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Paul M. Rea *Editor*

Biomedical Visualisation

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Preface

The utilisation of technologies in the biomedical and life sciences, medicine, dentistry, surgery and the allied health professions has been utilised at an exponential rate over recent years. The way we view and examine data now is significantly different to what has been done perhaps 10 or 20 years ago.

With the growth, development and improvement of imaging and data visualisation techniques, the way we are able to interact with data is much more engaging than it has ever been.

These technologies have been used to enable improved visualisation in the biomedical fields, but also how we engage our future generations of practitioners when they are students within our educational environment. Never before have we had such a wide range of tools and technologies available to engage our end-stage user. Therefore, it is a perfect time to bring this together to showcase and highlight the great investigative works that is going on globally.

This book will truly showcase the amazing work that our global colleagues are investigating, and researching, ultimately to improve student and patient education, understanding and engagement. By sharing best practice and innovation, we can truly aid our global development in understanding how best to use technology for the benefit of society as a whole.

Glasgow, UK — Paul M. Rea

Acknowledgements

I would like to truly thank every author who has contributed to the third edition of Biomedical Visualisation. By sharing our innovative approaches, we can truly benefit students, faculty, researchers, industry and beyond, in our quest for the best uses of technologies and computers in the field of life sciences, medicine, the allied health professions and beyond. In doing so, we can truly improve our global engagement and understanding about best practice in the use of these technologies for everyone. Thank you!

I would also like to extend out a personal note of thanks to the team at Springer Nature who have helped make this possible. The team I have been working with have been so incredibly kind and supportive, and without you, this would not have been possible. Thank you kindly!

About This Book

Following on from the success of the first four volumes, Biomedical Visualisation, Volume 5, will demonstrate the numerous options we have in using technology to enhance, support and challenge education. The chapters presented here highlight the wide use of tools, techniques and methodologies we have at our disposal in the digital age. These can be used to image the human body and educate patients, public, faculty and students in the plethora of how to use cutting-edge technologies in visualising the human body and its processes, creation and integration of platforms for teaching and education, to visualising biological structures and pathological processes.

Applications of CT and MRI Scanning

The first four chapters highlight the diverse uses of CT and MRI scanning. These chapters demonstrate the uses of modern scanning techniques currently in use both clinically and in research and include vascular modelling, uses of the stereoscopic model, MRI in neurovascular and neurodegenerative diseases, and how they can also be used in a forensic setting in identification.

Applications

The remaining six chapters truly demonstrate the diversity technology has in education, training and patient engagement. Multimodal technologies are discussed and include art and history collections, photogrammetry and game engines, augmented reality and review of the current literature for patient rehabilitation and education of the health professions. These chapters really do provide “something for everyone” whether you are a student, faculty member or part of our curious global population interested in technology and health care.

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Editor and Contributors

About the Editor

Paul M. Rea is Professor of digital and anatomical education at the University of Glasgow. He is qualified with a medical degree (MBChB), a M.Sc. (by research) in craniofacial anatomy/surgery, a Ph.D. in neuroscience, the Diploma in Forensic Medical Science (DipFMS) and an M.Ed. with merit (Learning and Teaching in Higher Education). He is Elected Fellow of the Royal Society for the Encouragement of Arts, Manufactures and Commerce (FRSA), Elected Fellow of the Royal Society of Biology (FRSB), Senior Fellow of the Higher Education Academy, Professional Member of the Institute of Medical Illustrators (MIMI) and Registered Medical Illustrator in the Academy for Healthcare Science.

He has published widely and presented at many national and international meetings, including invited talks. He sits on the Executive Editorial Committee for the Journal of Visual Communication in Medicine, is Associate Editor for the European Journal of Anatomy and reviews for 24 different journals/publishers.

He is Public Engagement and Outreach Lead for anatomy coordinating collaborative projects with the Glasgow Science Centre, NHS and Royal College of Physicians and Surgeons of Glasgow. He is also STEM Ambassador and has visited numerous schools to undertake outreach work.

His research involves a long-standing strategic partnership with the School of Simulation and Visualisation, The Glasgow School of Art. This has led to multi-million pound investment in creating world's leading 3D digital data sets to be used in undergraduate and postgraduate teaching to enhance learning and assessment. This successful collaboration resulted in the creation of the world's first taught MSc Medical Visualisation and Human Anatomy combining anatomy and digital technologies. The Institute of Medical Illustrators also accredits it. This degree, now into its 8th year, has graduated almost 100 people and created college-wide, industry, multi-institutional and NHS research-linked projects for students. He is Programme Director for this degree.

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Comparison of Magnetic Resonance Angiography and Computed Tomography Angiography Stereoscopic Cerebral Vascular Models

Gongchao Yang, Timothy D. Wilson, Michael N. Lehman and Dongmei Cui

Abstract

In this paper, we will discuss and compare the stereoscopic models developed from two types of radiographic data, Magnetic Resonance Angiography (MRA) images and Computed Tomography Angiography (CTA) images. Stereoscopic models were created using surface or volume segmentation and semi-auto combined segmentation techniques. Although, the CTA data were found to improve the speed and quality of constructing virtual vascular models compared to conventional CT data, small blood vessels were difficult to capture during the imaging and reconstruction process thereby limiting the fidelity of the stereoscopic models. Thus, high contrast Magnetic Resonance Angiography (MRA) images offer better resolution to visualize and capture the smaller branches of the cerebral vasculature than CTA images.

Keywords

3D stereoscopic models · Cerebral vasculature · Magnetic resonance angiography (MRA) images · Computed tomography angiography (CTA) images

1 Introduction

1.1 Literature Review

Stereoscopic virtual models are commonly created from computed tomography images for anatomy education. These models are purported to convey better depth information than non-stereo displays, and can potentially benefit image based medicine (Vernon and Peckham 2002; Held and Hui 2011). In recent years, new interface technologies and 3D virtual models have become possible due to advanced computer technology and software (Martin et al. 2013). These virtual anatomical models enable visualization, manipulation, and interaction with the computer, and stereoscopic 3D presentation of anatomic structures in a virtual environment (Trelease 1996; Nguyen and Wilson 2009;

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Sergovich et al. 2010; Adams and Wilson 2011; Roach et al. 2014; Kockro et al. 2015; Cui et al. 2016; Chen et al. 2017). 3D stereoscopic presentation has been particularly used in anatomical education with the evidence of improvement in students' learning (Luursema et al. 2006, 2008; Berney et al. 2015; Cui et al. 2017; Remmele et al. 2015, 2017). Use of 3D image displays can potentially decrease the learning curve of students and increase the understanding of spatial relationships as it provides a whole representation of the patient's anatomy (Luursema et al. 2008; Brewer et al. 2012; Cui et al. 2016).

1.2 Computed Tomography Angiography (CTA) Data and the Stereoscopic Models

Use of Computed Tomography Angiography (CTA) images is reported to successfully improve the construction of vascular virtual models for teaching vascular anatomy (Cui et al. 2016; Govsa et al. 2017). The CTA image acquisition requires the administration of intravenous iodinated contrast at a rapid rate, and the imaging is timed to optimize contrast in the arteries, thereby making the arteries easier to identify and evaluate (Cui et al. 2016). The CTA images are frequently used to detect intracranial aneurysms and other vascular abnormalities in clinical medicine and subsequent planning of therapeutic interventions in a clinical setting (Tomandl et al. 2004), the CTA images, when digitally combined can create 3D stereoscopic models of vasculature (Cui et al. 2016). Stereoscopic 3D rendered vasculature models of the head and neck derived from CTA images are not routinely used in clinical medicine or anatomy education (Cui et al. 2016). Using the CTA images to create the stereoscopic models is better than conventional CT for anatomical education due to the easily definable borders of most patent blood vessels. Furthermore, the CTA images are better suited for relatively large blood vessels using the surface segmentation method. Smaller blood vessels, however, are difficult to capture during the creation process. It takes considerable time to construct 3D models due to the requirement for manual identification and selection of the relevant anatomical structures on a slice-by-slice basis of the radiographic scans. Because dense tissue like cortical bone have a similar attenuation to contrast-enhanced vessels on CTA images, automated segmentation practices like volumetric segmentation is problematic as tissue differentiation is not readily possible (Cui et al. 2016).

