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3D printed phantoms for medical imaging: recent developments and challenges

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Abstract The rapid growth of 3D printing technology has transformed different fields in medicine, for example the fabrication of medical phantoms - physical models mimicking biological tissue in medical imaging and therapy. These phantoms play a crucial role in quality assurance, education, research and training. Unlike traditional methods, 3D printing enables the creation of anatomically accurate, cost-effective, modular, and customizable phantoms with high geometric freedom. A key advantage is the ability to produce patient-based models, tailored to individual anatomies and pathologies using medical imaging data. The workflow involves processing imaging data, refining 3D models, and selecting suitable 3D printing materials. This overview focuses on the workflow, types of phantoms, and the selection of printing techniques and materials. Besides numerous opportunities, challenges include standardization, validation procedures, and ensuring reliability across different systems. The potential of 3D printing in medical phantom development is evident, promising realistic, cost-effective, and personalized solutions for improved medical research.

1. Introduction

The rapid growth of three-dimensional printing technology (3D printing or additive manufacturing) has offered many new possibilities in the medical field. Traditional manufacturing methods, which are often time-consuming and expensive, have been complemented by the advantages of 3D printing. This technology allows for the creation of anatomically accurate, cost-effective, modular, and customizable models with a high degree of geometric freedom. One of the key advantages of 3D printing in medicine is its potential to produce patient-based and patient specific structures. The various applications in medicine, briefly summarized in Fig. 1, range from medical products and equipment, pharmaceutical products, tissue and biomaterials, medical devices to physical 3D models. Within the area of physical models, there are training and education models as well as models used for preoperative planning [1, 2]. Finally, there are also so-called phantoms. Phantoms are physical models designed to mimic biological tissue and its properties in medical imaging, playing a vital role in quality assurance, education, research, and training across medical disciplines. Additionally, phantoms are the primary application of 3D printing within the field of radiotherapy [3].

With 3D printing, the fabrication of medical phantoms has undergone a significant transition. This innovative technology has complemented and replaced traditional manufacturing methods, which are typically time-consuming and costly for phantom manufacturing. The increase of 3D printed phantoms in the past ten years can be seen in Fig. 2. The search of the database Scopus for publications with title, abstract or keyword of “phantom*” and “3D printing” or “additive manufactur*” showed a 14-fold increase in publications from 2013 to 2023.

In the field of 3D printed phantoms, various types are designed to address specific clinical needs and research requirements. Some phantoms focus on replicating specific organs or anatomical structures, while others focus on quality assurance. This review outlines recent developments, innovations, and challenges using 3D printing technology for phantom fabrication. It centers on two main aspects: (i) how 3D printed phantoms are being manufactured and

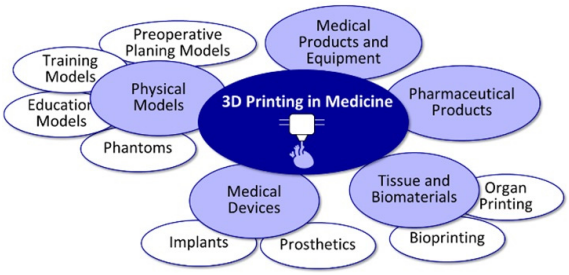

Fig. 1. Overview of the application areas of 3D printing in medicine.

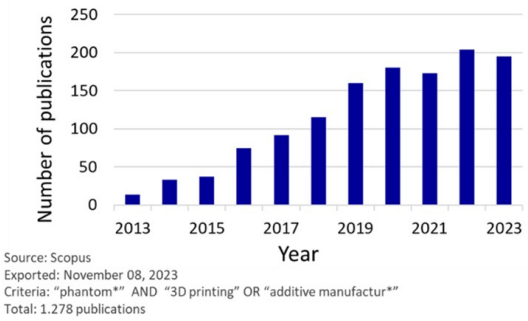

Fig. 2. Number of 3D printed phantom publications in the past ten years (search criteria listed below graph).

(ii) the workflow for developing a 3D printed phantom.

