can have elements of immersion (VR), augmentation (AR), or both (MR). Figure 1 presents the classification of digital technologies.

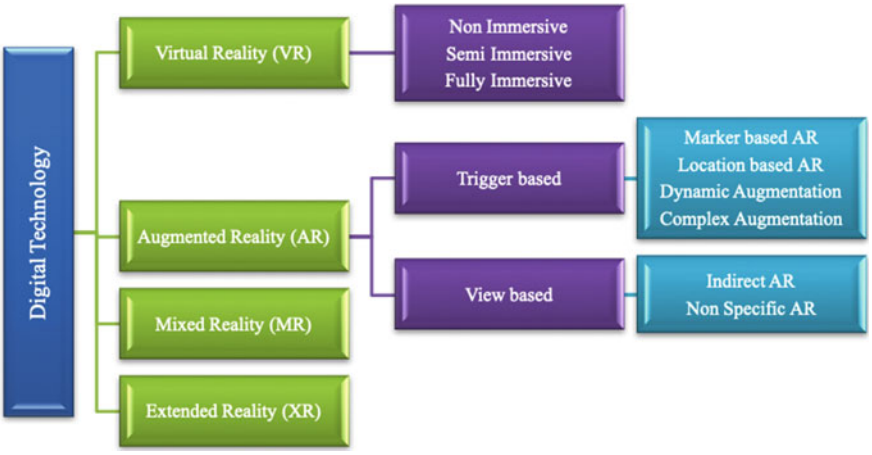

Fig. 1 Categories of digital technology

VR is practically omnipresent in every industry-education, healthcare, tourism, construction, architecture, entertainment, sports, art and design, event management, marketing, law enforcement industries, to name a few (Helsel 1992; Portman et al. 2015; Alcañiz et al. 2019; Bates 1992). Studies have shown that using VR in classrooms accelerates dynamic rendering, closed-loop interaction, and enhanced sensory feedback having a beneficial effect on retention (Helsel 1992). VR environments used in architecture and environmental planning can help plot designs, maps, and access remote territories (Portman et al. 2015). Marketing experts are showing keen interest in Extended Reality (XRs), technology similar to VR, to produce copacetic experiences for the consumer by reflecting those practiced in physical shops (Alcañiz et al. 2019). AR is generally maneuvered for applications like training, path planning, remote collaboration, warehouse logistics in manufacturing, tourism, medicine, and military services (Bates 1992; Ćuković et al. 2020; Petruse et al. 2019; Wei et al. 2014). Haptic and audio displays for tourism applications have shown an increased effect on interaction (Wei et al. 2014). Apart from training purposes, AR is used in military research for simulation of equipment like unmanned aerial vehicles (UAVs) in unknown areas (Ma'Sum et al. 2013). Similarly, MR interfaces are mainly designed for manufacturing and visualization processes. For instance, a "Needle biopsy" setup developed by Bajura et al. (1992) uses MR to overlay virtual ultrasound images onto a patient's body, allowing doctors to understand exactly where and how to insert the needle. Figure 2 indicates a video image presented to head mounted display (HMD), illustrating a sight of the subject's abdomen along with a superposed 2D ultrasound image. Therefore, these reality interfaces can enable a person to see, connect, and interact with different worlds in seemingly impossible ways. The research discussed in this paper, however, is limited to VR and AR technologies in the field of medical rehabilitation.

VR and AR are without doubt powerful tools to monitor, replicate, and alter the healthcare activities in a safe environment without changing anything on the user end and are therefore potential for improving recovery and aiding medical care. These

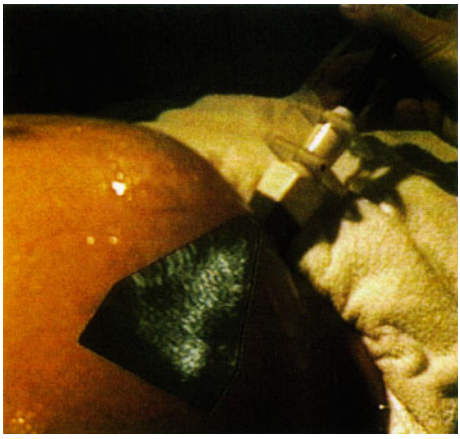

Fig. 2 MR system showing 2D ultrasound image superimposed on a subject's abdomen (Bajura et al. 1992)

tools provide optimized functional results and enhanced clinical benefits in post-surgery rehabilitation. For example, VR and AR technologies have proven to be practical and beneficial interventions in cases of vestibular rehabilitation, primary total knee arthroplasty (TKA), and Chronic Obstructive Pulmonary Disease (Stankiewicz et al. 2021; Gianola et al. 2020; Rutkowski et al. 2019). VR Exposure (VRE) therapy is a psychological treatment where doctors create a safe environment and expose the patients to things they fear or avoid in a controlled manner. VRE is used extensively to overcome clinical phobias and disorders like acrophobia, claustrophobia, Post-Traumatic Stress Disorder (PTSD), substance use disorders, social anxiety disorder, panic, generalized anxiety disorder, obsessive compulsive disorder, schizophrenia, psychosis, pain, addiction, eating disorders, and autism (Rus-Calafell et al. 2018; Maples-Keller et al. 2017; Sun et al. 2014).

Over last few years, the usage of VR and AR has been started in the domain of neurological reintegration, specifically in subjects with brain injury, Stroke, Parkinson's disease (PD), Multiple Sclerosis (MS), and Cerebral Palsy. Conventional therapy (CT) in view of stroke, PD, MS includes physiotherapy and kinesiotherapy sessions to reduce the difficulties regarding spasticity, pain, and fatigue in motor impairments (Maggio et al. 2019). However, these traditional approaches are not very effective due to reduced motivation, boredom, and lack of support, leading to decreased participation. Conversely, VR and AR therapy (VRT and ART) approaches cover the four fundamental aspects of rehabilitation: intensity, task-oriented training, biofeedback, and motivation. Such therapy approaches are repetitive and designed in accordance to tasks relevant to upper extremity or lower extremity. It is often used with CT, therefore increasing the intensity of traditional exercise. To compare the results of CT and AR/VR therapy, specific outcome measures are used. Outcomes like Box & Block Test (BBT) measures, Functional independence measures (FIM), Fugl-Meyer assessment (FMA) scores, modified Barthel index (MBI), Balance Performance Monitor (BPM), Berg Balance Scale (BBS) tests, 6 min walk test (6mwt), 10 min walk test(10mwt), GAITRite are crucial to determine the quality of the findings. Studies and clinical trials have shown the effectiveness of VR therapy to carefully detect the explicit FOG triggers and balance debilities in patients suffering from PD (Li et al. 2011). In the case of MS and post-stroke patients, VRT is oriented toward the reconstitution of both motor and cognitive dysfunction to favor the ADL, augmenting the enduring abilities and learning of fresh strategies for spasticity, pain, and fatigue (Maggio et al. 2019; Calabrò et al. 2017). This technology can also be adaptive by modifying itself in accordance with patients' feedback.

As several VR and AR systems have been designed and developed for rehabilitation purposes, there is an emergent need to review such systems comprehensively to understand their functionality and clinical efficacies. This paper aims to review VR and AR therapy approaches designed for rehabilitation purposes. The paper is organized as follows. Cases of VR and AR in health care, particularly post-stroke, MS, PD rehabilitation are first presented in Sect. 1. The adopted methodology along with a PRISMA report is presented, in Sect. 2, to support the inclusion-inclusion criteria of articles. Thereafter, the working and types of VR, AR systems are explained in brief in Sects. 3 and 4. Section 5 presents VR and AR therapy approaches for UE

motor rehabilitation. Section 6 discusses VR and AR therapy applications for LE rehabilitation. The existing shortcomings and related areas of technological improvement are discussed in Sect. 7. At last, concluding remarks of this review work are presented in Sect. 8.

2 Methodology Adopted for Systematic Review

A comprehensive literature was searched within various electronic databases such as Scopus, PubMed, Google Scholar, Institute of Electrical and Electronics Engineers (IEEE), and ScienceDirect was searched. The searched key inputs were like "(virtual reality OR game-based virtual reality OR computer-based virtual reality OR VR-based rehabilitation) AND (augmented reality or game-based augmented reality OR AR-based rehabilitation) AND (stroke OR PD OR hemiplegia OR brain injury OR multiple sclerosis OR traumatic brain injury) AND (Upper extremity OR cognitive OR motor OR Lower extremity OR executive function)." Using these key inputs, 72 out of 533 full-text articles are realized to be appropriate and, thereafter, studied in an exhaustive manner. The stepwise identification, screening, eligibility, and inclusion of 72 relevant articles are depicted in Fig. 3, utilizing a PRISMA flowchart (Moher et al. 2009). The final articles are included to refer VR, AR devices for UE, and LE rehabilitation for subjects suffering from Stroke, PD, MS (Tables 3, 4, 5 and 6). Exclusion criteria were (1) subjects without stroke or PD or MS; (2) subjects who were animals or children; (3) studies that did not affect physical UE/ LE rehabilitation; (4) studies that used methods other than AR/ VR for rehabilitation; (5) devices that did not provide feedback of any kind; (6) only design ideas were projected, no actual device included; (7) papers before year 2004.

The main study of this paper is AR and VR-based rehabilitation for patients suffering from deficits in upper limb and lower limb movements. Although few quality review works are already available in the literature (Schultheis and Rizzo 2001; Sveistrup 2004; Howard 2017; Kim 2005); however, either they were published more than a decade (Schultheis and Rizzo 2001; Sveistrup 2004; Kim 2005) or having non-systematic presentation in view of upper extremity and lower extremity dedicated devices (Howard 2017). In case of other review papers published recently (Penn et al. 2018; Huang et al. 2018a; Dunn et al. 2017), the VR and AR technologies for the rehabilitation purposes are not presented exhaustively and discussed either specific to a certain disease or specific to an extremity. To the authors' best knowledge, this review work has explored all the possible design features and functionalities of VR and AR solutions for the rehabilitation of upper and lower extremity.

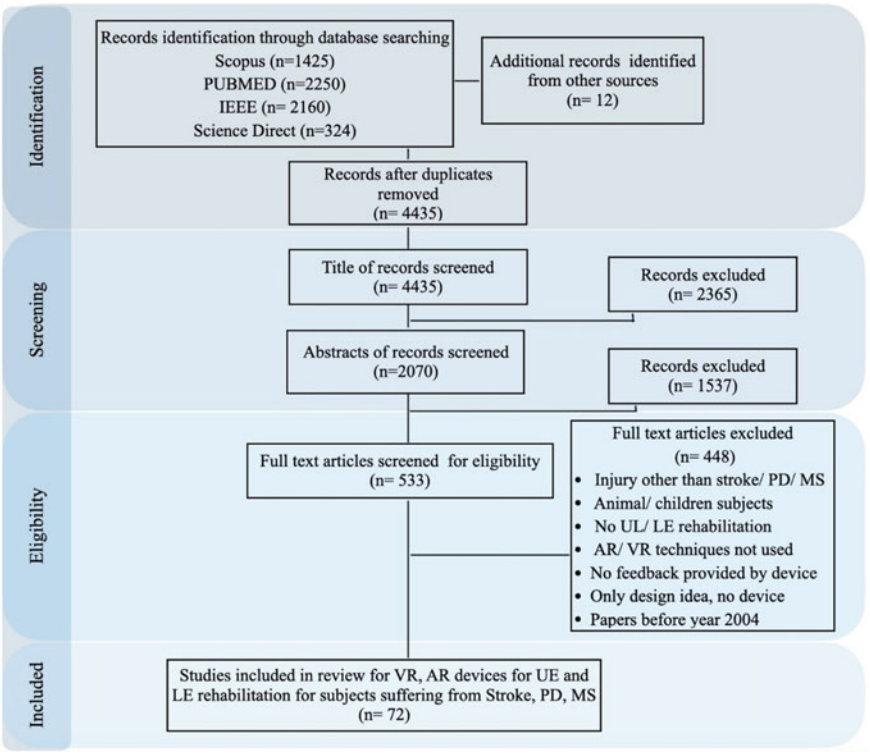

Fig. 3 Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flowchart (Moher et al. 2009)

3 Virtual Reality Systems

Immersion in VR is the effect caused by a situation, environment, or graphic representation which makes the user perceive the projected environment as reality. Jennett et al. (2008) define VR in terms of user involvement; and consider it as the reason behind lack of awareness of time and actual world, along with a feeling of "being" in the work surroundings. While talking about immersion in general VR cases, the term "spatial immersion" is used, which means being physically present in a fabricated environment. This occurs when a user's senses are partially/ fully stimulated by a VR system using images, sound, and other feedback sources to feel the said world as real. Considering an important element of a VR system, the levels of immersions can be varied for different purposes. There are three primary categories of VR simulations, differentiated on the degree of immersion as seen in Fig. 1.