1.3 Magnetic Resonance Angiography (MRA) and the Stereoscopic Models

Magnetic Resonance Angiography (MRA) uses a magnetic field to evaluate and identify abnormal vasculature, and unlike CTA, MRA is usually undertaken without an intravenous contrast agent. Instead of using tissue attenuation of ionizing radiation, MRA uses magnetic field properties, and spin characteristics of the hydrogen protons of blood (Kiruluta and González 2016). The contrast-enhanced MRA method has advantages of a large field of view, without ionizing radiation, thus reducing the probability of nephrotoxic harm. The MRA method also reduces the allergic reaction related to the iodinated contrast media compared to the computed tomographic angiography (CTA) images (Grist 2000). MRA is also less sensitive to calcification and ossification, rendering bone less revealing than CTA. In addition, soft tissues are better visualized and blood vessels have a similar diagnostic accuracy as an enhanced CT scan (Çelebioğlu et al. 2017). The MRA method visualizes the arteries and veins by measuring the velocity of H proton flow. The resulting images demonstrate details of vascular structures that, in many situations, are superior to those seen on angiograms (Haines 2006; Keller et al. 1989). The greatest benefit of MRA is its minimal invasiveness, namely its ability to precisely delineate intracranial arteries without puncture of the arteries or administration of contrast media

(Çelebioğlu et al. 2017; Igase et al. 2018). In addition, MRA has often been used in the clinical setting to detect cerebral aneurysms, and arterial steno-occlusive disease (Fushimi et al. 2017; Igase et al. 2018).

2 Methods

2.1 Computer Tomography Angiography (CTA) Data

The CT angiography (CTA) images were acquired with a Siemens SOMATOM Definition CT scanner with anisotropic voxel dimensions (0.35 × 0.35 mm in axial dimension and 0.75 mm in craniocaudal dimension), using a routine CT angiography (CTA) technique that included intravenous iodinated contrast administration and bolus timing for an optimal arterial phase. The mean intensity of arteries was about 350 Hounsfield Units for creating the volume rendering model using Computed Tomography Angiography data (Cui et al. 2016).

2.2 Magnetic Resonance Angiography (MRA) Data

The MRA images were acquired with a Siemens 3 T Skyra MRI scanner with voxel dimensions (0.25 × 0.25 mm in axial dimensions and 0.55 mm in craniocaudal dimension), using a routine 3-dimensional (3D) Time Of Flight (TOF) acquisition protocol. The raw data were saved as DICOM (Digital Imaging and Communications in Medicine) format files.

2.3 Creating and Rendering of the 3D Model

The stereoscopic 3D virtual models were created with Amira software, version 5.6 (FEI Visualization Sciences Group, Burlington, MA). To create a virtual 3D model, the DICOM MRA data that contained the head region was uploaded into the object pool using a Dell Precision T7600 computer workstation (Dell Incorporated, Round Rock, TX) with an NVIDIA Quadro K6000 video card (NVIDIA Corporation, Santa Clara, CA). The cerebral vascular structures were grouped by using "labels." This process allows like-labeled structures to be displayed individually or with other label groups for selective visualization. Previously, the CTA vascular head and neck virtual models were developed using two general approaches: surface and volume segmentation construct the models (Cui et al. 2016). In order to increase the speed and efficiency of the creating process and avoid errors during the segmentation, a newly developed semi-auto combined methodology in our lab was used for creating MRA stereoscopic models. The semi-auto combined segmentation technique combines both volume and surface approaches. Within the software a *blow tool* was often used as it maximally identified density differences at segmentation edges, thus enabling the operator to identify lumenal edges. This technique is better able to differentiate minor gray-level contrast differences in slice images within structures that have similar attenuation values (Chen et al. 2017), consequently making their differentiation sometimes ambiguous manually.

2.4 Visualization and Presentation of 3D Stereoscopic Models

After the segmented model is rendered with an operator-chosen color or color bitmap, the stereoscopic cerebral vascular model can be exhibited by using the stereo presentation to project the 3D models stereoscopically in a virtual reality-like environment via a stereoscopic projection system. To project the model sterescopically required a virtual reality configuration within the software to project the model using a passive stereo display (dual high-definition projector system: InFocus IN3128HD; InFocus, Portland, OR). The models can be displayed as a 3D virtual model on a large silver screen in a dimly lit ambient environment (Nguyen and Wilson 2009; Adams and Wilson 2011; Brewer et al. 2012; Cui et al. 2016).

Viewers wear linear polarized 3D glasses and sit in a small theater-like classroom. The MRA cerebral vascular stereoscopic model can be manipulated 360° in all axles, model rotation, translation, and zoom manipulation are possible by using a 3D mouse or a computer mouse interface.

3 Results

3.1 Comparison of CTA and MRA Stereoscopic Models from Window Display

A virtual stereoscopic model of the major cerebral vascular structures created from MRA radiographic images includes: internal carotid arteries, vertebral arteries, basilar artery, posterior cerebral artery (right), anterior cerebral arteries, middle cerebral arteries. Both the large and most of small artery structures are easily detected through segmentation based on selecting density thresholds of the arteries using the volume segmentation selection. Undesired structures can be efficiently removed using surface editing, or semi-auto combined segmenting, thereby highlighting tissues of interest. The vascular structure of the MRA 3D mode (Fig. 1a) appears smoother and more complete than the CTA model (Fig. 2b). The two models in lateral orientation highlight the appearance and contiguous nature of MRA versus CTA rendered models. A stereoscopic virtual cerebral vascular model was created from CTA data and used as comparison. The vascular structures included arterial inputs to the circle of Willis (internal carotid arteries, vertebral arteries and basilar artery) while the entire anastomosis is also visible (posterior, middle, and anterior cerebral arteries, and their bilateral communicating arteries. The large arteries were easy to be segmented, but small arteries were more difficult to be manipulated. In addition, small arteries appear disconnected and had gaps in the lateral model orientation (Fig. 1b).

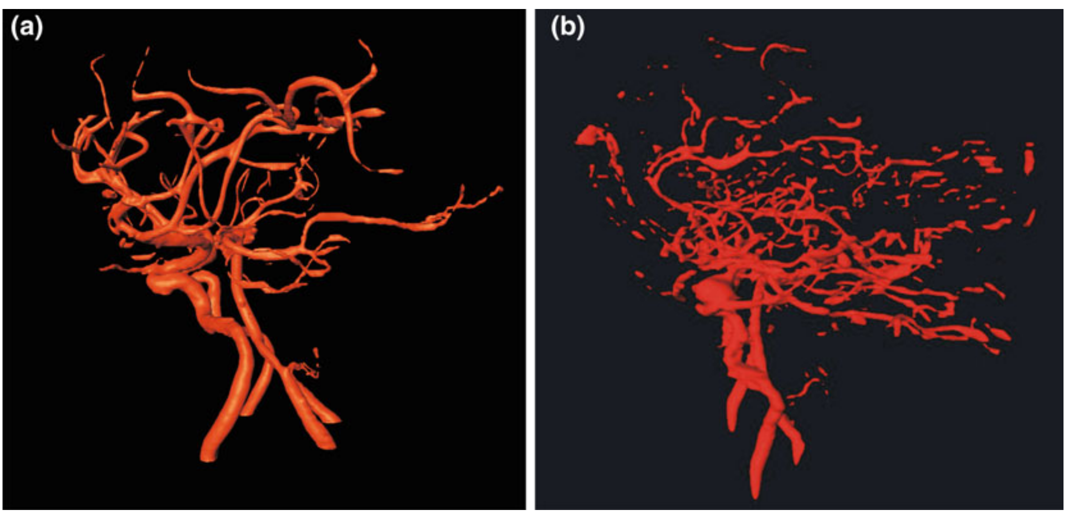

Fig. 1 Examples of Magnetic Resonance Angiography (MRA) model and Computed Tomography Angiography (CTA) model of cerebral vasculature. The model on the left **a** was created from the Magnetic Resonance Angiography data; blood vessels appear smooth with no gaps. The model on the right **b** was created from Computed Tomography Angiography data, which failing to show the connections between the large blood vessels and some smaller vessels. *Photo credit* Reproduced with permission from Dongmei Cui

3.2 Comparison of MRA and CTA Models from Segmentation and Rendering

Visual comparisons of MRA and CTA models in Fig. 2 anterior (left) and superior views (right) after volume segmentation based on the tissue density. The vasculature of the MRA model appears smooth and identifiable, and there are few bony structures remaining. These extra bony structures can be efficiently removed later using surface editing (Fig. 2a, b). However, the CTA model contains large amounts of cancellous bony structures remaining after the volume rendering, which are difficult to remove using surface editing (Fig. 2c, d). Creating a CTA vascular model required more effort and time compared to the MRA vascular model due to its contrast-enhanced