2. Types of 3D printed phantoms

The key to a phantom is the tissue-equivalent material (also known as surrogate), which replicates specific properties of a tissue in the human body in order to imitate it as realistically as possible for medical imaging. As displayed in Fig. 3, there are two manufacturing options for producing phantoms using 3D printing [4, 5]. One approach involves the direct production of the desired model or segment using 3D printing. Alternatively, indirect production occurs through the creation of tools and molds. The latter is used when a mold or mold inserts of the phantom are manufactured using 3D printing. Material requirements for tissue equivalence of the printing material only have an influence on direct production, whereas they play no role in the indirect production of a mold. Direct production can be achieved either by printing a tissue-equivalent material, or by producing a hollow structure that is filled with an additional surrogate. Furthermore, a combination of both direct and indirect manufacturing methods be employed within a single phantom, enabling, for instance, the fabrication of diverse organs with distinct characteristics. Application examples of the different production methods are described in the following subsections.

2.1 Direct manufacturing

In the direct production of a 3D printed phantom, the representation of the material used in the investigated imaging modality is crucial. Consequently, the manufacturing material must

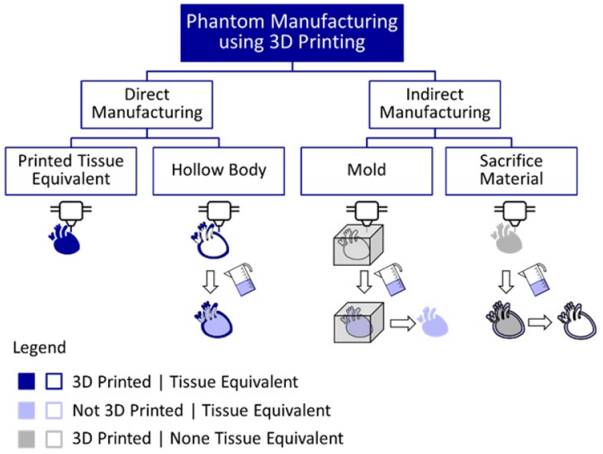

Fig. 3. Phantom manufacturing options using 3D printing (adapted and expanded from Refs. [4, 5]).

mirror the properties that are essential for the given imaging technique, such as appropriate x-ray absorption, sound velocities, or magnetic resonance relaxation times. These properties are influenced among others by materials attenuation coefficients, mass density, effective anatomic numbers, speed of sound or acoustic impedance [6]. Printing resolution and costs should also be considered when choosing a 3D printing material and method for direct phantom manufacturing [7].

Nevertheless, there are still limitations to overcome. In their review on 3D printing for imaging phantoms, Filippou et al. [6] discussed several challenges regarding materials and printing accuracy. They highlighted that printing accuracy and the ability to mimic all tissue properties adequately is still challenging. For instance, while certain materials can replicate specific properties such as tissue density, they may fall short in replicating others, such as speed of sound or attenuation.

Relevant 3D printing techniques for the production of phantoms include fused deposition modeling (FDM) and stereolithography (SLA) [4, 6, 8]. In their review Tino et al. summarized 3D printed phantoms for radiotherapy applications [9]. They included 53 studies listing the printing process, printer and the material used [9]. These range from PLA, ABS, acrylic polymer, epoxy resin to HIPS with printing processes from FDM, SLA to polymer jetting technology (PJT), digital laser printing (DLP), selective laser sintering (SLS), multi-jet printing (MJP) [9].