3.1 Non-Immersive VR

Non-Immersive VR allows the subject to interact in a simulated world and can be straightforwardly deployed using input devices like joystick, monitor, keyboard, or a mouse (Robertson et al. 1993). Even though it is a computer simulated world, the user is well-aware about the surroundings and can control aspects of this environment. Non-immersive systems are also considered economic and are generally easier to set up as compared to immersive VR. Video game systems or movie systems are common examples of this system. Non-immersive VR is also used in rehabilitation, for instance, a RAPAEL smart glove experience developed by Lee et al. (2020) proved beneficial to improve the upper limb function of stroke patients.

To reduce fall risk and improve gait rehabilitation in older adults, a non-immersive VR system with a motion-capture (MOCAP) camera setup and a computer-aided simulation demonstrated positive results (Mirelman et al. 2016). The VR system consisted of a motion-capture camera and a computer-generated simulation projected on to a large screen, which was specifically designed to reduce fall risk in older adults by including real-life challenges such as obstacles, multiple pathways, and distracters that required continual adjustment of steps. Figure 4 illustrates this VR system. Non-immersive VR systems are therefore considered as a powerful tool to improve the neurological disorder-related symptoms and to elevate cerebral and motor function of the brain.

Fig. 4 Treadmill training using a non-immersive VR system (Mirelman et al. 2016)

3.2 Semi Immersive VR

Semi-immersive simulated practices provide the feeling of presence in a different certainty while still staying aware of the surroundings. Quality details of the graphic along with the feedback provided by the system are directly proportional to the immersive feeling. Hardware for these systems generally includes high-resolution screens, powerful processors, and projectors to partly imitate the design and functionality of practical real-world scenarios. This class of VR is often utilized for educational or vocational training. Studies suggest that semi-immersive VR could be a beneficial approach for therapy of patients with traumatic brain injury, potentially leading to better cognitive and behavioral outcomes (Luca et al. 2019).

3.3 Fully Immersive VR

Fully immersive is the most realistic simulation experience to perceive and indulge with complete immersion-based virtual reality, where the operator needs the relevant supporting tools. VR headsets are most commonly used to offer high-resolution data with a varied field of view for a surreal immersive VR experience. The display creates a stereoscopic 3D effect and follows with the input tracing and feedback to create an authentic experience. A Cave Automatic Virtual Environment (CAVE) is a completely immersive VE wherein the user wears 3D glasses and is surrounded by projection screens or flat displays. It is widely used for education and training purposes (Ott and Pozzi 2008). VR glasses and Head Mounted Displays (HMD) deliver visual and auditory cues in the form of detailed graphics and auditory information. In addition to the benefits mentioned above, VR systems like Oculus Rift also allow for precise tracking of the user's movements, thus making it very useful for education, training, and rehabilitation purposes (Basu and Johnsen 2014). While CAVE systems are more expensive and difficult to move, HMD, VR glasses, and Oculus Rift are relatively cheaper and easy to handle.

3.4 Tools Supporting VR Technologies

VR systems are commonly used for medical training purposes to perform tasks, enhance skills and simulate complicated procedures. Lap Mentor is a frequently used semi-immersive system, to simulate laparoscopic surgery (Alaker et al. 2016). Khalifa et al. (2006) review the Eyesi VR system to train prospective students for cataract and vitreoretinal surgery training. A non-immersive VR-based tool, named as modified IREX program, was designed by Thornton et al. (2005) to assist in brain traumatic injury. Subramanian et al. (2007) discussed CAREN VR, a CAVE type immersive-based simulation system, to improve hand impairments in stroke patients

effectively. Another immersive system-nVisorSX was used in a work by Sharar et al. (2007) while providing therapy for severe burn patients. The Novint Falcon along with a leap motion controller assisted in upper limb VRT for patients suffering from hand motor impairments (Ramírez-Fernández et al. 2015). The key details of the VR-based medical devices are enlisted in Table 1).

Table 1 VR-based devices used in medicine

Tool	Author (year)	Use	Type of VR	Hardware details
Lap mentor (LAP Mentor III)	Alaker et al. (2016)	Laparoscopic surgery-Tasks, skills and suturing simulation	Semi-immersive	LCD Display with haptic feedback and modular design
Eyesi VRMagic (Eyesi Surgical)	Khalifa et al. (2006)	Eye surgery—Cataract and vitreoretinal surgery training	Semi-immersive	Monitor-based display. The tool can be equipped with different interfaces to reproduce complex interactions
Modified IREX program	Thornton et al. (2005)	Traumatic brain injury	Non-immersive	Computer based display
CAREN VR simulation system	Subramanian et al. (2007)	Stroke	Immersive	HMD/CAVE along with treadmill with force-sensing plates, a moveable base and motion-capture analysis
nVisor SX (discontinued)	Sharar et al. (2007)	Severe burn	Immersive	HMD with high-resolution color microdisplays and custom optics
Novint Falcon + LMC	Ramírez-Fernández et al. (2015)	Hand motor impairments	Non-immersive	Computer display. The Novint falcon is a 3 axis device with haptic feedback

4 Augmented Reality Systems

AR can be explained as a modification of the actual environment by adding visual or sound or other stimuli to it. The user interacts with the digital world and the system does the changes to the world by augmenting elements to it. Edwards-Stewart et al. (2016) classify AR systems into two main categories-triggered and view-based augmentation; shown in Fig. 1. Triggers refer to characteristics like object markers, GPS location, and dynamic augmentations of objects that initiate the augmentation.

4.1 Triggered-Based Augmentation

Trigger-based AR comprises Marker-based AR, Location-based AR, Dynamic Augmentation, and View-based AR. Marker-based AR can be either object based or paper/ image based. The object or image containing the marker is called the trigger object and it can be recognized by the AR system upon scanning. The scan triggers an additional sequence where more relevant content can be displayed on the device. Marker-based AR has been instituted successfully with patients suffering from animal phobias. Location-based AR is geo based and marker-less—it relies on GPS, accelerometer, digital compass, and other technologies to accurately identify a device's location. Dynamic AR, usually included with motion tracking, is receptive to the object's view as it alters. Lastly, the fourth kind of triggered AR is complex augmentation, defined as a hybrid form of location-based AR and dynamic amplification. A popular example of this is Google Glass, where users can access information regarding local spots depending upon their GPS location (Edwards-Stewart et al. 2016).

4.2 View-Based Augmentation

View-based AR consists of Indirect AR and Non-specific Digital AR. Indirect AR means augmenting static images as per the user's preference. For example, trying on clothes virtually by superimposing clothes onto an existing image of the person. Non-Specific Digital AR refers to digitize a dynamic outlook of the environment without having any reference to what is being perceived (Edwards-Stewart et al. 2016). This is a common policy to be found in mobile games. The operator intermingles with the augmentation like tapping the augmented scenarios upon viewing without having a reference to the operator's surroundings. However, it is pertinent to mention that view-based augmentation is not considered to be a part of AR in accordance with Milgram et al. (1994).

4.3 Tools Supporting AR Technologies

Some AR devices used in health care for visualization and training purposes are listed in Table 2. For anatomy education, a "Magic mirror" is used, where the system contains a sensor which tracks the user and displays all the anatomical organs and parts of the user on a LCD display (Ma et al. 2016). A projector-based MRI system enables simulated navigation of tracked interments on pre-defined routes and conception of risk structured on the subject undergoing MRI (Mewes et al. 2019). The Endosight system is a guidance system that assists in oncology procedures by visualizing 3D anatomical structures, tumor targets, and interventional tools on subject's body (Solbiati et al. 2018). Sutherland et al. (Sutherland et al. 2012) explore an AR Haptic simulation system which uses an optical tracking system, a haptic device, and a GUI to offer visual feedback for spinal needle insertion process. AR BOOK is an educational tool with AR modules concentrating on the lower limb's anatomy (Ferrer-Torregrosa et al. 2015). In another case, smart glasses were used as an educational tool to provide visual feedback for AR simulation of central venous catheters (CVCs) to train novice operators (Huang, et al. 2018b).

Table 2 AR-based devices used in medicine

Tool	Author	Use	Features of AR, feedback and hardware
Magic mirror	Meng et al. (2016)	Anatomy education	RGB-D sensor-based tracking device to detect the user movement on LCD a display
Projector-based interventional MRI system	Mewes et al. (2019)	pre-plan paths of tracked instruments visualize risk structure of patients	Visual navigation, tracking via markers
Endosight system	Solbiati et al. (2018)	Interventional oncology procedures	Markers on needles, radiopaque tags on patient's skin. Display using tablet/ PC
AR Haptic simulation system	Sutherland et al. (2012)	spinal needle insertion training	MicronTracker2 optical tracking system, PHANToM haptic device + GUI
AR BOOK	Ferrer-Torregrosa et al. (2015)	anatomy of the lower limb	
AR glasses	Huang et al. (2018b)	AR simulation of central venous catheters	Display unit + control box with visual feedback

5 Upper Extremity (UE) Rehabilitation

Damage or impairment of motor function in the UE of patients compels to not move their upper extremities flexibly and accurately. Therefore, a system for UE rehabilitation needs to be developed to help the patients to retain these motor functions and improve the quality of their life (Narayan et al. 2021). Traditionally, for these cases, CT primarily consists of repeated movements involving upper or lower limbs, which makes the patient disinterested and reduces the effects of rehabilitation (Ying and Aimin 2017). However, applying digital technology to CT provides an interactive experience for the users, enhancing the rehabilitation quality and results.

5.1 VR Technology-Based Upper Extremity Rehabilitation

VR techniques allow for repetitive learning, well-rounded feedback to all the senses, augmented practice and can be paired with robotic devices/ exoskeletons to increase effectiveness (Cameirão et al. 2008). Users react with virtual objects in a directly using hand gestures and body movements or via devices like glove, joystick, and mouse. Table 3 discusses and provides evidence concerning current applications of VR Therapy for UE motor recovery.

In a clinical trial conducted by Yin et al. (2014), the feasibility of VR training on early stroke subjects was investigated. Substantial improvement in FMA was obtained when participants were subjected to 30 min of VR therapy for weeks, 5 times each week, in addition to CT. VRT consisted of a Sixense unit, an electromagnetic sensor system that identifies the movement in 3D and a customized training program that consisted of highly repetitive tasks and different difficulty levels. Afsar et al. (2018) used the Microsoft Xbox 360 Kinect video game system to provide 30 min of VR therapy per day in addition to 60 min of CT for 4 weeks. The delta-BBT score for the experimental group has shown the significant improvement as compared to the control group ($p = 0.007$), proving that the Kinect-based game system may have added advantage for stroke patients. Figure 5 illustrates Jintronix, a virtual reality exergame system used to improve motor function in stroke survivors (Norouzi-Gheidari et al. 2020). Conducting VRT in addition to CT, post-intervention improvements were observed in ADL measures. Choi et al. (2016) used convenient VR via a mobile phone for 10–30 min of VRT sessions for 2 weeks. Notable results were seen in the FMA-UE, B-stage, and MMT after treated with the MoU-Rehab as compared to the conventional therapy.