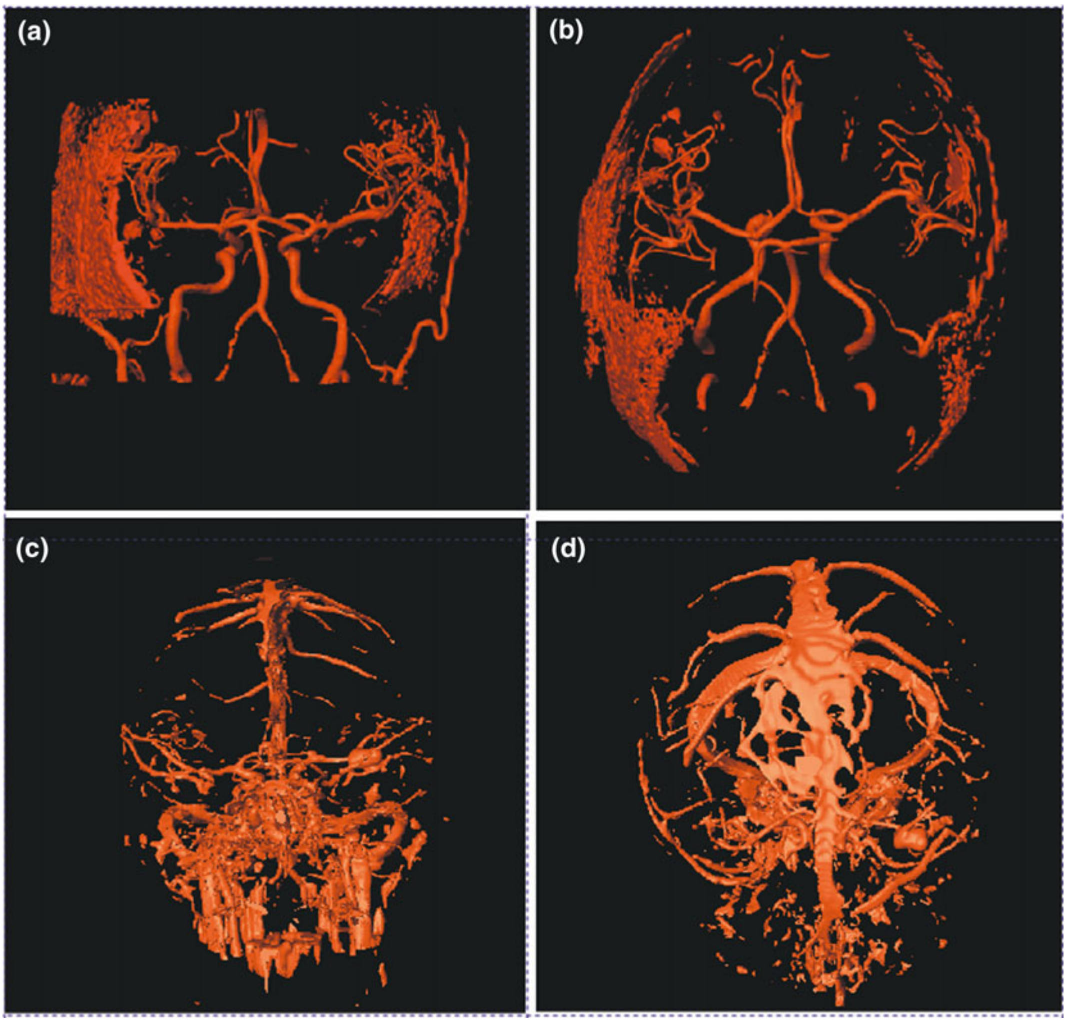

Fig. 2 Comparison of MRA and CTA models after volume segmentation. The anterior view (**a**) and superior view (**b**) of MRA models using the volume segmentation method. The cerebrovasculature appears smooth and identifiable, and has only a small amount of other tissues (cancellous bony structures) remaining in the MRA models. The anterior view (**c**) and superior view (**d**) of CTA models using the same segmentation method. A large amount of cancellous bony structures remain, the cerebrovasculature is difficult to view and no clear border can be defined between the blood vessels and other blood riched structures

blood vessel has a similar attenuation to cancellous bone, which need additional time to remove the bone.

3.3 Overview Comparison of MRA and CTA Models

The criteria for creating stereoscopic 3D models created from the MRA and CTA radiographic data are taken into account with both angiographic methods. The criteria include ease and time for vessel reconstruction, model surface appearance and completeness, capability of segmentation methods to detect the entirety of the circle of Willis without pollution of other structures, and stereoscopic presentation for comparison of stereoscopic models created from Magnetic Resonance Angiography (MRA) and from the Computed Tomography Angiography (CTA) data were listed in Table 1.

4 Discussion

The most commonly used data for anatomic stereoscopic 3D model creation includes computed tomography (CT) images and magnetic resonance (MR) imaging (Nguyen and Wilson 2009; Sergovich et al. 2010; Adams and Wilson 2011; Yeung et al. 2011; Brewer et al. 2012; Cui et al. 2016). The use of histological sections has been used for creating ultrastructure (Roth et al. 2015). Recently, use of Computed Tomography Angiography (CTA) images has been reported to successfully improve the construction of vascular virtual models for teaching vascular anatomy (Cui et al. 2016; Govsa et al. 2017). Although MRA has often been used in the clinical setting to detect cerebral aneurysms, and arterial steno-occlusive disease (Fushimi et al. 2017; Igase et al. 2018), MRA material has not commonly use surface segmentation due to time consideration. In this paper, we compared the stereoscopic virtual vascular models developed from both CTA and MRA data.

4.1 Stereoscopic Models Created from Computed Tomography Angiography Data

CT data is excellent for creating models of bony structures due to the high density and contrast of bone, but cannot easily differentiate soft tissue,

Table 1 Comparison of the models created from the magnetic resonance angiography (MRA) and from the computed tomography angiography (CTA) data

Comparative criteria/types of models	Computed tomography arteriogram (CTA) model	Magnetic resonance arteriogram (MRA) model
Large vessels reconstruction	Excellent	Excellent
Small vessels reconstruction	Poor	Excellent
Smoothness	Good	Excellent
Vasculature continuation	Poor/minimum	Excellent
Volume rendering	Excellent on bone and large blood vessels	Excellent on soft tissue and both large and small vessels
Surface editing for vasculature	Difficult, poor	Easy, excellent
Semi-auto combined rendering	Excellent on large vessels; poor for small vessels	Excellent on both large and small vessels
Stereoscopic presentation	Excellent	Excellent
Time needs for completing the models	>80 h	30–60 min

especially vasculature. In order to improve the stereoscopic vascular model reconstruction, contrast-enhanced computed tomography angiography (CTA) is used to create 3D stereoscopic models (Cui et al. 2016). CTA data serve as an excellent resource for creating bony and vascular structures using volume segmentation methods as the contrast difference between enhanced tissue and bone are much higher than surrounding tissues. However, this method has its limitation. Because bone has the attenuation levels very similar to contrast agent so cannot tell them apart digitally, but only after the volume segmentation has occurred where user's knowledge of anatomy enable further filtering. Also, cancellous bone (spongy bone) contains large numbers of blood cells, and injected contrast reaching intra-and extra cerebral structures simultaneously, resulting in a similar density to the contrast-enhanced blood vessels, it is difficult to separate blood vessels from cancellous bone when selecting the thresholds for volume segmentation using CTA data. As a consequence, manual surface segmentation methods are usually needed to separate blood vessels from cancellous bone. Manual surface segmentation has the advantage of the operator of the software having the ability to create different vascular structures in a separate digital "materials". Having a vascular structure with multiple materials that correspond to anatomical borders permits a user-controlled and flexible view of virtual models. The disadvantage here is the manual nature of the segmentation requiring significant time (>80 h) and the model surface has a slight edge (Cui et al. 2016).

4.2 Stereoscopic Models Created from Magnetic Resonance Angiogram Data

The Magnetic Resonance Angiogram (MRA) images are performed without an intravenous contrast agent. It uses instead magnetic field properties, and quantum spin characteristics of hydrogen protons found mainly in water. Blood in the center bore of the magnet is pulsed with radio frequency energy (Kiruluta and González. 2016). MRA does not use ionizing radiation, and it is able to show neuroanatomical structures in more detail than CTA (Vieco et al. 1997; Çelebioğlu et al. 2017). In addition, MRA radiographic images reveal arterial structures well, and are insensitive to the presence of bony structure, thereby providing a unique and innovative way to create 3D cerebral vascular virtual models. The Magnetic Resonance Angiogram (MRA) images, not only reveal large artery structures well, but also capture small arteries better than the CTA data during the rendering process. Also, the Magnetic Resonance Angiogram (MRA) data reveal soft tissue well and less cancellous bone can be selected, so after volume rendering, the surface editing was easy to apply. The Magnetic Resonance Angiogram (MRA) images work well with the vascular system. The Magnetic Resonance Angiogram (MRA) images, particularly work well for modelling the arterial system. In this case, the pathological condition was captured in a timely manner, the posterior cerebral artery hemorrhage was nicely revealed in a few minutes during the volume segmentation process. This approach can serve as a potential diagnostic tool for medical students and clinicians, and for the purpose of educational training. Volume-base segmentation process is often used in other commercial software for similar purposes. The volume segmented models have fine detailed textures, a natural, smooth appearance, and with surface editing, they can be created in a timely manner (30–60 min).