In FDM, the object is produced layer by layer from a filament that can be melted. This process is particularly interesting since different tissue-mimicking properties can be obtained by varying the infill parameters achieved [6, 8, 10–14]. For example, Hong et al. evaluated different infill ratios of ABS, TPU, and PLA materials for computed tomography (CT) phantoms [15] and manufactured different lung phantoms, see Fig. 4(f). Their study demonstrates that a wide range of CT values can be achieved by controlling the internal filling of the 3D printing material. There are also other studies, like the one conducted by Rai et al., who looked at 3D printed material for magnetic resonance imaging (MRI) phantoms [16]. They successfully 3D

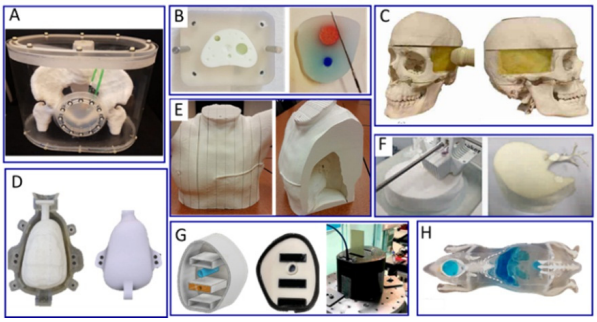

Fig. 4. Selection of 3D printed phantoms: (a) pelvic phantom from Ref. [4]; (b) prostate mold and prostate phantom from Ref. [4]; (c) head phantom from Ref. [17]; (d) bladder mold and bladder phantom adapted from Refs. [4, 18]; (e) sliced thorax phantom from Ref. [19]; (f) lung phantom from Ref. [15]; (g) arm slice phantom from Ref. [20]; (h) mouse phantom from Ref. [21].

printed test phantoms using a combination of visible and non-visible materials, achieving adequate MRI signal and contrast [16]. Craft and Howell printed a thorax phantom using 100 % PLA infill as well as air cavities [19], see Fig. 4(e). Another example for FDM printing PLA and PETG, in this case for nuclear medicine, can be found in Gillet et al. [22].

Material properties can be influenced by producing an individual print filament and thus adapted to specific tissue types [23]. For example, adding additives into commercial printing resin, as demonstrated by Badiuk et al. [24], who achieved CT-values for bone by adding calcium carbonate and strontium carbonate powders into SLA resin. Another advantage of 3D printing a phantom directly is the possibility of applying several materials at once with a multi-material printer [14, 23]. Even the classic support material of an FDM printer can later be used as a second tissue in imaging.

As another example of a printing method used for direct phantom manufacturing, Wegner et al. used SLA to print a mouse phantom body for preclinical radiotherapy applications [21], see Fig. 4(h). Leaving un filled cavities that are later filled with other none 3D printed surrogate materials [21]. Leonov et al. combined FDM and liquid cristal display (LCD) 3D printing to produce a head phantom for transcranial ultrasonography [17], see Fig. 4(c). They also used non 3D printed polyvinyl chloride plastisol to fabricate an acoustic window in the skull [17].

Next to the direct printing of tissue-equivalent parts, the 3D print can also be used as an anatomic shell filled with a surrogate. In Breslin et al., an application of this process can be seen regarding an 3D printed arm phantom [20], see Fig. 4(g). The outer shell and radiation dosimetry compartments for the upper arm segment are printed with a FDM process [20]. Badiuk et al. [24] also used a combination of 3D printing and classical fabrication. Specifically, the bone structure and a skin shell of the head were 3D printed, with the soft tissues subsequently mimicked by filling the shell with polyurethane rubber [24].

2.2 Indirect manufacturing

The use of 3D printing as an indirect manufacturing method for phantoms involves 3D printing of a mold or a sacrificial material used in phantom creation, rather than of the phantom itself. For instance, Adams et al. [25] demonstrated the use of a 3D printed mold for a kidney phantom, incorporating a 3D printed wax structure within the mold structure as well, which was later removed after polymer molding. A similar process is used by Kadoya et al. [26]. Another example in Wegner et al. involves the creation of a mold for a deformable anatomical silicon bladder, with a dissolvable core material (PVA), also 3D printed and subsequently removed post-molding [5], see Fig. 4(d). These examples combine to advantages of printed sacrifice material and a printed mold. A mold without a sacrifice material can be found in Wegner et al. where a 3D printed mold is used to fabricate a prostate phantom [4], see Fig. 4(b).