Rutgers arm is a system involving a low-friction table with a 3D tracker and a library of virtual reality (VR) exercises. A telerehabilitation extension of this was developed by Kuttuva et al. (2006). The device was examined on a chronic stroke patient for over 5 weeks and improved FMA test scores were recorded for shoulder range of motion. In a similar study by Burdea et al. (2011), Rutgers arm II was introduced to sense and support the arm movement and thereafter, tilted to resist or

Table 3 VR tools for UE Rehabilitation

Author year	Group/sample	Disease	Type of VR	Sessions	Outcome measures
Yin, et al. (2014)	VRG (n = 11) CG (n = 12)	Stroke	Sixense unit + LCD	9 × 30 min VR therapy for 5 weekdays over 2 weeks + CT	FMA (mean change (SD) = 11.65 (8.56), $p < 0.001$), Action Research Arm Test, Motor Activity Log, FIM
Afsar et al. (2018)	VRG (n = 19) CG (n = 16)	Stroke	Microsoft Xbox 360 Kinect video game system	(30 min VR + 60 min CT)/day, 5 times a week for 4 weeks	Delta-BBT ($p = 0.007$), Delta-FIM self-care score ($p = 0.677$), Delta-FMA-UE ($p = 0.057$)
Norouzi-Gheidari et al. (2020)	VRG (n = 9) CG (n = 9)	Stroke	Jintronix-exergame systems	4 weeks of exergaming sessions + CT	MAL-QOM, SIS (stroke impact scale) shown a mean difference of 1.0%, 5.5%, and 6.7% between the intervention and control group, respectively) at post-intervention
Choi et al. (2016)	VRG (n = 12) CG (n = 12)	Stroke	Mobile game-based upper extremity VR program smartphone and a tablet PC (MoU-Rehab)	30 min CT + 30 min MoU-Rehab for 10 sessions over, 5 days per week, for 2 weeks	FMA-UE, B-stage, modified Barthel index (MBI), EuroQol-5 Dimension [EQ-5D]
Kuttuva et al. (2006)	VRG (n = 1)	Stroke	Rutgers Arm	5 weeks of training	FMA
Burdea et al. (2011)	VRG (n = 4)	Stroke	Rutgers Arm II + VR games	6 x (3-1 h sessions/week)	FMA increase up to 9 points
Kang et al. (2012)	VRG (n = 18) CG (n = 18)	Stroke	Virtual mirror with visual modulation	–	MEP amplitudes increased by 46.3%

(continued)

Table 3 (continued)

Author year	Group/sample	Disease	Type of VR	Sessions	Outcome measures
Elor et al. (2019)	VRG (n = 6) CG (n = 3)	Stroke	HTC Vive with soft robotic exoskeletal support	–	post-gameplay interviews using mixed 5-point Likert Scale questions and open-ended questions. Score of 111/130 or higher was seen
Shin et al. (2016)	VRG (n = 46)	Stroke	RAPAEL Smart Glove	4-week (20 sessions for 30 min per day) + 30 min standard CT	FMA (F = 6.48, df = 1.46, p = 0.006), JTT (F = 4.073, df = 1.497, p = 0.032), SIS (F = 6.048, df = 1.46, p = 0.015)
Sánchez-Herrera-Baeza et al. (2020)	VRG (n = 6)	PD	Immersive virtual reality technology—Oculus Rift 2 + leap motion controller	–	BBT, speed of movement, fine motor dexterity PPT, CSQ-8. Improvements in strength (p = 0.028), fine (p = 0.026 to 0.028) and speed movements (p = 0.039) in the affected side were seen
Maggio et al. (2019)	VRG (n = 10) CG (n = 10)	PD	BTS Nirvana (BTS-N) system	3 (60 min) sessions/week, for 8 weeks	Mann–Whitney U test, Bartlett test, Wilcoxon signed rank test
Cuesta-Gómez et al. (2020)	VRG (n = 30)	MS	Leap Motion Controller (LMC) based Serious Games	2–60 min sessions/ week over a 10 -week period CT + 15 min LMC with each session	Grip strength, follow up measures compared to pre-treatment investigation; BBT for more affected side (p = *0.016*), PPT assemblies (p = 0.038), NHPT, FSS, MSIS, CSQ-8

Fig. 5 The Jintronix rehabilitation exergaming system (Norouzi-Gheidari et al. 2020)

assist reach. The VR games adapted automatically according to each individual's motor abilities and significant positive FMA scores were obtained along with self-reported changes in the participants' ADL. Improvements were also reported in active ROM and grasp strength. Kang et al. (2012) used virtual mirrors with visual modulation in a study including healthy and stroke patients. The study presented positive results for the virtual mirror task and proved that visual modulation is an effective form of therapy for UE rehabilitation in stroke patients. Another VR visual feedback therapy via HTC Vive HMD was explored in the butterfly project by Elor et al. (2019). The users experienced physiotherapy by following and guarding a virtual butterfly, with the help of a robot-based wearable device to assist the subject's UE movements. Shin et al. (2016) introduced a biofeedback system containing a glove-shaped sensor device and a software application, called the RAPAEL Smart Glove which indicated improvements in the FMA, JTT, and SIS scores of patients with problems of distal UE function.

Sánchez-Herrera-Baeza et al. (2020) conducted a study for PD patients, using immersive VR technology—Oculus Rift 2 and a leap motion controller—OR2-LMC. They observed significant improvements in strength, fine and gross coordination dexterity, and mobility speed in the impaired side with an outstanding agreement. In a novel experimental setup by Maggio et al. (2019), a semi-immersive therapy system called BTS-N was used by PD patients. The results indicated an improvement in cognitive functioning pertaining to executive and visuospatial activities among the subjects. Cuesta-Gómez et al. (2020) used a Leap Motion Controller (LMC) System, which incorporates non-wearable sensors to capture the movement of the forearms and hands. Concluding results showed significant improvements in the post-treatment examination for coordination, locomotion speed, fine and gross UE dexterity.

5.2 AR Technology-Based Upper Extremity Rehabilitation

In most cases of AR therapy assisting UE recovery, gaming systems including virtual and real objects are used. Markers are attached to real objects and the systems track the moment, position, and orientation of these objects using a webcam. The system then seamlessly augments the real environment with the virtual world to present different tasks to the user which engages the user's UE movements. Some cases mentioned below include robotic devices and exoskeletons to assist UE rehabilitation. Table 4 lists the development of AR-based UE rehabilitation prototypes.

Bank et al. (2018) implemented three AR games that used a HMD and tracked the user's hand and body without any contact. Figure 6 demonstrates the setup of this system. The game objectives included speed of movements, adjustment of hand opening, and obstacle avoidance. For the first game, maximum reach distance was slightly greater in controls ($98.0 \pm 2.9\%$) than in PD patients ($96.8 \pm 2.9\%, p = 0.04$) and stroke patients ($95.5 \pm 2.9\%$, $p = 0.06$). In the second game, it was observed that PD patients moved slower than controls. In the third game, success rate did not differ much between controls (100 [100–100] %) and PD patients (100 [75–100] %, $p = 0.21$) or stroke patients (100 [75–100] %, $p = 0.09$). Thus, results obtained were almost similar for the CG, PD, and Stroke patients.

In a case study for post-stroke patients, Luo et al. (2005) created a training environment that integrated augmented reality (AR) and virtual objects with assistive devices like gloves containing body-powered orthosis (BPO) or pneumatic-powered device (PPD). This method demonstrated beneficial results. A NeuroR system developed by Assis et al. (2016) works by providing visual feedback of the illusion of injured UE movements while the affected limb is resting, resulting in increased FM

Table 4 AR tools for UE Rehabilitation

Author, year	Group/sample	Disease	Type of AR	Sessions	Outcome measures
Bank et al. (2018)	ARG: (Stroke: n = 10) (PD: n = 10); CG: (n = 10)	Stroke PD	Games on AIRO II HMD + Leap Motion webcam	–	Mann–Whitney U-tests, *t*-tests (PD vs. control-, stroke vs. control) (*see text for score values*)
Luo et al. (2005)	ARG: (BPO: n = 1) (PPD: n = 1); CG: (n = 1)	Stroke	Gloves consisting of BPO or a PPD	6-week training	BBT and Rancho
Assis et al. (2016)	ARG: (n = 1); CG: (n = 1)	Stroke	Visual illusion feedback	–	FMA-5% increase, computerized biophotogrammetry
Van der Meulen et al. (2016)	ARG: (n = 11)	PD	Virtual movement targets + haptic controller	–	System Usability Scale (SUS: 47.5 to 95; M = 70.7, SD = 14.6)

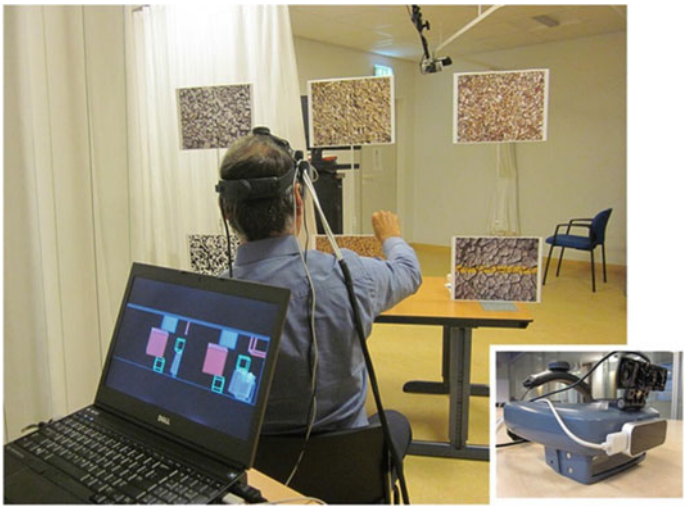

Fig. 6 Participant with AIRO II system (Bank et al. 2018)

scores. In an interactive game proposed by Van der Meulen et al. (2016) for PD patients, the system engages participants' UE movements by employing AR to show simulated motion targets, (like candies drop from a conveyor belt, and a haptic game controller to grab the candies).

6 Lower Extremity (LE) and Gait Rehabilitation

After reviewing the VR and AR devices for UE rehabilitation, the design of such devices for rehabilitation of lower extremity is discussed in this section. Diseases such as stroke, PD, MS affect the motor controls of the body and as a consequence, the patient's ability to walk is impaired. Therefore, the primary focus of rehabilitation is gait recovery and balance. In recent years, VR, AR technology (with or without Robotic interventions) have shown improved locomotion evidence in patients with motor defects. Kalita et al. (2020), Narayan and Dwivedy (2021, 2020). To find the effectiveness of these technologies, VR/ AR digital therapies are often tested in clinical trials along with patients receiving only CT. The most frequently used outcome measures in the different trials are gait speed, balance, and improvement of the motor function.

6.1 VR Technology-Based Lower Extremity Rehabilitation

Several studies have shown positive effects of VR-based treatments for LE motor rehabilitation. Specific VR, interactive video games, reflection therapy, and robot-assisted VR are some interesting approaches to the patient's rehabilitation. Table 5 categorizes VR-based rehabilitation therapy for neurological conditions and also summarizes current research in LE application.