4.3 Which Data Is More Advantages for Creating Stereoscopic Cerebral Vascular Models?

Based on the comparison of the two methods presented in this paper, the stereoscopic vascular models created from CTA data were superior to conventional CT data, due to the enhanced CT angiogram (CTA) having much better vascular visibility as blood vessels were much easier to capture than when using CT images (Cui et al.

2016). The CTA data is excellent on segmentation of high density tissue, such as bone and contrast enhanced blood vessels. Although the (CTA) has a good blood vessel contrast and the large blood vessels were easy to manipulate, small vessels were much more challenging, and often appeared disconnected and had gaps in CTA models. The Magnetic Resonance Angiogram (MRA) images not only reveal large artery structures well, but also capture small arteries better than the CTA data during the segmentation process. Furthermore, the Magnetic Resonance Angiogram (MRA) data reveal soft tissue well with less cancellous bone, this enables the volume segmentation methodology to be superior for time and quality. If required, surface editing was easy to apply to the segmentation. The 3D model created from MRA images has the advantage of creating excellent vascular stereoscopic models. The production process is easier and more time-efficient than when using CTA data. Both large and small blood vessels can be captured, and appear smooth and without gaps compared to the CTA models in which only large blood vessels were well captured and smaller vessels were lost or were discontinuous. The finished MRA models are attractive, clear and have an excellent stereoscopic visualization.

4.4 Visualization of Stereoscopic Cerebral Vascular Models

Both the CTA and MRA data can be used to create cerebral vascular 3D models, and these models can be displayed in the stereoscopic view via a stereoscopic projection system. In this case, stereoscopic view needs to have the stereo Preferences (VR setting) option, that allows virtual images to project via the dual or multiple projectors. Projected images were filtered through the polarized lens, and viewers wearing 3D glasses experience the models popping out of the screen, moving and floating in front of the viewers' eyes. Models can be rotated freely and zoom in and out. In additional, the both CTA and MRA cerebral vascular models can be implicated and integrated with their slices of data. The slice data can be dynamically manipulated by users to demonstrate cross-sectional data simultaneously with the resulting 3D models (Cui et al. 2016). Stereoscopic presentation with orthoslice module visualization allows medical students to integrate viewing of both a cerebral vascular model and MRA images in sagittal, coronal, and transversal orientation, and in solid or transparency views. This feature allows students to freely explore the relationship between the vessel structure model and radiographic images in more than a hundred different levels with multiple orientation. Although, the finished MRA models are attractive, clear and have an excellent stereoscopic visualization, the CTA models have better visualization and integration with skull model.

4.5 Limitations

Although Magnetic Resonance Angiogram (MRA) data offers greater advantages in general than computed tomography angiography (CTA), they have some limitations when creating the stereoscopic 3D models. MRA images naturally reveal blood vessels and soft tissue well, but are less sensitive to bone, and often do not capture bony structures well. This is a positive feature for MRA during volume rendering when blood vessel models are needed and cancellous bone was intentionally avoided. However, the visualization of bone with vasculature is less well defined when compared to the 3D models created from the CTA data.

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Use Stereoscopic Model in Interventional and Surgical Procedures

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Abstract

The 3-dimensional (3D) stereoscopic modeling software allows anatomists to create high-resolution 3D models from computed tomography (CT) images. In this paper, we used high resolution CT images from a cadaver and a patient to develop clinically relevant anatomic models that can be used to teach surgical trainees different surgical procedures and approaches. The model facilitates visualization, manipulation, and interaction. It can be presented in stereoscopic 3D in a virtual environment, either in a classroom setting or immediately preceding a surgical procedure.

Keywords

3D stereoscopic models · Paranasal sinuses · Cervical vertebrae · Trigeminal ganglion · Computed tomography (CT) · Surgical and procedure perspective

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1 Introduction

1.1 Literature Review

Computer models have gained attention as a means to delineate detailed clinical anatomy (Nicholson et al. 2006; Qayumi et al. 2004), but few medical schools use virtual models in their clinical anatomy course (Adams and Wilson 2011; Cui et al. 2017; Yeung et al. 2011). In order to remain clinically relevant, anatomy education should focus on models that are based on real patients and models that enable trainees to simultaneously visualize and manipulate any part of the surface or re-construct interior structures (Li et al. 2006; Liu et al. 2011).

Blockade of trigeminal ganglion is a valuable treatment for many facial pain syndromes such as trigeminal neuralgia, persistent idiopathic facial pain, herpes-zoster or cancer-related pain (Peters and Nurmikko 2002). Trigeminal ganglion has three main branches, including ophthalmic (V1), maxillary (V2) and mandibular (V3). The V3 branch goes through the foramen ovale, which is an essential access to trigeminal ganglion for the interventional procedure such as radiofreuquency ablation. Currently, the most common practice of trigeminal ganglion block is performed under fluoroscopy guidance (Horiguchi et al. 2005). Since the fluoroscopy does not show soft tissues or blood vessels, the procedure is always challenging for an inexperienced trainee especially not knowing the regional anatomy well.

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Endoscopic (trans-sphenoidal) pituitary surgery has replaced craniotomy or oral and is a minimally invasive technique that uses a small incision at the back of the nasal cavity, resulting in little disruption of the nasal tissue. There has been continued development and advancement of minimally invasive surgeries and procedures that have made pituitary or spine surgery safer with improved patient recovery times (Guiot et al. 2002; Levi et al. 2017). These procedures require a detailed knowledge of the regional anatomy, much of which is not covered in classic medical school anatomy. For clinical trainees, it is crucial to be able to thoroughly understand the structures of the paranasal sinuses and the surgical pathway during the procedure of trans-sphenoidal pituitary surgery. The segmentation of the vertebrae is challenging, and the pathologic alterations frequently encountered in real cases explain the difficulties of an automatic segmentation in daily practice patients (Courbot et al. 2016). To prevent complications of cervical epidural injections, it is also essential for the trainee to understand the spatial relationship between cervical vertebrae and the surrounding structures, such as spinal nerves and blood vessels (Botwin et al. 2003).

1.2 Purpose of Using the Stereoscopic Model in Interventional Procedures

Interventional procedures are good alternative to treat different diseases or symptoms. In the field of chronic pain, due to the ongoing opioid crisis (Dhalla et al. 2011), physicians prefer non-opioid medication or interventional procedures to improve patients' chronic pain. The pain physicians now have more options to help patients with different kinds of interventional procedures under fluoroscopy guidance, including joint injection, medial branch block, peripheral nerve block or radiofrequency ablation (e.g. trigeminal nerve), epidural injection, spinal cord stimulation, kyphoplasty, and dorsal root ganglion stimulation, etc. (Krames 2015). More studies have been focusing on interventional procedures toward neuromodulation to regulate pain centers both centrally and peripherally (Rigoard et al. 2013). The pain management fellows are in the era of learning the classical procedures and new procedures which likely to be popular in the coming years. The trajectory safety view is recommended for needle placement for most procedures. This is because the procedure was done under fluoroscopy guidance which only show well of high density organs (bone) and it is two-dimensional. There is a steep curve for fellows to understand the regional anatomy before confidently put a needle or electronic leads into the right location. Most of learning materials are either plastic model or cadaver based (which are expensive), or image based (which is two-dimensional). With the assistance of the stereoscopic model based on real patient data, a more realistic and practical model likely to decrease the steep learning curve. The research on the stereoscopic model can be potentially used to discover new safety trajectory views for the physicians.

1.3 Interventional Procedure Pathway

There are many procedures that depend heavily on how physicians understand the regional anatomy. To be confident of final needle placement, it's critical for physicians to understand the procedure pathway to avoid "danger zone" or important structures which might cause severe complications. For the trigeminal ganglion model, we describe the pathway for trigeminal ganglion injection. After trajectory image was achieved, the needle first goes through the skin about 3 cm lateral to the corner of the mouth and aims towards 90° intersection of the pupillary line with a point 3 cm in front of the tragus (Hartel 1914). The needle passes through buccinators, masseters, medial/lateral pterygoid muscle, maxillary artery and vein, branches of the trigeminal nerve, and foramen ovale to the trigeminal ganglion.