This indirect approach is particularly advantageous when the incorporation of solid walls may cause unrealistic boundaries in the phantom, or when the 3D printing material does not align with the imaging modality requirements for a specific tissue or application, since the printing material doesn't have to be a tissue equivalent. Thus, this technique ensures greater flexibility in tailoring the phantom composition and properties to the desired anatomical and imaging specifications.

2.3 Combination of direct and indirect manufacturing

The combination of both direct and indirect manufacturing processes in the creation of a phantom offers a versatile approach to phantom development. This hybrid methodology harnesses the strengths of each technique. Direct manufacturing allows for the precise printing of tissue-equivalent materials, ensuring fidelity to specific patient characteristics. Meanwhile, indirect manufacturing introduces flexibility by utilizing 3D printed molds that can be filled with various tissue-equivalent mixtures, accommodating a broader range of anatomical structures. This synergistic approach enables the fabrication of complex, multi-component phantoms, where more than one organ or tissue are incorporated in the phantom, like phantoms of the whole abdomen [4].

3. Workflow for developing a 3D printed phantom

For a future standardization of phantom development, it is necessary to adopt a well-established production workflow. Conventional product development processes are structured to facilitate the creation of technical products. Examples of such methodologies include VDI 2221 [27] and the V-model outlined in VDI 2206 [28], which is specifically tailored for the development of mechatronic models. The basic steps can be adapted and applied to the development workflow for 3D printed phantoms. They consist of (i) a planning phase, (ii) a concept phase, (iii) a design phase and, finally, (iv) a validation phase, as seen in Fig. 5.

Fig. 5. Four basic phantom development phases.

3.1 Planning phase - phantom requirements

3D printed medical phantoms encompass a diverse array of applications, each tailored to specific needs within the medical imaging field. When developing a phantom, the first step should be to gather information on phantom requirements (cf. Fig. 5). This should include the application of the phantom, which consist of phantom purpose, area of application and represented anatomy. Phantom purposes can range from quality assurance/ control and calibration to research and education or training phantoms [29]. It is important to specify the purpose, since it defines the depth of the imaging properties, which should be as accurate as needed with a fitting effort to benefit ratio. Area of applications for phantoms are medical imaging modalities, like CT and MRI, as well as image-guide therapies where imaging is also used, such as radiotherapy. Material properties could be for one or more (multimodal) applications.

The application-specific and class-related requirements for the phantom must be systematically documented and categorized in a list into mandatory and optional requirements. This process involves not only product developers but also the phantom end-users, which may include medical clinicians, engineers, or physicists.

3.2 Concept phase - material testing

The subsequent phase involves the development of the phantom concept. This includes categorizing the phantom into components. It is likely that the phantom is supposed to represent a certain section of a human body, such as the head. In this case, the phantom components are the organs or tissue types making up the phantom, like the skull or bone, the brain and other. What kind of anatomical structures, organs or tissues and to what extent they are to be included is defined in the planning phase.

Following this categorization and conceptual design, a crucial step involves the material analysis (see Fig. 6). This analysis is conducted to assess and determine the suitability of various printing materials for the intended application in the phantom.

The material testing procedure for a phantom can be structured based on the hierarchical product component test pyramid proposed by Schwan et al. [30]. Fig. 7 adapts this methodology to phantoms. The phantom structure, which represents the physical test object, and the reality, i.e., the patient, are each displayed on a pyramid side. The structural complexity levels are the material level, which is equivalent to biological tissues for phantoms, the structure and component level as well as the product, like the final phantom or, on the reality side, the patient.

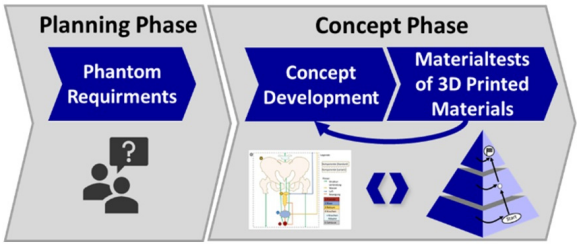

Fig. 6. Planning and concept phase for developing a 3D printed phantom.