Jaffe et al. (2004) conducted a trial wherein post-stroke subjects were requested to step over virtual objects or real objects on a 10 m treadmill (TM). The VR system provided visual, auditory, and vibrotactile feedback. The subjects expressed improvement in gait velocity, stride length, walking endurance, and obstacle clearance capacity, proving the effectiveness of obstacle training for improving gait velocity. Mirelman et al. (2009) used a robotic VR system to improve balance, speed, step time, step length, and stride in patients suffering from stroke. In a separate trial, the Rutgers Ankle, a 6-DOF robot with a VR simulation interface was used. Results from this trial intimated improved motor control of the ankle-ankle ROM changed by 19.5% (Mirelman et al. 2010). A VR gait training program for stroke patients was designed by Cho et al. (2013) by exploiting a video recording of the actual environment. The findings exhibited a greater improvement of the VR group on the BBS and TUG test, suggesting that this program may be a valid approach to improve gait performance. A virtual reality rehabilitation system (VRRS), appended to a MOCAP system, was successfully used (Luque-Moreno et al. 2016) to improve leg stance and walking speed in two post-stroke individuals.

Virtual reality reflection therapy (VRRT) was used effectively in a study performed by In et al. (2016) among post-stroke patients. The setup used is illustrated in Fig. 7. Significant improvements were observed in BBS, FRT, TUG, and postural sway outcomes among the concerned patients. VRRT can also be applied at home along with CT to improve affected LE function. Bergmann et al. (2017) introduced VR-augmented robot-assisted gait training (RAGT) to induce balance and gait recovery in stroke patients. The intervention manifested positive results like high acceptability and motivation, and slashed dropout rate, and an extended training period as compared to the standard control group. Fifteen PD patients with FOG took part in a trial designed by Janeh et al. (2019) that included VR-based gait modulation tasks on a GAITRite walkway system. The tasks effectively improved step width and swing interval parameters, proving to be a beneficial for manipulating gait characteristics in PD. Figure 8a, b demonstrate the experimental setup for the GAITRite walkway system. In a study conducted by Mendes et al. (2012), subjects with PD took part in Wii Fit training along with warm up exercises specifically designed to improve motor and cognitive skills. After more than 7 games, PD patients were capable to transfer the motor functionality attained through the games to an equivalent new task. In a similar study, Liao et al. (2015) used virtual reality-oriented Wii Fit exercise (VRWii) to enhance obstacle avoiding features and dynamic stability of PD patients. Wii Fit training is, therefore, a potential training method to improve motor controls and reduce FOG in PD patients.

Table 5 VR tools for LE Rehabilitation

Author, year	Group/sample	Disease	Type of VR	Sessions	Outcome measures
Jaffe et al. (2004)	VRG (n = 20)	Stroke	Virtual objects on treadmill with visual, vibrotactile, and auditory feedback	six sessions of approximately 1 h duration over 2 weeks	Balance Test, Walking Test, Obstacle Test, and 6 min Walk Test (6MWT) maximum walking speed improvement by 101.7%
Mirelman et al. (2009)	VRG (n = 9) CG (n = 9)	Stroke	Rutgers Ankle Rehabilitation System	3 times per week for 4 weeks for ≈1 h	gait speed increase up to 105% over a 7-m walkway, 6MWT
Mirelman et al. (2010)	VRG (n = 9) CG (n = 9)	Stroke	VR based on game technology with a hybrid NR and MNP system	three times a week for 4 weeks for approximately 1 h	FMA, BBS,19.5% change in ankle ROM
Cho et al. (2013)	VRG (n = 7) CG (n = 7)	Stroke	Virtual gait training using a real-world video record	30 min a day, three times a week, for 6 weeks	BBS (VRG: 4.14 *vs.* CG: 1.85), Timed Up and Go test (−2.25 *vs.* −0.94)
Luque-Moreno et al. (2016)	VRG (n = 2)	Stroke	VRRS + motion tracking capture system	15 treatment sessions 1 h VR + 1 h CT	3MWT, kinematic parameters
Taesung In et al. (2016)	VRG (n = 13) CG (n = 12)	Stroke	VR reflection therapy	30 min, five times a week for 4 weeks	BBS (3.62 ± 1.85), FRT (5.14 ± 3.57), TUG test (−3.80 ± 3.72), postural sway, 10 mWV (0.11 ± 0.06) for VRG
Bergmann et al. (2017)	VRG (n = 10) CG (n = 10)	Stroke	VR-augmented robot-assisted gait training	12 sessions (over 4 weeks)	FAC, Intrinsic Motivation Inventory (IMI), individual mean walking time
Janeh et al. (2019)	VRG (n = 16)	PD	GAITRite® walkway	1.5 to 2 h	Comparison of gait parameters

(continued)

Table 5 (continued)

Author, year	Group/sample	Disease	Type of VR	Sessions	Outcome measures
Mendes et al. (2012)	VRG (n = 16) CG (n = 11)	PD	Nintendo Wii Fit	10 games over 8 sessions + follow up session after 60 days	scores of 10 Wii Fit games over eight sessions, UPDRS-II test showed results of 8.3 (SD 3.6) post-training for VRG
Liao et al. (2015)	VRG (n = 12) TE (n = 12) CG (n = 12)	PD	VR-based Wii Fit exercise	VR/ TE for 45 min, + 15 min of TM in each session for a total of 12 sessions over 6 weeks	obstacle crossing performance, dynamic balance, SOT, PDQ-39, FES-I, TUG
Peruzzi et al. (2017)	VRG (n = 14) CG (n = 11)	MS	VR-based TM training	six weeks of treadmill training (TT), while the subjects in the experimental group received six weeks of virtual reality-based treadmill training (VR-TT)	Clinical measures and gait parameters
Fulk et al. (2005)	VRG (n = 1)	MS	BWS + TM + VR locomotor training	2 days a week for 12 weeks	10mwt (21% improvement), 6mwt (24.6%)

Studies have shown that VR-based TM training tasks have managed to improve factors like speed, cadence, stride length, walking endurance, and lower limb joint ROMs in MS patients (Peruzzi et al. 2017). In a case study of an individual lady suffering from MS, a body weight support (BWS) with a treadmill and over ground walking activity was conducted in association with VR-based balance intervention for 12 weeks. In addition to high motivation, improved test results were observed for her during the LE rehabilitation tests (Fulk 2005). Another VRT (Fung et al. 2006) consisted of a locomotor training system involving a self-paced TM mounted onto a 6-DOF motion platform. Different scenario VEs were woven into the gait training program that provided various levels of complexity. With practice, patients could effectively adjust their walking style and speed pertaining to changes in the game and as required for the task. This study, therefore, demonstrated that patients with

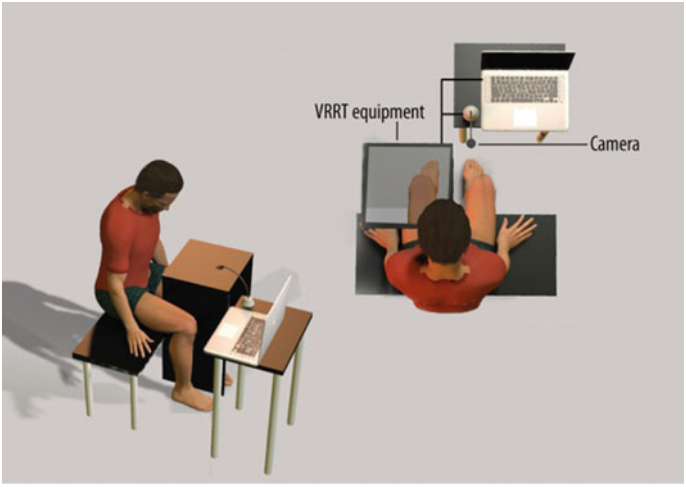

Fig. 7 Setting for virtual reality reflection therapy (In et al. 2016)

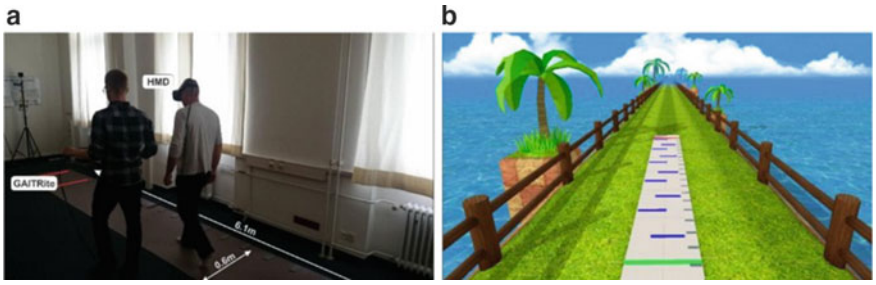

Fig. 8 Experimental system: **a** subject walking with HMD over the actual surface of GAITRite® **b** subject's view of the simulated environment on the HMD (Janeh et al. 2019)

stroke were capable to regulate themselves as per the VR system and were immersed effectively for gait training.

6.2 AR Technology-Based Lower Extremity Rehabilitation

AR Therapy includes visual and auditory augmentation using systems like smart glasses, HOLOLens, smart treadmills for postural training, gait and balance stabilization to enhance LE rehabilitation. Table 6 presents the experiences of tools based on AR focusing on LE rehabilitation.

AR-based postural balance activity for stroke patients in addition to CT indicated positive results on the TUG test, BBS, cadence, velocity, step length, and stride

Table 6 AR tools for LE Rehabilitation

Author, year	Group/sample	Disease	Type of AR	Sessions	Outcome measures
Lee et al. (2014)	ARG: (=10) CG: (n = 11)	Stroke	AR-based postural control training	AR therapy: 30 min/ day, 3 days/ week over 4 weeks + CT	TUG, BBS-(ARG vs CG post-training scores-49.9 ± 6.0 vs 45.8 ± 5.6)
Held et al. (2020)	ARG: (n = 1)	Stroke	ARISE system	–	BBS, FMA-LE, MI-LE
Janssen et al. (2020)	ARG: (n = 16) CG: (n = 1)	PD	AR visual cues through HoloLens	–	Friedman test and post-hoc Wilcoxon
Janssen et al. (2017)	ARG: (n = 25)	PD	3D AR visual cues delivered smart glasses + auditory cueing	–	Rank tests

length of impaired and non-impaired sides (Lee et al. 2014). A recent study by Held et al. (2020) introduces the ARISE (Augmented Reality for gait Impairments after StrokE) system which provides evidence of gait adaptation via visual and auditory augmentation. This approach is a combination of HoloLens 2 glasses and a sensor-oriented MOCAP system, as shown in Fig. 9. It was used by one post-stroke patient where he completed gait assignments and an AR parkour program. HoloLens with auditory and visual cues was used in a study for PD patients with FOG, where the subjects performed 180° turns with two control settings (one with auditory cues and one without cues). The study showed that visual cues worked better than auditory cues and the AR visual cues reduced the peak angular velocity and step height compared to both control conditions (Janssen et al. 2020). In another study by Janssen et al. (2017), PD patients with FOG performed walking tasks under different conditions. Three-dimensional AR visual cues were conveyed by smart glasses and auditory cueing via a metronome was also included depending on the control conditions. However, augmented visual cues conveyed by smart glasses were not found to be advantageous for subjects with PD and FOG.