1.4 Purpose of Using the Stereoscopic Model in Minimal Invasive Surgical Procedures

Minimal invasive surgery gains its popularity because its less traumatic and quick recovery. Open reduction and internal fixation tibia fracture in orthopedics is a good example of traditional surgery. It provides a good anatomical view, but patient takes longer time to recover due to deeper tissue dissection and long open wound. The minimally invasive surgery is less involved in cutting and opening, but more exploratory with either fluoroscopic guidance or endoscopic guidance. In the field of neurological surgery, the residents or fellow not only need to learn open craniectomy but also more advanced endoscopic surgery for the spine and brain (pituitary) (White et al. 2004). The process of learning new surgical technical skills has required visual spatial ability and can be difficult for some learners; however, none has probed the impact of a three-dimensional video learning module on the acquisition of new surgical skills (Roach et al. 2012). Using stereoscopic 3D visualization to learn a surgical skill in resident training is less common than using a 3D video due to the accessibility to the relatively new technology and equipment. Stereoscopic 3D learning is a more advanced learning tool and particularly helped students with low spatial ability in the study of anatomy structures (Cui et al. 2017).

1.5 Minimal Invasive Surgical Procedure Pathway of Pituitary Gland and Intraarticular Injection Procedure of Cervical Vertebrae

In this section, we briefly describe one minimal invasive surgery pathway- transsphenoidal pituitary gland surgery. An image-guidance system (CT or MRI) is likely to be used during the surgery for mapping. The endoscope advances to the back of the nostril, then a small portion of septum will be removed for better camera view. After removing the sella of sphenoidal sinus, the pituitary gland is exposed for tumor removal (Messerer et al. 2018). There have been reports demonstrating use of 3D reconstruction of cervical vertebrae for different purposes (Courbot et al. 2016; Chen et al. 2017). To prevent complications of cervical epidural injections, it is also essential for the trainee to understand the spatial relationship between cervical vertebrae and the surrounding structures, such as spinal nerves and blood vessels (Botwin et al. 2003; Chen et al. 2017).

1.6 Significance (or Current Clinical Educational Training Session)

The current procedures or surgery training done during the residency or fellowship are case based. The trainee has the teaching material provided by physicians. During the procedure, the physicians show trainees how it is accomplished with minimal complication with hand-on experience. For the simple procedures like skin biopsy, the trainee learning curve is very short. Because the regional anatomy is straight forwards. However, when it comes to the complicated procedure like trans-sphenoidal surgery, high cervical steroid injection or trigeminal ganglion radiofrequency ablation, it usually takes longer time for the trainee to grasp the essence of the procedure. Due to the longer learning time and steep learning curve, case based teaching on those difficult procedures might not be the most efficient way to learn. Take a trigeminal ganglion block as an example, the teaching during the procedure is based on two-dimensional fluoroscopic images. Even if the foramen ovale shows clearly on the trajectory view, the trainee will still feel inconfident especially if complication happens. Most anatomy teaching is two-dimensional based and does not provide the depth of the structures. Stereoscopic model, hence plays important role in not only delivering three-dimensional regional anatomy, but also letting the trainee experience the depth of the structure. The spatial ability necessitates trainee better understanding the regional anatomy (Garg et al. 2001). By this way, the trainee has a better understanding of the anatomy adjacent to the procedure target. This likely assist trainees to well prepared for the procedure than mere improvising.

In this paper. The stereoscopic 3D models of the paranasal sinuses, cervical vertebrae, foramen ovale and related surface tissue are demonstrated to help with clinical training of trigeminal ganglion radiofrequency ablation procedure, cervical vertebral injection and endoscopic (transsphenoidal) pituitary surgical procedure.

2 Methods

2.1 Computer Tomographic (CT) Data

The 3D models were developed from a de-identified patient without any clinical or radiological head and neck pathology. The CT images of the patient were acquired by the Department of Radiology at the University of Mississippi Medical Center with a Siemens SOMATOM Definition CT scanner (Siemens, Erlangen, Germany) using routine high resolution imaging techniques, resulting in voxel dimensions of 0.35 × 0.35 mm in axial dimension and 0.75 mm in cranio-caudal dimension. The raw data was saved as de-identified Digital Imaging and Communications in Medicine (DICOM) format.

2.2 Creating and Rendering of the 3D Model

The 3D models were created using Amira® software, version 5.6 (FEI, Hillsboro, Oregon, USA) using a Dell Precision T7600 computer (Dell Incorporated, Round Rock, TX) with an NVIDIA Quadro K6000 video card (NVIDIA Corporation, Santa Clara, CA). DICOM data 283 axial images were uploaded into the Amira® object pool with the final model in the graphic window. DICOM data were reconstructed using a combination of surface rendering, volume rendering and semi-auto-combined rendering as we described in the previous papers (Chen et al. 2017; Cui et al. 2016). Models were used to provide clinical trainees better visualization of the subject's clinical anatomy for different interventional or surgical procedures.

2.3 Visualization and Presentation of 3D Stereoscopic Models

The high-resolution 3D model with sub-millimeter resolution was then stereoscopically visualized by dual projection with a passive stereo display using dual high-definition projector system InFocus model IN3128HD, (InFocusVR Corp., Portland, OR). A linear polarized filter (polarizer film; Edmond Optics Inc., Barring, NJ) was equipped for visualization of the final model. Like other 3D visualization tools, the AmiraVR software platform (FEI, Hillsboro, OR) allows the user to generate interior views of the models. These models can be explored in a virtual window that allows for viewing the structures at any angle while zooming and rotating 360° (Chen et al. 2017). For example, it was possible to view the inner surface of each paranasal sinus cavities by passing through the walls of the sinuses and navigating through horizontal or vertical axes. It is possible to view the interior of the skull base model. Such interior views enhanced visualization and understanding of the spatial relationships between various structures such as the cervical vertebrae, spinal cord, associated spinal nerve root and artery that pass through the intervertebral foramen (Chen et al. 2017). Similarly, it creates unique visual angles of the infratemporal fossa that potentially enhance learners' 3D rotation imaginary ability.

These models can be explored in a virtual window that allows for viewing the structures at any angle while zooming and rotating 360°. More specifically, the models can be rotated to visualize structures from different perspectives according to the viewer's needs, such as from the inside of the skull where you can follow the optic chiasm into the sella turcica, to the optic nerve in optic canal, and then onward into the eyeball, or from the medial side of mandible appreciate the relationship between medial pterygoid muscle and the trigeminal nerve.

In order to view the images stereoscopically, the observer wears glasses that have polarized lenses that match the polarization axes of the filters on the projector, so the observer's left eye sees only the projected left eye image and the observer's right eye sees only the projected right eye image. The models can be displayed on a large silver screen with a dim ambient light environment. Students wear linear polarized 3D glasses and sit in a small theater-like classroom. The experience of viewing 3D stereoscopic models is similar to viewing a 3D movie in an IMAX 3D theatre. These features allow users to explore and better understand the spatial relationships of difficult clinical anatomy structures. Stereoscopic 3D presentation and visualization give trainees a true experience that feels like being physically inside the human structures for surgical exploration.

3 Results

In this paper, we will discuss three stereoscopic models in the procedures which are trigeminal ganglion radiofrequency ablation, high cervical facet injection and trans-sphenoidal pituitary surgery.

3.1 Stereoscopic Viewing of Trajectory Targeting of Trigeminal Ganglion as a Procedure for Trigeminal Neuralgia Treatment

The trigeminal ganglion is the target for radiofrequency ablation if other conventional treatment not relieving patients facial pain (e.g. trigeminal neuralgia). The foramen ovale is the anatomical target where the needle tip of radiofrequency should be located. We used a female CT image to create the 3D structures related to the foramen ovale on the right side. All internal structures were segmented with high-resolution detail before the surface generation. The structures had been labeled included skin, masseter muscle, medial pterygoid muscle, lateral pterygoid muscle, maxillary branches of external carotid artery, foramen ovale and trigeminal ganglion, internal jugular vein, branches of the carotid artery, and parotid gland. With stereoscopic view, students can visualize the important anatomical structures from the most commonly used anterolateral approach. Figure 1 shows a trajectory region from the anterolateral view of the stereoscopic model. For example, during the needle trajectory targeting the foramen ovale for conventional treatment to relieve patient's facial pain, the needle passes through the skin, lateral pterygoid muscle (Fig. 1a), potentially medial pterygoid muscle (Fig. 1b), potentially maxillary artery (Fig. 1c), through the foramen ovale (Fig. 1d).