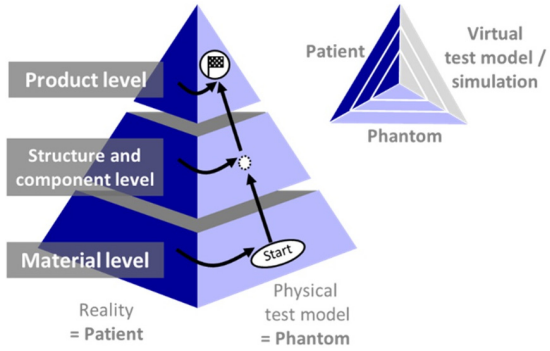

Fig. 7. Product component test pyramid (adapted from Ref. [30]).

The testing procedure for 3D printed phantoms is also illustrated in Fig. 7. Material testing for surrogate tissue initiates the process as the starting point. Understanding the properties of 3D printed materials is foundational before making further material choices. Even if known material from the literature is used, testing should still be considered, since its properties could be different when using different imaging systems or printer settings. Comparisons to reality are made at each testing cycle, using patient imaging data or literature data to verify the material application in the phantom. The reality side can be equivalent to a single data set for all patient pyramid levels, like a CT scan of the head, while the phantom side is tested step by step, first only at material level, then component level, and finally the entire phantom.

A third side of the pyramid can represent a virtual model or simulation, which can be used to verify tests as one moves up the pyramid (cf. right corner of Fig. 7). This testing procedure can be adapted to the user's scenario, serving as a preliminary guideline that can be modified for specific phantom development needs.

Discoveries during the material testing phase have the potential to alter the initially defined concept, leading to adjustments such as transitioning from a direct to an indirect 3D printing process. This initiates an iterative loop between the conceptual and material testing phases (cf. Fig. 6). Once all aspects are finalized, the design phase can begin.

3.3 Design phase – 3D printing

The design phase addresses the complete design and

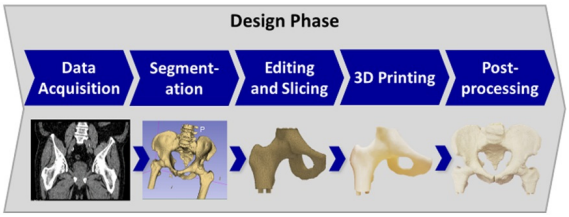

Fig. 8. Design phase for phantom development with steps (adapted from Ref. [4]).

manufacturing, including 3D printing. The standard workflow for designing and manufacturing a 3D printed medical model, that can be found literature, involves processing imaging data into a digital 3D model [1, 31]. This process was adapted for 3D printed phantoms by several authors [4, 6, 8, 9, 13]. The steps from the literature are summarized and illustrated in Fig. 8.

The distinct advantage lies in the use of a three-dimensional data set derived from a medical imaging source, such as CT, MRI, or other patient images. After acquisition, the data can be segmented into various tissue types (exemplified by a pelvic bone in Fig. 8). Image data processing programs, commonly capable of exporting segmented structures as 3D models (STL files), are typically employed for this purpose, for example via thresholding algorithms.

In the next step, the model undergoes editing in a computer-aided design (CAD) program, where adjustments are made according to specifications, such as suitable interfaces, or it is positioned as a negative in a designed casting mold. The designed model is then sliced by the 3D printing software using an STL file as input. Subsequently, the product undergoes 3D printing and concludes with post-processing. Post-processing is a crucial aspect, particularly in indirect manufacturing, where the 3D printed casting molds can be filled with tissue-equivalent mixtures to create anatomical organ phantoms. In the case of direct printing, post-processing might involve support material removal or curing procedures, depending on the chosen printing method.

3.4 Validation phase – application and validation

The validation of a 3D printed phantom is a critical step in ensuring its accuracy and reliability for its intended applications. Upon completion of the manufacturing and finalization processes, the 3D printed phantom evolves into a complete model, culminating in the crucial phase of final validation within the chosen application. This validation entails comparisons with other phantoms documented in literature or available commercially, along with a comprehensive evaluation against the gold standard – a comparison with a human patient.