7 Discussion and Future Opportunities

VR and AR Technologies are extensively employed in the area of medicine, showing positive effects especially for disability management, rehabilitation, surgical training, and psychological diseases therapy. In this review work, VR- and AR-based therapy for both UE and LE rehabilitation purposes, especially in case of brain injury, stroke, PD, and MS. Recent devices and intervention techniques used for therapy are listed in

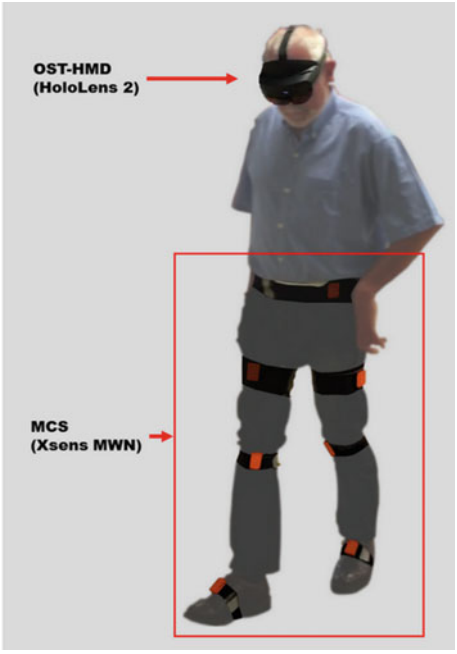

Fig. 9 Post-stroke patient wearing the ARISE system (Held et al. 2020)

tables and compared, keeping in mind-feasibility, effectiveness, and result outcomes. Using VR, AR systems for rehabilitation therapy promotes neuroplasticity and motor learning while making sure that challenging tasks are practiced in a safe environment. The motor cognitive or limbic challenges can be tailored to fit specific patient needs and can follow customized straining strategies. The therapies, in most cases, are adaptive, i.e., task variation and progression happens in accordance with the patient and his/ her performance. Some of these systems also have an added advantage of portability, accessibility, ease of use, and no need of professional supervision. Almost all cases of VR, AR systems mentioned in this paper have shown increased motivation, enjoyment, and acceptability among patients-leading them to complete the therapy and a significant reduction in dropout rates (Canning et al. 2020).

However, intense nature of physical and cognitive challenges may cause unwarranted fatigue and might cause dizziness, eyestrain, motion sickness, and loss of coordination. Feedback can also sometimes play an adverse role. Excessive feedback may confuse the patient; discouraging feedback might put a damper on spirits; incomplete or inaccurate feedback does not tell the patient how to proceed precisely. Apart from this, VR and AR systems are not always feasible in the sense that sophisticated systems are usually costly and inaccessible. VR- and AR-based interventions are therefore considered inevitable steps toward revolutionizing the digital technology-based approach toward neuro-rehabilitation. Some points to be considered to make these interventions even more effective are:

- Most of the control groups are very exclusive and take into account very specific details of a disease. Control groups need to be broadened, bit by bit, to include a larger group of people with some variations. Researchers need to be thorough and clearly define the intervention factors such as frequency, dosing, number of repetitions, and ardency (Proffitt and Lange 2015).
- Methods to track the patients' movements or gestures should be error free. More than one process can be used in a single tracking system. Feedback provided by the system should be accurate, should provide further steps to improvement (Ying and Aimin 2017).
- AR, VR game therapies should include a wider range of tasks which can guide the patients accurately (Ying and Aimin 2017). Increased number of tasks should be made available on easily accessible hardware. Currently, in many cases, standard controllers are used; these need to be modified as per need of PD/ Stroke patients. VR and AR technology can be made "wearable" so it can be used more easily for ADL.
- Furthermore, the research and development should be more focused to address concerns regarding standardization, power consumption, measurement validity, interoperability, and discretion of devices.
- At home, low-cost therapy options can make VR and AR approaches accessible for everyone. In addition to this, professional supervision will not be needed everywhere and the patient can practice therapy by himself.

8 Conclusion

In the last decade, extraordinary improvements have been made regarding the development of virtual and augmented reality systems for motor rehabilitation. Several target populations have been considered, especially stroke PD and MS patients suffering from UE and LE defects. In this work, at first, the knowledge base of different digital technologies has been established. Thereafter, in the context of VR and AR applied to the therapy of UE and LE, this chapter has reviewed some of the main developed systems and described their major findings. Related paradigms and therapy concepts have been grouped in four different categories: VR-based therapy for UE, AR-based therapy for UE, VR-based therapy for LE, and AR-based therapy for LE. All these techniques have a few common concepts like learning by imitation, reinforced feedback, haptic feedback, augmented practice and repetition, video capture virtual reality, exoskeletons, mental practice, and action execution/observation. VR- and AR-based approaches allow us to add to the conventional therapy to make it more effective, in a short period of time. In general, the patients that used VR and AR environments have experienced significant improvements in several performance parameters which directly impacts the activities of daily living. This review will act as a guide for research communities to use digital technologies for rehabilitation purposes.

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Chapter 11
Artificial Intelligence-Based Technological Advancements in Clinical Healthcare Applications: A Systematic Review

Shivansh Mishra, Mohamed Abbas, Kanak Jindal, Jyotindra Narayan, and Santosha K. Dwivedy

1 Introduction

Artificial Intelligence (AI) is a set of technologies to simulate human intelligence processes by machines. The AI covers a broad spectrum of applications such as automation of cars and industries (Shadrin et al. 2017; Hyder et al. 2019), Internet-of-things (IoT) (Chiang and Zhang 2016), computer vision (Guo et al. 2016; Jiang et al. 2017; Caffe 2021; Abadi et al. 1603), Natural language processing (NLP) (Alshahrani and Kapetanios 2016; Sarrouti and Alaoui 2017a, b; Kim 2010), and robotics (Rath et al. 2018; Narayan et al. 2018, 2020; Shademan et al. 2016). Shadrin et al. (2017) designed an autonomous car maneuvering decision system based on AI to increase automation efficiency. AI-integrated automation of trucks for mining applications can benefit the mining industry in terms of operation cost reduction (Hyder et al. 2019). Chiang and Zhang (2016) presented a dedicated architecture for data storage and computation to increase the efficiency of embedded AI. The performance of embedded AI can be enhanced by utilizing the storage and computational powers of IoT-connected devices instead of using a data center in the cloud server. Deep learning or deep neural network is an AI function and has many applications in computer vision (Guo et al. 2016). Convolution neural network (CNN) is widely used for computer vision applications because of its excellent image processing capabilities (Jiang et al. 2017; Caffe 2021; Abadi et al. 1603) as well as for sentence modeling, sentiment

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categorization, and question answering (Alshahrani and Kapetanios 2016; Sarrouti and Alaoui 2017a, b). NLP is a branch of AI that helps machines interpret human language. NLP can be implemented to learn a foreign language in a computer-based learning module (Kim 2010). AI has also been implemented in humanoid robots (Rath et al. 2018), surgical robots (Narayan et al. 2018; Shademan et al. 2016), rehabilitation robots (Narayan et al. 2020), and so on.

AI is revolutionizing healthcare widely. It has various fruitful applications in different fields of healthcare. The areas of AI application in healthcare can be divided into—clinical settings, biomedical computations, and pharmaceutical industries. A brief discussion about the current and prospective applications of AI in these fields is presented below:

Clinical Settings: AI application in the clinical setting can be categorized into (a) Bio-imaging (b) Big Data and Applied Text Mining in healthcare, (c) AI-assisted surgery, (d) Medical robots, (e) Diagnosis and Prediction of Disease. AI techniques like Support Vector Machine (SVM) and Convolution Neural Network (CNN) can detect lesions from MRI and CT-scan imaging (Griffis et al. 2016). AI has application in big data processing in rehabilitation (Rong et al. 2020), home assistance (Lloret et al. 2015; Dahmani et al. 2016), facial expression operated-controller (Rabhi et al. 2018), memory rehabilitation (Man et al. 2003). AI-based question-answering systems (Sarrouti and Alaoui 2017a, b) and various other applications (Rodriguez-Esteban et al. 2006; Athenikos and Han 2010) of AI use data-mining of the medical database. AI systems can assist in surgeries for surgical procedures (e.g., stitching) (Shademan et al. 2016) and surgical robots (Attanasio et al. 2021). Neuro-prosthesis are designed to monitor urinary bladder volume in patients with neurological disorders (Mendez et al. 2013a, b). A functional-genetic method is proposed to predict convulsion by the classification of brain signals (Assi et al. 2017). A man–machine interface in the upper body prosthesis is also designed (Farina et al. 2017). Robotic process automation (RPA) (Kepka et al. 2005) is a software technology to regulate the medical platforms used for radiotherapy authentication purposes. Diagnosis and prediction have two methods where AI can be implemented—signal processing (Cook et al. 2013) and medical imaging (Stoitsis et al. 2006). The AI integrated with clinical decision systems or fully automated clinical decision systems is being applied for diagnosis in healthcare. An AI-integrated clinical decision system for diagnosis and treatment (Jiang et al. 2017) of disease is shown in Fig. 1 below. This cyclic process of clinical decision-making is driven by data generated using clinical trials. The physical examination notes and clinical laboratory results are generated from clinical activities. The ML and NLP AI algorithms assist in the process of decision-making. NLP interprets the medical data, and ML analyses the output of NLP. NLP distinguishes the image, genetic and electrophysiological (EP) data from unstructured clinical notes. The unstructured data is converted to electronic medical record (EMR) data which is understandable by machine. ML techniques analyze the unstructured data taken as input from output of NLP and outputs structural data like probability of disease. AI is being tested to be applied for diagnosis of cancer (Somashekhar et al. 2017; Sweilam et al. 2010; Ford and Land 2014; Shi et al. 2017),

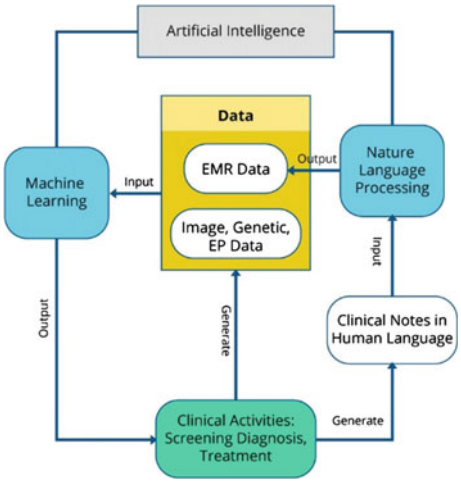

Fig. 1 AI-integrated clinical decision system. ML and NLP (Jiang et al. 2017) assist the cyclic process of clinical decision-making

heart diseases (Safdar et al. 2018) and, stroke (Ye et al. 2017; Asadi et al. 2016), which are deadly. AI also has applications in precision medicine (Lee et al. 2018).

Biomedical Computations: The process of AI assistance in biological research is shown in Fig. 2 (Rong et al. 2020). The doctor provides medical data and his imagination (model) to the AI system as input. The AI systems, based on the data and input model, contribute to the realistic models. The doctor or researcher can then decide on one of the most suitable models and generate its simulation codes for further study (Christley and An 2012). Computational Modeling Assistants (CMA) are the AI technology, which makes simulation models of the disease out of which a doctor or researcher can choose the best one (Liu and Yu 2014). Ontologies provide structured vocabulary for a scientific domain and focuses on class-structure and properties among the concepts in the domain. Many bio-ontologies are being developed which are used to define specific life science information like gene ontology (GO), foundational model of anatomy ontology (FMA), systems biology ontology (SBO), and physio-chemical process ontology (REX) (Rong et al. 2020). Gene Ontology (GO) is a systematic language to describe features of gene and gene products. Foundational Model of Anatomy Ontology (FMA) is a systematic language for human body phenotype and its features. Systems Biology Ontology (SBO) is for system biology, which is the field related to computational modeling of biological systems (e.g., organism). Physiochemical Process Ontology (REX) is ontology for physiochemical processes, which are physio-chemical changes happening over time, such as biochemical processes from gene ontology (GO). AI can search for research works and order them according to relevance for the ease of researchers (Névéol et al. 2009). AI is helpful in genetic engineering for aligning and giving momentum to research processes. One of the major research areas in this field is the design of remedial treatments for diseases. Microsoft Research Station B and Distributed Bio are AI technology companies working in this field (Using and To Engineer Biology 2021).