3.2 Stereoscopic Viewing of Trajectory Targeting of an Intraarticular Injection Procedure for Head and Neck Pain Treatment

Higher cervical facet (atlantoaxial joint) is the target for cervical facet arthropathy for both diagnostic and treatment purposes. This procedure is usually done by an experienced physician who knows the atlantoaxial anatomy well due to high risk of nerve damage and intravascular injection. Figure 2 (Chen et al. 2017 ASE) shows a digital model of the atlas, axis, skull and clinically relevant anatomic structures, including the spinal cord and vertebral artery. Intraarticular injection or transforaminal injection for headache or neck pain is usually done under X-ray fluoroscopic guidance using a 2D view, as shown in the cartoon drawing (Fig. 2a). With the semi-auto-combined method, the atlas over the

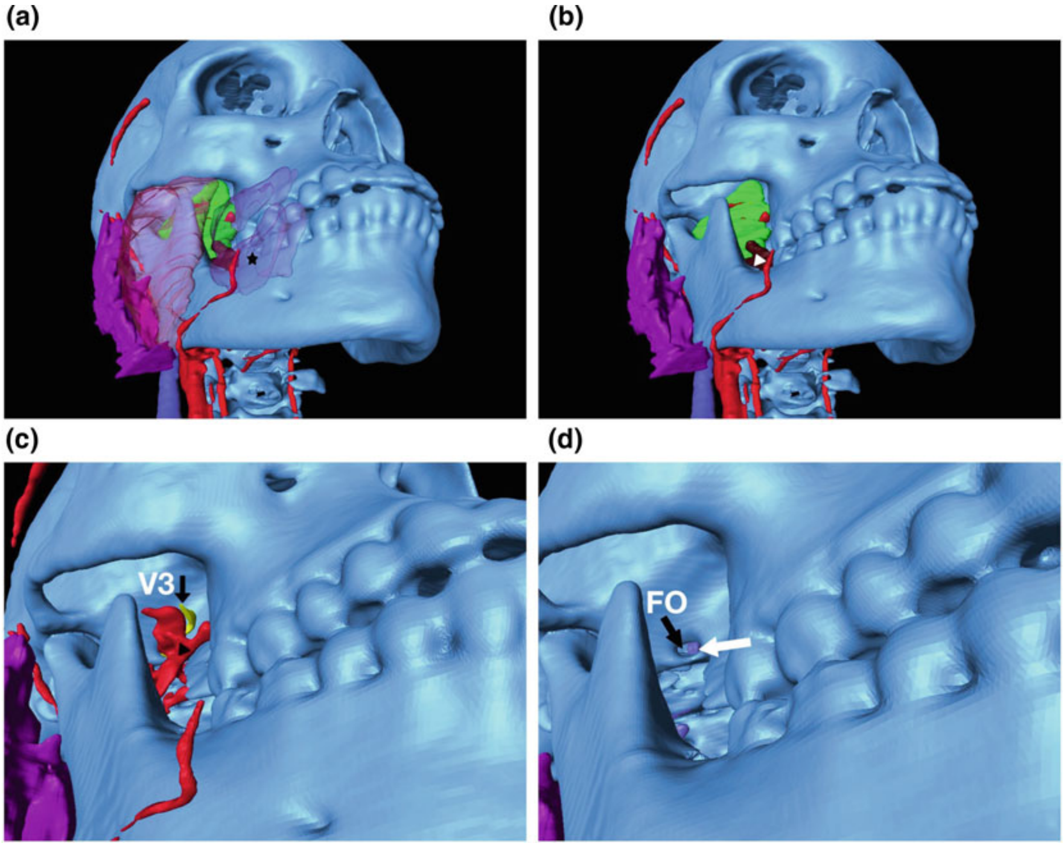

Fig. 1 From anterolateral region, the needle trajectory passes through the skin, potentially buccinators (transparent purple, asterix, **a**), lateral pterygoid muscle (green, **b**), medial pterygoid muscle (brown, white arrow head, **b**), maxillary artery (red, black arrow head, **c**), which occupies the foramen ovale in front of V3 (yellow, black arrow, **c**), foramen ovale (FO, black arrow, **d**), part of transverse sinus (white arrow, **d**). *Photo credit* Reproduced with permission from Chen and Cui

axis and the atlanto-axial joint can be visualized (white arrow in Fig. 2b). The atlanto-occipital joint is indicated by a black arrow with the vertebral artery (right side, red) passing through the transverse foramen (Fig. 2b). A more oblique lateral view in Fig. 2c shows that the nerve root (transparent yellow, black arrowhead) and vertebral artery are very close to the atlanto-axial joint, which can potentially cause complications from procedures. Figure 2d shows an anterior-posterior view, indicating that the vertebral artery (right side, red) is located lateral to the atlanto-axial joint space (white arrow). By removing the skull, the relationship between of C1 and C2 is easier to understand, especially how the dens sits right behind the arch of C1 to provide stability when head turning. Two white arrows indicate transverse foramen where the right vertebral artery goes through. The black asterisk locates the groove for right vertebral artery. Figure 2f is a better demonstration of inferior view of skull (white) with isolated C1 (transparent blue), showing how vertebral artery (right side, arrow head, red) passing through