A validation is conducted to analyze whether the phantom meets the predefined requirements outlined in the planning phase. The validation process encompasses both quantitative and qualitative assessments, ensuring that the phantom properties align with the intended purpose and accurately replicate the targeted anatomical features. This comprehensive validation framework serves as a critical quality assurance step, fostering confidence in the reliability and effectiveness of the 3D printed phantom across various medical scenarios. Even though this step is crucial, the reliability and reproducibility of phantoms across different imaging systems and institutions are often not analyzed.

4. Discussion and conclusion

The field of medical imaging has seen significant advancements with the rapid growth of 3D printing technology. Thanks to its versatility, this technology enabled a significant transition in the fabrication of medical phantoms. The traditional manufacturing methods, which are often time-consuming and expensive, have been complemented by the advantages of 3D printing, thus allowing for the creation of anatomically accurate, cost-effective, modular, and customizable phantoms with a high degree of geometric freedom.

Indirect and direct manufacturing techniques complement each other for manufacturing phantoms with tissue equivalent materials. 3D printing material requirements and characteristics impact only direct production. This method includes printing an existing tissue-equivalent material or a hollow structure filled with additional surrogate. Alternatively, indirect production is applied when molds or mold inserts are created using 3D printing. Phantoms can integrate both methods, enabling diverse organ fabrication with distinct characteristics.

The typical workflow for developing and manufacturing 3D printed phantoms involves a planning phase, a concept phase, a design phase and a validation phase. First the required type and the specific clinical needs and research requirements are defined. Some phantoms focus on replicating specific organs or anatomical structures, while others focus on quality insurance. Afterwards the concept with material testing is conducted. This involves analysis 3D printed material on a material level bevor modelling substructures or structures like organs.

The final design of a phantom involves utilizing three-dimensional patient data obtained from medical imaging, such as CT scans or MRI, to create phantoms tailored to patients' unique anatomies and pathologies. The design workflow processes imaging data into a digital 3D model using advanced algorithms, refining it for accuracy, and printing materials to match tissue properties. While personalized human body model fabrication holds a significant advantage, challenges such as data collection constraints pose significant challenges. Privacy concerns surrounding the sensitive patient data necessitate robust protocols for secure handling and storage. Addressing these limitations requires interdisciplinary collaboration and the development of ethical research methodologies that prioritize both scientific advancement and patient welfare.

Ideally, a singular phantom should closely emulate its human counterpart across all pertinent parameters, although achieving this parity is not yet fully realized. Presently, most phantoms represent only a subset of measured parameters and are typi-

cally tailored for a specific application. Beyond physical equivalences, factors like spatial resolution, production costs, and the feasibility of the 3D printing process also need consideration. Material analyses for 3D printed phantoms have been done by a handful of studies but are still limited, with often only addressing one aspect or one 3D printing process. Comprehensive material studies encompassing various printing processes, different materials, and consistent test conditions remain to be explored. While the materials presently available may not be suitable for all applications. In the future customized new materials, incorporating additives, could enable a closer mimicking of tissues than what is achievable with commercial 3D printing material.

Despite the numerous opportunities presented by 3D printed medical phantoms, there are still challenges to overcome. Standardization and validation procedures are crucial to ensure the reliability and reproducibility of these phantoms across different imaging systems and institutions. Efforts must be made to establish robust quality assurance protocols and conduct comparison studies between 3D printed phantoms and traditionally manufactured ones to validate their accuracy, uniformity and performance. Printing parameters, accuracy, costs, manufacturing time and durability are often not analyzed or even mentioned in the literature. Furthermore, development processes are often not outlined. More guidance, in form of detailed phantom material catalogs, and comparisons study would be beneficial for the research field. The validation processes could be supported using checklists, questioners or a weighted evaluation form.

In conclusion, the development of 3D printing for medical phantoms represents a transformative advancement in the field of medical imaging. The ability to create anatomically realistic, cost-effective, modular, and customizable phantoms using patient-specific data has immense potential in improving medical research.

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