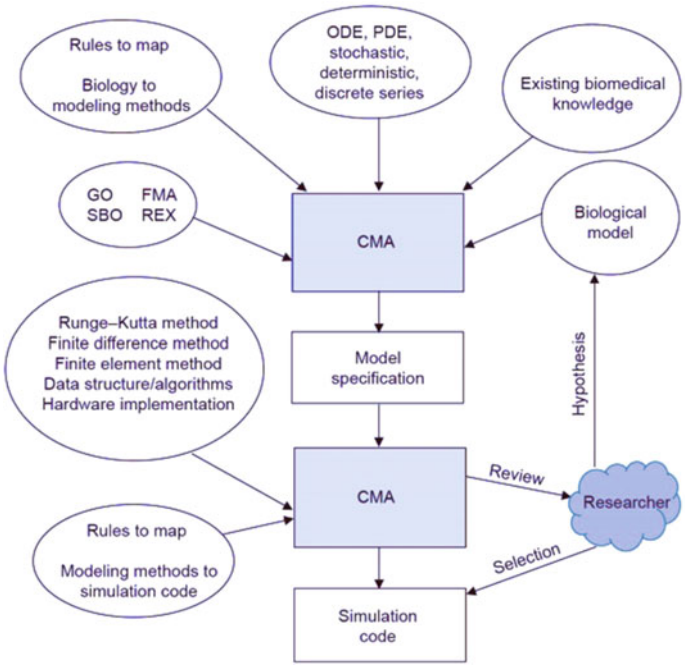

Fig. 2 Process of AI assistance in biomedical computations. ODE: ordinary differential equation; PDE: partial differential equation; GO: gene ontology; FMA: foundational model of anatomy ontology; SBO: systems biology ontology; REX: physicochemical process ontology (Rong et al. 2020)

Microsoft Research Station B has tied up with Oxford Biomedica to perfect the gene-remedial treatment for leukemia and lymphoma.

Pharmaceutical Industries: The process from a medicine discovery to deploying it for use is an extensive journey. It requires a lot of time and money for discovery, laboratory trials, and clinical trials. AI can be used to reduce time and make every step of this process cost-effective. Pharmaceutical industries are tying up with big AI technological start-ups for medicine development. 'Moderna' company has utilized Amazon's AWS cloud platform to make a cancer vaccine in 40 days only (Big Pharma is Using AI and Machine Learning in Drug Discovery and Development to Save Lives 2020). 'Riffyn' has designed a cloud-based software for biotech companies that collects and analyzes experimental data. This helps researchers to utilize their time on scientific works rather than experimenting and collecting data. Synthesizing new proteins for study purposes is one of the major concerns of pharmaceutical industries. AI technology companies viz., Atomwise and Arzeda provide ML computational platforms to run and monitor these computational biology studies. Atomwise provides an ML platform named 'AtomNet', which designs molecules and analyzes their performance (How AtomNet® Technology Improves Drug Design Using Convolutional Neural

Networks 2021). AtomNet is a CNN-based platform that identifies the target-protein structure and designs molecules to interact with them (How AtomNet® Technology Improves Drug Design Using Convolutional Neural Networks 2021).

Moving further with hardware requirements, CPU and GPU are exploited to implement AI in the domain of robotics (Rong et al. 2020). Although conventional NN models can be implemented on a regular computer's CPU, CNN models require GPU to be implemented on computers. CPU in combination with GPU can outperform CPU alone for spiking NNs (Naveros et al. 2017). Field-Programmable Gate Array (FPGAs) and Application Specific Integrated Circuits (ASICs) can be better hardware to implement ML algorithms as they are application-specific, compact, and efficient (Nurvitadhi et al. 2016). To implement AI on mobile devices or for IoT devices, Memristor Crossbar Circuits (MCC) are used by programming and storing its resistance. A memristor is defined as the fourth fundamental two-terminal circuit element having the resistor, the capacitor, and the inductor settings. Therefore, they are more stable and do not lose their state even if device loses power. MCC uses memory disk space for computation also, and this makes them storage-efficient and power-efficient. In the IoT application of AI, the data collected using sensors or Radio frequency identification (RFID) tags are stored in places like the cloud and can be used when needed. RFID uses the radio frequency waves to transfer the wireless data which helps in unique identification of an object.

Although several state-of-the-art reviews on the application of AI in healthcare are available; however, they have not covered the related topics systematically. Therefore, in this work, the role of AI in clinical settings is extensively presented, followed by an overview of AI in different healthcare applications. The rest of the chapter is structured as follows. In Sect. 2, different AI-based fundamental learning algorithms and associated recent developments are discussed. In Sect. 3, A PRISMA statement is provided to show the inclusion and exclusion criteria of the articles reviewed while conducting the systematic review. Thereafter, in Sect. 4, the integration of AI techniques in clinical settings is reviewed and presented. The impact of AI-based learning models is described for prior estimation of neurological diseases, surgical facilities, physical rehabilitation, and robot-assisted biomedical care units. Furthermore, in Sect. 5, the ethical and legal issues pertaining to AI implementation in different healthcare domains are reviewed. Section 6 discusses hurdles and related possible opportunities of deploying AI in real-life settings in the future. Finally, the conclusion of the current work is presented.

2 Fundamental and Advanced AI Forms

The basic form of AI, i.e., machine learning (ML), is explained in this section along with few state-of-the-art algorithms. Thereafter, advanced AI forms like deep learning (DL), reinforcement learning (RL), and natural language processing (NLP) are briefly presented.

2.1 Machine Learning

Machine Learning is the most common form of AI, which involves making models based on training data and learning of the model. Machine Learning (ML) models can be classified into supervised ML and unsupervised ML based on the utilisation of the results in the training data during model formation (Jiang et al. 2017).

Supervised ML: Algorithms relate input (parameters' value) and output (results' value). Supervised learning uses training data to make a model/algorithm which relates training data to results. Some popular supervised ML models are neural networks (Wilde 2013), support vector machine (SVM) (Suthaharan 2016), and random forest (Kaur et al. 2019). The neural network uses weighted parameters relating to input and output, similar to neurons. Extending the ML concept, deep learning uses a number of layered weighted parameters relating to input and output (Goodfellow et al. 2016).

Unsupervised ML: Algorithms, which identify patterns among input data values and group them. This grouping is used for extracting dominant features of the data. Principal component analysis (PCA) (Bro and Smilde 2014), clustering (Caron et al. 2018), and generative adversarial networks (GAN) (Creswell et al. 2018) are the main unsupervised ML techniques. Further post-processing of unsupervised model results can be used to increase the accuracy of supervised models. The algorithm in GAN evolves by training on a given dataset using a variable classifier. GANs use the game theory of learning. Recently, GANs have application in image generation, generation of 3D models from images, advising drugs for disease, and so on (Alqahtani et al. 2019).

2.2 Deep Learning

Deep learning is an expanded form of supervised ML technique with many hidden layers of the neural network (Goodfellow et al. 2016). Deep learning technology is a dense neural network comprised of an input layer, an output layer, and one or more hidden layers in between. In various types of modern neural networks, these layers may be interconnected in many ways. They may be classified into feedforward, perceptron, auto-encoder, and recurrent neural networks. Deep learning is a modified version of the classical neural network, which has gained popularity in recent years (Schmidhuber 2015). This is due to its ability to handle complex and large amounts of data. Deep Learning models are effective and popular in oncology and other modalities related to scan imaging data processing.

Convolutional Neural Network (CNN): It is one of the most popular deep learning techniques. CNN is used for image processing. CNN takes the image pixels' data and processes them after weighing at different layers (Albawi et al. 2017; Abbas et al. 2020). The training goal is to optimize the weights for minimum error at estimating

the output. Various tools using CNN have been developed, such as TensorFlow by Google (Abadi et al. 1603) and Caffe from Berkeley AI Research (Caffe 2021). CNN has made image processing easier as it does not require an image to be analyzed before feeding to the algorithm for training. CNN has application in medical imaging due to the increased computational power of modern-day computers. CNN has gained popularity in medical image diagnosis due to its ability to analyze complex and high-dimensional data (Jiang et al. 2017). Another CNN technique, You Only Look Once (YOLO), is designed to identify the objects from an image (Du 2018). It uses only one neural network to solve regression problems on bounding boxes made across the images. It has the advantage of faster identification and increased accuracy. Therefore, it is helpful for applications requiring real-time object identification. However, it has demerits of non-general nature for different aspect ratios of objects and chances of loss of accuracy.

2.3 Reinforcement Learning

Reinforcement learning (RL) is an AI technique that performs tasks based on rewards while learning (Zoph and Le 1611). In RL, some reward is given when the algorithm learns the task; otherwise, it loses the reward with a penalty. This algorithm learns intending to maximize the reward gain and minimize the penalty. The reward can result in the accuracy of the architecture of a neural network (Zoph and Le 1611). Zoph and Le (1611) used reinforcement learning for a Recurrent Neural Network (RNN), which trains itself using resulting accuracy on a given dataset as a reward. Reinforcement learning has applications in robotics and customized suggestions (Ritschel et al. 2017). RL has the disadvantage of high computational power requirements.

2.4 Natural Language Processing

NLP is an AI technique used to read and interpret human language both, verbal and written (Murff et al. 2011). NLP is related to understanding human language, interpretation (defining), and its application. NLP has two types: statistical and semantic; statistical is based on a deep neural network and requires large training data, i.e., 'corpus'. Semantic analysis works with the help of machine learning algorithms. The task of semantic analysis is to find the proper meaning of the sentence while interpreting the meaning of each word. NLP algorithms can assess a medical report (clinical note) with as excellence as a doctor. It works on two significant aspects, i.e., text-mining and categorization. The algorithm searches for relevant words and phrases for the outcome of interest in the text-mining of clinical notes and reports. Then after identifying the words and phrases, the algorithm matches them whether they are related to the disease detection. Then the recognized words and phrases

are included in the vocabulary for post-processing the data based on AI techniques. NLP can be used majorly in two areas of clinical settings—medical assistance for accurate adverse event reporting (Miller et al. 2017) and disease diagnosis (Castro et al. 2017).

3 Methodology Adopted

Many articles were searched from digital sources such as Scopus, the Institute of Electrical and Electronics Engineers (IEEE), PubMed, and Science Direct. Moreover, other sources such as websites and organizations' web links were also explored. The keywords for the search were '(artificial intelligence OR machine learning OR deep learning OR natural language processing) AND (healthcare OR biomedicine OR clinical-setting OR drug discovery OR pharmaceutical industry) AND (bio-imaging OR applied text-mining OR rehabilitation OR surgery OR medical robotics OR diagnosis OR clinical decision system OR prediction OR mental health OR psychopathology) AND (ethical OR legal OR safety)'. Initially, using these keywords, 17,003 articles were found from digital databases, and 239 sources were accessed from other sources. After removing the duplicate records, 6391 articles were relevant, including the title and abstract inclusions. Further, excluding the title and abstract only documents, 1109 articles were found to be eligible and assessed additionally for specific exclusion points. Exclusion criteria were (1) AI applications other than healthcare; (2) AI in environment-related diseases; (3) patents in AI-aided healthcare system; (4) papers before the year 2010. Following the exclusion criteria, finally, 87 out of 1109 articles were found to be appropriate and reviewed in a detailed manner. However, it is pertinent to mention that 26 articles out of 87 were included to highlight the literature on different AI techniques.