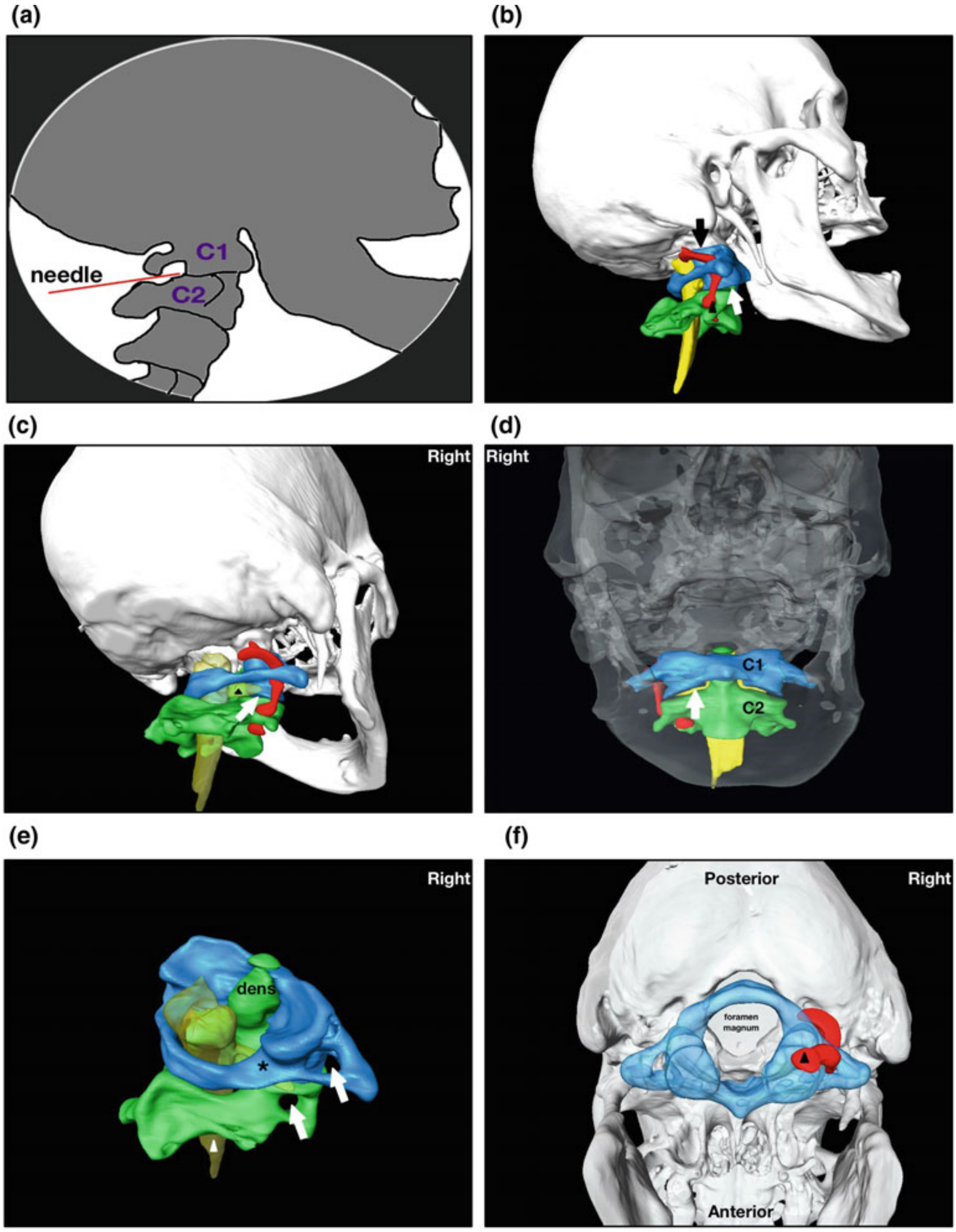

Fig. 2 **a** Lateral fluoroscopic view of C1 (atlas) and C2 (axis) joint injection, pink line indicated the injection needle; **b** lateral view, right side, black arrow indicates atlanto-occipital joint formed between atlas (blue) and occipital bone (part of the skull, white), white arrow indicated atlanto-axial joint formed between the axis (green) and atlas (blue), black arrow head indicated right vertebral artery, cervical spinal cord is labeled with (yellow); **c** lateral oblique view, right side, atlanto-axial joint indicated by the white arrow, cervical spinal cord (transparent yellow), second cervical nerve root indicated by a black arrowhead; **d** anterior view, with transparent skull, atlanto-axial joint indicated by the white arrow, C1 in blue and C2 in green, cervical spinal cord in yellow, right vertebral artery in red; **e** C1 in blue and C2 in green, cervical spinal cord, transparent yellow, indicated by the white arrow head, two white arrows indicate transverse foramina, asterisk marks groove of posterior arch; **f** inferior view of skull, anterior to posterior orientation, C1 in transparent blue, right vertebral artery in red indicated with black arrow head. *Photo credit* Reproduced with permission from Anat Sci Educ 10:598–606 (2017)

transverse foramen, turning inwards over the groove of the posterior arch of C1 and continue going up into the foramen magnum of the skull.

3.3 Stereoscopic Viewing of Pathway for the Endoscopic Trans-Sphenoidal Pituitary Surgery

The trans-sphenoidal surgery is to target the pituitary gland through endoscopy. The stereoscopic models of the skull, paranasal sinuses, the atlas (C1), axis (C2) and the selected surrounding structures were created from CT images of a cadaver. All internal structures were segmented with high resolution detail. The general pathway of trans-sphenoidal approach to pituitary gland surgery begins at nasal canal, passing nasal septum and turbinates, locating sella turcica before reaching pituitary gland. The simulation starts with a potential patient (digital model) lying on the surgical table in supine position (Fig. 3a). The user then proceeds to endoscopic views of the right nasal canal (Fig. 3b, asterisk right nostril), with visualization of internal structures including the middle and inferior turbinates (Fig. 3c). Further going through the turbinates, these structures may be made transparent to give the viewer a better 3D spatial sense of surrounding structures, including turbinates and nasal septum (purple), bone (including body of sphenoid bone labeled in the figure, transparent white), sphenoid sinuses (pink), and ethmoid sinuses (blue) (Fig. 3d). In order to visualize what's behind the sphenoid sinus, proceeding further by removing the sphenoid sinus allows the viewer to appreciate the relationship with critical surgical landmarks such as the location of the optic nerve, carotid canals and normal anatomic variants of sella turcica endoscopically (Fig. 3e). This is important, as the trans-sphenoidal approach is commonly used for pituitary tumor surgery. The normal surgical path is very deep and narrow, and a direct view is usually blocked by crucial osseous or soft tissue structures, such as turbinates (Fig. 3c), sphenoid sinus (Fig. 3d), neurovascular structures, the carotid artery, optic nerve and sella turcica as labelled (Fig. 3e). The close proximity of the sphenoid sinus to the carotid artery and the optic canal, and increased anatomic variations between sphenoid sinus and sella turcica floor (Fig. 3d, e) makes the approach even harder, and hence the familiarity with anatomical landmarks on the surgical route is of paramount importance. The better view of relative spatial relations of the pituitary gland (blue), carotid artery (red) and optic chiasm (yellow) can be achieved using the internal views and by making skull bone temporarily transparent (Fig. 3f).

4 Discussion

4.1 Stereoscopic Versus Conventional Learning Approach for the Trajectory Targeting of Trigeminal Ganglion Procedure

The purpose of creating the stereoscopic anatomy model is to facilitate trainees' learning curve of trigeminal ganglion injection or radiofrequency ablation and help them to learn the special relations of important surgical anatomy structures like maxillary artery, middle meningeal artery to avoid procedure complications. The most common procedure complication is a hematoma.

The conventional learning for the trigeminal ganglion procedure is based on two-dimensional fluoroscopic images. The ideal pathway of injection needle is described as "trajectory view" where the target can be seen directly on the fluoroscopic image. The successful needle placement is described as "bull's eye" as the only dot on the screen theorectically for ideal needle placement. However, two factors challenge the learner's understanding of clinical anatomy. First, the structure best seen on the fluoroscopic image are the bones, which are the only landmarks for the trainee to rely on. Teaching the anatomy during the procedure demands the trainee having a very good spatial ability to "see" the none-bone structure by the best guess and

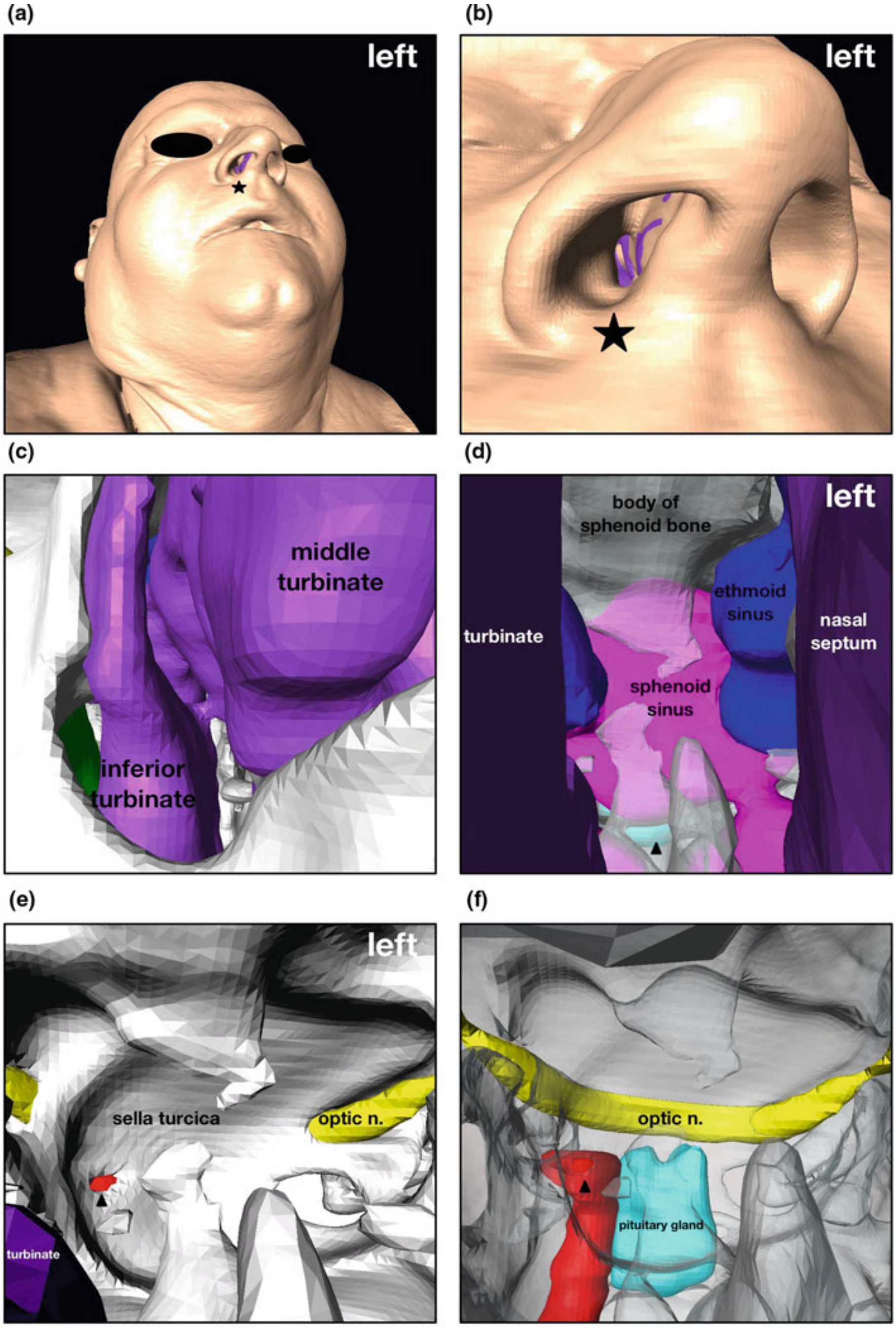

Fig. 3 **a** Supine position, the asterisk sign indicates the right nostril; **b** magnified right nostril, gross view of the right nasal canal; **c** subtracted soft tissues with the middle turbinate on the right and inferior turbinate on the right and inferiorly; **d** view posterior turbinate level with septum (purple), part of body of the sphenoid bone (transparent white), ethmoid sinuses (blue), and sphenoid sinus (pink); **e** more posterior part of the turbinate (purple, left lower corner), the view after sphenoid sinus (pink structure in **d**) removed, showed sella turcica with optic nerve (yellow) behind it and right internal carotid artery, indicated by small black arrowhead; **f** view with all sinuses, and turbinates removed with transparent bone (transparent white), showed the optic chiasm (yellow), below which is the pituitary gland (blue) as indicated by the arrow, and right internal carotid artery (black arrowhead). *Photo credit* Reproduced with permission from Anat Sci Educ 10:598–606 (2017)