Opinions of all the authors were considered in reaching a conclusion to include an article based on the methodology. A consensus was made when a conflict of opinions for inclusion did arise. A PRISMA flowchart illustrating the inclusion and exclusion of records is shown in Fig. 3.

4 AI in Clinical Settings

In this section, the applications of AI in clinical settings such as bio-imaging, applied text-mining, surgery, medical robotics, and diagnosis and prediction of disease are elaborated systematically.

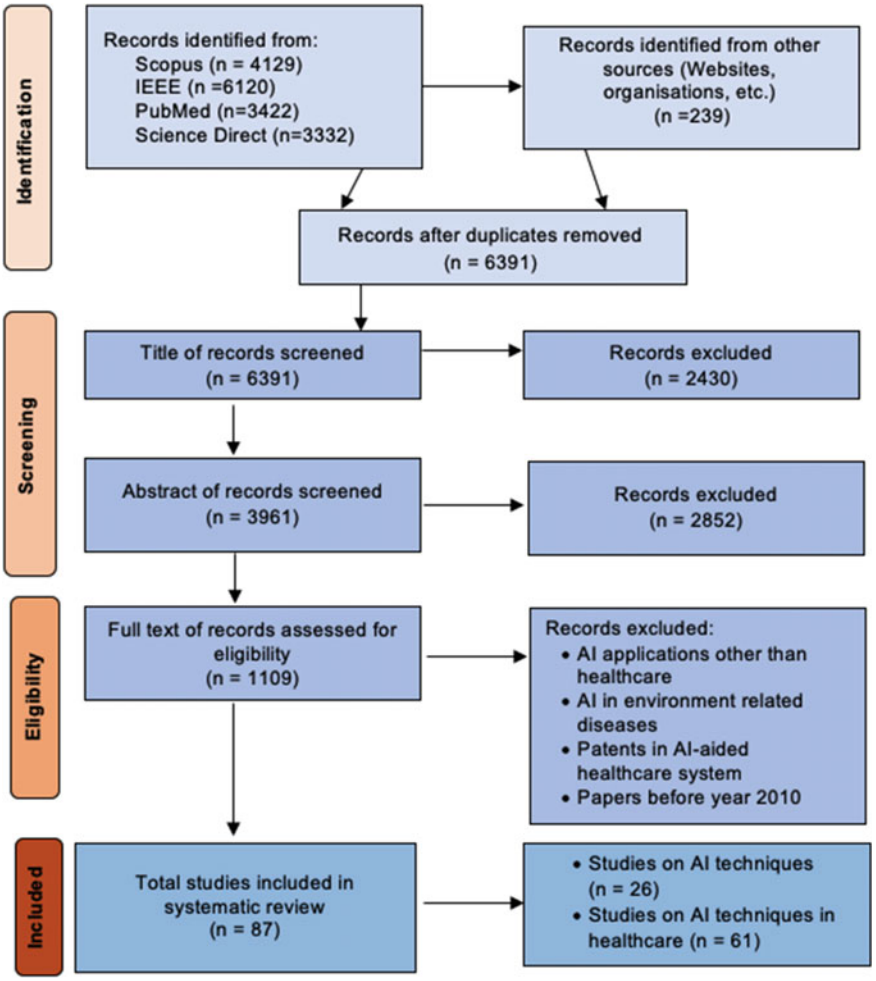

Fig. 3 Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flowchart

4.1 Bio-Imaging

ML models such as CNN and SVM have the ability to identify lesions from MRI and CT-scan images (medical images). Figure 4 illustrates the percentage-wise application of different ML algorithms in the field of imaging (Jiang et al. 2017). Griffis et al. (2016) developed an ML model based on Naïve Bayes classification to identify the injured portion of the MRI of the nervous system. Thornhill et al. (2014) developed three ML models which detect a blood clot in a CT-scan image of the nervous system, which is not possible by classical methods. They created artificial neural network (ANN), SVM, and discriminant function analysis models having an

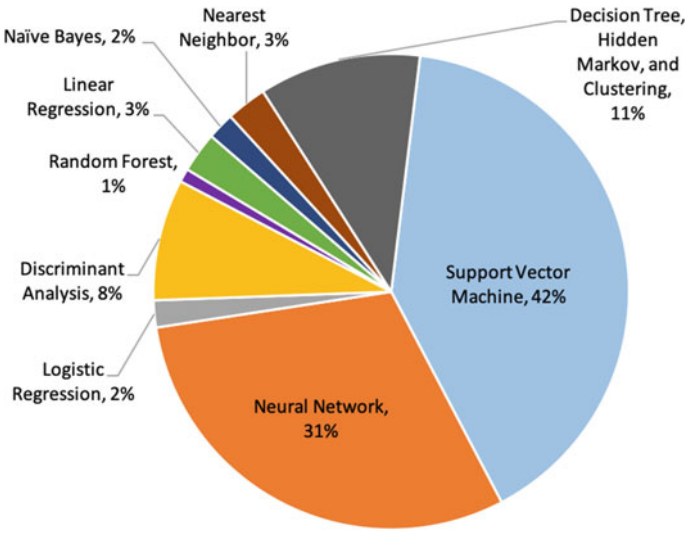

Fig. 4 Application of different ML algorithms in imaging (Jiang et al. 2017)

accuracy of near about 70%. In medical imaging, AI can increase the quality of images and thus increase the efficiency of diagnosis (Stoitsis et al. 2006). Miller et al. (2017) used NLP to identify and report adverse events in clinical trials. The medical data obtained from the trials were analyzed and found to predict an adverse event accurately.

4.2 Applied Text Mining in Healthcare

Applications like rehabilitation and personal care require big data to be considered while augmenting the AI system (Rong et al. 2020). The big data in rehabilitation may be walking data of joint angles, joint moment, and ground reaction force. In the case of personal care, it may be data about one's living environment and one's daily activities (Lloret et al. 2015). Dahmani et al. (2016) proposed a personal care AI system for home assistance for people with loss of autonomy (PLA). The home assistance AI system model was based on wireless sensor networks (WSN) and data-mining. It provided independence and better quality of life to the PLA. Rabhi et al. (2018) developed an AI-enabled controller for rehabilitation devices for the disabled, which was controlled using facial expression. The AI-enabled controller was trained to recognize human facial expressions using image processing and perform tasks accordingly. Man et al. (2003) developed a memory rehabilitation AI system to assist people with memory damage. The AI system gathers big data from a person's (user's) surroundings (home) and essential daily activities in the cloud or mobile

device. Then it takes a decision using the computational powers of the device and reminds the user of crucial tasks through SMS or alarm alerting signals.

NLP has excellent potential in biomedical question answering and applied text-mining of medical data (Rong et al. 2020). An NLP system can answer a patient's questions by making decisions after identifying, searching for words and phrases in a medical database. NLP can gather information based on a questionnaire in the form of yes or no (Sarrouti and Alaoui 2017a). This is one of the four types of biomedical question-answering using NLP (Sarrouti and Alaoui 2017b). NLP has applications in organizing and updating medical data to be utilized efficiently (Athenikos and Han 2010). NLP can mine for data from a lot of sources, categorize them and, then arrange. NLP deep learning models are also used to make reports based on radiology, extract relevant information, and note down doctor-patient conversations.

4.3 Surgery Facilities

AI application in surgery is limited to assistance in surgical procedures like stitching an incision (Jiang et al. 2017). Narayan et al. (2018) proposed an adaptive neuro-fuzzy inference system (ANFIS) for path planning of a 5-DOF medical robot while performing minimal invasive surgery (MIS). The ANFIS approach is a hybrid form of neural networks and fuzzy logic. Shademan et al. (2016) developed a medical robot based on supervised ML to perform stitching surgery. The robot used information from a light field imaging system to perform stitching in surgery on pigs. When integrated with processing systems or computers of devices, AI technologies like image processing become 'intelligent' physical robots and have application in head, neck, and prostate surgery (Attanasio et al. 2021).

4.4 Medical Robots

The urinary bladder in people with a neurological disorder and elderly malfunctions, and thus excess urine volume and pressure can be harmful. Mendez et al. (2013a, b) designed a neuro-prosthesis to monitor urinary bladder volume and inside wall pressure. The neuro-prosthesis also regulates the mechanoreceptors to send signals (neural signals) to the brain for timely urination. The device consists of two modules—a sensor to be put inside the bladder and a wearable computer device. The two are connected via Wi-Fi (wireless), and the sensor can exchange neural signals with the computer using an ML algorithm to make a decision based on them. Convulsion is a neurodegenerative disorder, which can pose a lifetime threat to a patient due to its unpredictability. BouAssi et al. (2019) developed a method based on directed transfer function (DTF) and AI to predict convulsion. They detected the brain signals using the directed transfer function (DTF). Then, they used intracranial electroencephalography (iEEG) signals of dogs to train the ML algorithm. The

AI-based method classifies the intracranial electroencephalography (iEEG) signals into normal, onset, and intermediate. This can be used to design a device that can predict an onset of a seizure. Farina et al. (2017) used SVM supervised ML model for man–machine interface in an upper body prosthesis. Robotic Process Automation (RPA) is a structured rulebook that can be implemented in information systems of clinical settings. These virtual robots behave as 'semi-intelligent users' who perform repetitive works like authenticating systems. RPA is used in healthcare for authentication, updating patient data, and bill-payment automation. AI is also being used in making a set of 'if–then' rules for decision-making purposes in healthcare (Ravi et al. 2016).

4.5 Diagnosis and Prediction of Diseases

Cancer is a deadly disease, and its early diagnosis can be life-saving. The SVM supervised ML models have been used for cancer's (Dheeba et al. 2014) and Alzheimer's (Khedher et al. 2015) early detection. AI-enabled gene expression is a new technique for cancer diagnosis application using microarray data categorization (Shi, et al. 2017). In work by Dheeba et al. (2014), Neural Network has been used to diagnose breast cancer using mammography images. The consistency of mammography images was analyzed using a neural network. Based on the classification, unusual cases were identified more accurately than conventional diagnosis techniques. IBM Watson is a promising AI technology for oncology applications, which uses ML (for structured data) and NLP (for unstructured data). Researchers have used IBM Watson to predict cancer with an excellent efficiency of 99% (Somashekhar et al. 2017). The assistive decision system assists the clinical decision-making and performs diagnosis management. Safdar et al. (2018) used AI as an assistive clinical decision system to diagnose heart diseases.

Stroke causes many deaths in North America, China, and other countries (Jiang et al. 2017). Stroke can be deadly when not detected and treated in time. ML models can be helpful in the early diagnosis and medical treatment of stroke (Jiang et al. 2017). Villar et al. (2015) contributed a gait monitoring ML model. This ML model was embedded in a device and detected any change in the gait pattern. It further finds ways to treat the stroke based on the symptoms observed. Treatment efficiency is one of the major concerns for doctors as well as patients. Treatment of stroke is done using intravenous thrombolysis (tPA). ML models can optimize a treatment procedure based on the set of rules and clinical trial data available. Ye et al. (2017) developed an ML model based on 'interaction trees' and 'subgroup analysis' to decide 'tPA treatment frequency' considering the individual patient data. Post-treatment safety is needed to be ensured for the patients. ML model with increased prediction accuracy offers a safer way for monitoring post-treatment complications. Asadi et al. (2016) developed an SVM and ANN-based prediction model to analyze patient health after brain surgery. They predicted the outcomes with 97.5% accuracy over 43% of conventional regression-based prediction. AI can prevent harmful consequences of

epileptic seizures by predicting them by analyzing EEG (electroencephalography) signals (Cook et al. 2013). Castro et al. (2017) used NLP to diagnose neurological disease-related words from clinical notes. An accuracy of 95% and 86% were obtained in NLP-enabled diagnosis of training and testing, respectively. Recently, in Yu et al. (2020), a stroke diagnostic and prediction system is developed using real-time electromyography signals (EMGs). The proposed approach utilizes the random forest (RF) and long-short-term-memory (LSTM) as ML and DL algorithms. The stepwise procedure to predict the stroke using AI techniques is shown in Fig. 5. There are two modules, offline and online processing. The offline module includes ML and DL algorithms analyzing EMG data. The online module is based on real-time collected bio-signal detection and prediction. In offline module, daily data is collected and stored in the system for pre-processing of EMG bio-signal using ML and DL algorithms. For early detection, attribute subset selection is done on pre-processed data. The ML LSTM-based training models are developed and sent to the second module for online processing then used for real-time stroke prediction. The online module collects real-time EMG data whenever requested by user or system. Incomplete data is handled by 'pre-processing and normalization'. The accuracy can be improved by attribute subset selection. The DL LSTM-based model detects and

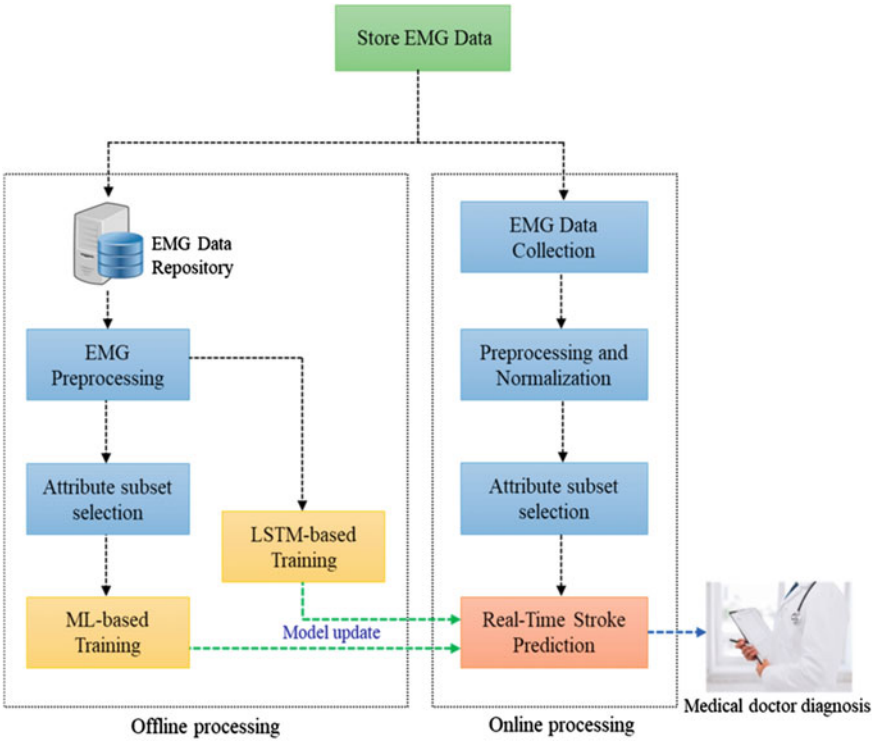

Fig. 5 Schematic diagram of ML- and DL-based stroke prediction (Yu et al. 2020)

predicts stroke in real time by processing the data obtained after pre-processing. In the end, predictions are provided to staff and the patients will be provided assistance based on medical doctor's diagnosis.

4.6 Psychopathology and Mental Disorder

Psychological and mental disorders viz., depression, bipolar disorder, post trauma stress disorder (PTSD) show common symptom of defective semantics (tone, words, written). Semantic analysis for the pathology of psychological and mental disorders can be done using AI (Corcoran and Cecchi 2020; Glaz et al. 2021). At first, the data is collected from medical database and social media (Glaz et al. 2021). Secondly, this data is analyzed for medical terms using NLP (for unstructured data such as doctor-patient interaction) or information extraction algorithms (for structured data viz., EHRs) and stored as medical vocabulary. Now SVM, random forest and neural network, categorization ML algorithms are used for classification of the text or medical terms. Based on the classification, patients are diagnosed or an analysis is performed on their medical data. Metzger et al. (2017) developed an AI algorithm to predict the proportion of emergency cases because of suicidal attempts in France. It used EHRs to extract features and then classify them based on ML algorithms viz., random forest, naïve Bayes. Post-trauma stress disorder (PTSD) is a major concern among population affected by accidents. In another such work, McCoy et al. (2016) used NLP for suicide risk-categorization in patients discharged from hospital. They collected discharge-statements of patients from the EHR database of hospital. Further, they evaluated and categorized the statements based on a rating. The rating was obtained by comparing them against a list of key terms using Pattern, version 2.6: Python, an open source sentiment analysis tool. They demonstrated that AI-enabled risk-categorization can effectively augment post-discharge monitoring of patients based on their EHR. Timely diagnosis of PTSD is important for further treatment. An efficient prediction model would help reduce the time and cost for identifying the needy population. He et al. (2017) proposed a technique to diagnose PTSD using NLP and text-mining on statements obtained from trauma survivors. They compared various ML algorithms viz., SVM, decision tree, naïve Bayes, product-score model (PSM) for text classification. Further, they used a combination of text classification and data representation to identify attributes and classify the data. Their study demonstrates the credibility of PTSD prediction using AI-based prediction model.

5 Challenges and Future Directions

The deployment of AI in the medical field comes with many hurdles, which need to be considered and resolved. The AI application in the medical field needs to have guidelines associated with it for safety and efficiency. The US FDA has made guidelines with primary concern over three aspects—the safety of the users, applicability in the practical world and, assessment for iterations in design (Intelligence et al. 2021). Data sharing for machine learning databases also poses a challenge for AI applications in the medical field (Jiang et al. 2017). There is a lack of motivation for hospitals and research labs to share their patient data and clinical trial data. Following this, the problem of non-generalized ML algorithms arises as the training for an ML algorithm is limited to only one clinical setting (say, one hospital) (Obermeyer and Emanuel 2016). Non-generalized ML models do not predict outcomes accurately since the problem of overfitting of testing data may arise (Kallianos et al. 2019). In such cases, the decision of the best ML model can be taken by a group of experts, known as consensus diagnosis (Krause et al. 2018; Ribeiro et al. 2016). The difficulty of elucidation of ML algorithm leads to another issue for doctors who don't have the necessary skills. Elucidation of ML algorithm is important as then only its result can be utilized and trusted for decision-making. Efforts are being made to explain ML algorithm's results to a doctor who does not have the needed data engineering skills. Ribeiro et al. (2016) proposed an optimization technique to elucidate the deep learning ML model used for non-imaging data. They also demonstrated that this technique can be applied to text-based (random forest) as well as image-based (neural network) classifiers. The research in this field is still going on.

Application of AI in mental health can unexpectedly fail on the criteria of fairness and plausibility. The programmers may outweigh certain parameters over others in the algorithm based on their knowledge and experience. AI can be used as a virtual doctor for people who feel less confident in explaining their symptoms to a doctor (Glaz et al. 2021). Studies have shown that people open up more to a computer than to a person. This way AI can provide an effective solution for people with mental and psychological disorder. For example, an algorithm to predict outcomes of psychosis may be coded to outweigh clinical parameters over socioeconomic (Martinez-Martin et al. 2018). The outcome of such AI algorithm would exclude potential patients based on only clinical neglecting socioeconomic parameters.

5.1 Conceptual and Modeling Issues of AI in Healthcare

There is a lack of capability of existing ML algorithms to handle and utilize features of patient medical data for broader diagnosis purposes (Yu et al. 2018). For such broader diagnosis, an ML model that can utilize the patient's demographic data, previous medical complications data, etc., can be designed. Third-party software is needed with a secure computing environment to use the patient medical data across all

clinical settings. For example, the 'Substitutable Medical Applications and Reusable Technologies on the Fast Health Interoperability Resources platform' (SMART on FHIR) (Mandel et al. 2016) is an application that integrates the medical data of patients across all healthcare settings. The clinical trial data for training AI systems are mainly obtained from laboratories and are not taken from clinical settings. Other clinical setting-based trials need to be explored and use their medical data to make use of the AI systems better.

Radiologists use non-imaging data in addition to imaging data to make decisions. So, it is necessary for AI-based CDS to take into account both. Currently only medical-imaging data are being used for training deep learning models as the capability for analyzing non-imaging data is in the developmental stage. Therefore, there is a challenge for inclusion of clinical context in the form of non-image data in the training data. There is also a challenge of gap in knowledge-sharing due to lack of standards for publication. The researchers do not elaborate computational techniques used to develop their ML models. This might be due to un-awareness, inexperience with new ML techniques and, word-limit. Therefore, other researchers can't apply others' findings in their own research, being unable to interpret the ML model. Therefore, there is a need for implementation of standards of articles to include the ML techniques. For that, journals need to define rules and regulations for publishing an article (Kallianos et al. 2019).

5.2 Ethical and Legal Issues of AI in Healthcare

Implementation of AI systems raises some genuine ethical and legal issues, which need to be addressed. There is a significant concern for the safety and privacy of a patient's medical data (Lee and Gostin 2009). When shared for training an ML model, a patient's medical data contains confidential information and, when shared for training an ML model, can risk a patient's privacy. AI implementation in healthcare clinics and hospitals will remove the workload of doctors from daily tasks. Thus, doctor-patient interaction can be enhanced for better treatment outcomes. However, this might affect a healthcare personnel job who performs such daily tasks. AI-enabled clinical assistants may hamper the daily clinical tasks; therefore, keen monitoring will be needed. Also, Electronic Health Record (EHR) systems need to be designed and implemented in a user-friendly way (Middleton et al. 2013). American Medical Informatics Association (AMIA) suggests that by using a user-friendly EHR, better, safer, and profitable healthcare services can be provided. As the AI systems keep evolving with data and trial results, it needs to be developed according to standard rules. To address this, administrative bodies are required which set those rules and provide licenses to AI developers. Implementation of AI in Clinical Decision Support (CDS) poses critical legal challenges (Yu et al. 2018). CDS gives the person-specific information which is intelligently filtered. CDS includes tools that enhance decision-making. It is unclear now who will be accountable for mismanagement that occurred while implementing AI in Clinical Decision Support (CDS).

Moreover, health insurance does not have remission guidelines for AI systems implemented in healthcare. To overcome such ethical and legal challenges, AI technology companies and developers must work in unison with healthcare professionals.

6 Conclusions

AI is a set of technologies which has application ranging from autonomous cars to healthcare. AI application in healthcare can be categorized into the clinical setting, computational biology, and pharmaceutical industries. In this work, a brief discussion has been made about AI applications in all three fields. Fundamental and advanced AI techniques, which are being used for healthcare applications, have been reviewed. Thereafter, the clinical settings of healthcare application, which exploits AI, have been reviewed and discussed in detail. AI application in the clinical settings has been categorized into bio-imaging applied text-mining, surgery facilities, medical robots, diagnosis and prediction of disease, and psychopathology and mental disorder. NLP has great potential in biomedical question-answering and applied text-mining of medical data. Medical robots in the form of neuro-prosthesis, convulsion prediction systems, and authentication systems are being used. From the review, it has been observed that AI is efficiently applied to diagnose and predict deadly diseases like cancer, heart diseases, and stroke. NLP and text-mining AI techniques have been found effective in psychopathology and diagnosis of mental disorder. The ethical and legal issues for the successful implementation of AI in the clinical setting have been demonstrated. This work has reviewed the issues related to the patient's privacy, changing environment of the clinical setting due to AI implementation, lack of rules and regulations for AI in clinical settings. Moreover, non-generalized ML algorithms facing difficulty in the elucidation of results have been noticed as key hurdles in implementing AI in clinical settings.

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