imagination. Second, the depth of the needle or probe is depend either on the bony landmarks or lateral view. For example, in the trigeminal ganglion block procedure, the trainee can only be sure about the depth of needle placement by "feeling" the touch of pterygoid bone or lateral fluoroscopoic view that needle does not go through the sella. Even with the above technique, sometimes, the return of blood or cerebral spinal fluid will still confuse the learner due to these are not shown in a two-dimensional X-ray image when using conventional learning approach. By using stereoscopic models, the trainee could overcome the above barricade of learning, because stereoscopic learning requires minimal visual spatial ability from learner and the teaching material provides a good visualization.

The model of trigeminal ganglion block trajectory was demonstrated from three different views: anterolateral, lateral and inferior regions. The anterolateral approach is the most commonly described in literature (Fig. 1). By studying the model, the lateral approach could potentially avoid the risk of hematoma by avoiding the maxillary artery, and avoiding intra-oral risk during the procedure.

The stereoscopic model requires the learner to wear a pair of stereoscopic glass by looking at the model based on real patient CT/MRI images. The model not only demonstrate the bony structure, but also the structures like the external carotid artery, maxillary artery, middle meningeal artery, vertebral artery, medial and lateral pterygoid muscle, parotid gland, branches of the trigeminal nerve and trigeminal ganglion. Now the trainee can see that after needle or probe penetrate the skin, it will go through lateral pterygoid muscle and potentially medial pterygoid muscle. Before the needle reaches near to the foramen ovale, the maxillary artery/vein block the anterior medial part of foramen ovale, which is a vulnerable region and can be penetrated by the needle. This is most likely the reason why hematoma is very common here. Some patients might have an electric shock feeling during the procedure, and trainee can see that some branch of the trigeminal nerve, especially maxillary branch when the needle is positioned more anteriorly or mandibular branch when the needle is positioned more posteriorly. The model guides learners to avoid procedure complication or re-direct the needle if blood or paresthesia comes during the procedure. All the above findings cannot be achieved with two-dimensional fluoroscopic image teachings.

4.2 Stereoscopic Versus Conventional Learning Approach for the Trajectory Targeting of Intraarticular Injection Procedure

The high cervical facet steroid injection is used for both diagnostic and treatment purposes of neck pain and headaches. The target area is the space in between the first and second vertebra process (C1–C2). The working space is very small, and the target is surrounded by vital structures including vertebral artery, cervical nerve root and cervical spinal cord. This procedure is the "no man zone" for most interventional pain physicians. The three-dimensional stereoscopic view can be used to help trainee be less scared of this procedure by clarifying the structural relationship of the high cervical regional anatomy. The model of the atlas and the axis that allows trainees to better understand the relationship between the C1 and C2 vertebrae. The corresponding 3D model clearly demonstrated the important anatomical features such as the atlanto-occipital and atlanto-axial joints, interarticular facets and the transverse foramina.

The conventional learning for cervical facet steroid injection procedure is based on two-dimensional fluoroscopic images. The ideal pathway of injection needle is described as "trajectory view" where the target can be seen directly on the fluoroscopic image. The successful needle placement is described as "bull's eye" as the only dot on the screen theorectically for ideal needle placement. However, two factors challenge the learner's understanding of clinical anatomy. First, the structure best seen on the fluoroscopic image are the bones, which are the only landmarks for the trainee to rely on. Teaching the anatomy during the procedure demands the trainee having a very good spatial ability to mentally "see" the soft tissue structures by the best guess and imagination. Second, the position and depth of the needle or probe is depend either on the anatomy bony landmarks or lateral view of the structures. For example, in the cervical facet procedure, the trainee can only be sure about the depth of needle placement by "feeling" the touch of vertebral pillar or contralateral oblique fluoroscopoic view that needle does not go further than the anterior part of zygophysial joint of vertebral process. Even with the above technique, the trainee still needs lots cases of practice and inconfident to do the procedure.

By using stereoscopic models, the trainee may overcome the above barricade of learning due to the limited visual spatial ability from either learner himself or teaching materials. Particular thickness can be assessed with ease using this model and can also provide important anatomic information for doing C1/C2 injection for both diagnostic and therapeutic interventions. The anatomy could then be related to routine 2D X-ray fluoroscopic images that are used during the epidural injection or biopsies.

With the 3D model, the trainees can visualize these vertebrae at any angle and from any position (including internally) to better understand the anatomic relationships and their impact on a variety of clinical procedures. The model not only demonstrate the bony structure, but also the structures like vertebral artery, cervical spinal root and spinal cord etc. Now the trainee can see that after needle or probe penetrate the skin, it will go through facet joint. The vertebral artery lays laterally against the C1–C2 joint which is different comparing to the other cervical joints where the vertebral artery located medial to the facet joint. The nerve root goes posterior to the facet joint. Some patients might have the electric shocking feeling during the procedure, and trainee can see that the cervical nerve root runs from transverse foramen towards the facet. Thus, it is recommended minimal sedation or no sedation for such procedure to avoid irreversible permanent nerve damage. The model guides learners to avoid procedure complication or re-direct the needle if paresthesia or paralysis comes during the procedure. All the above findings cannot be achieved with two-dimensional fluoroscopic image teachings.

4.3 Stereoscopic Versus Conventional Learning Approach for the Endoscopic Trans-Sphenoidal Pituitary Surgery

Pituitary surgery carries risks of compromising complicated regional anatomy. It requires trainees to have a good grasp of depth and spatial relations of targeted structures. The conventional learning approach for neurosurgical residents are from textbooks, teaching video or cadaver lab. Only the cadaver lab provides some in depth spatial learning, other teaching methods are two-dimensional based. Not all the residents or institute has free access to cadaver lab. Most of the cadavers are not plastinated with colored silicone which labels the vessels. The biggest limitation per author's observation is that trainee cannot freely manipulate the model to visualized the structures from any angle, which is very helpful to create a better spatial location of different structures in trainees' mind. The use of three-dimensional computer models for neurosurgical guidance and navigation has been described in the past (Komotar et al. 2012; De Notaris et al. 2014), but without stereoscopic virtual presentation.

The flexible and spatial competent three-dimensional models of the paranasal sinuses from the perspective of the surgical approach, which allows clinical trainees and surgeons to explore and visualize the route from the nasal cavity to the sphenoidal sinus and help them better understand the spatial relationships between the sphenoid bone, the sinuses and their surrounding structures. In some patients with complex sella anatomy, non-pneumatized or overtly pneumatized sphenoid sinuses, the appearance of the sella turcica and its relationship with the tuberculum and dorsum sellae and adjacent clivus may be anatomically challenging and may substantially increase the risk of complications during surgery. An accurate and thorough understanding and review of the anatomy of the region and important landmarks relevant to trans-sphenoidal surgery is of paramount importance to patient safety. Even the degree of sphenoid sinus development and location and deviation of the sphenoid septum can be appreciated in three-dimensional. Furthermore, the degree and extent of sella floor bulge, related to the degree of the sphenoid sinus pneumatization, and the location and prominence of the carotids are all critical landmarks when planning the surgical approach and understanding the complex anatomy.

The stereoscopic model can be used in the simulation lab for surgical trainees. Each trainee can manipulate the models from any perspective before the surgical procedure or for routine practice. This provides personalized anatomy education for clinical trainees. The size of the model can be enlarged, its perspective can be changed according to the viewers' satisfaction, and interior structures can be demonstrated without opening or breaking down the model. With stereoscopic glasses, this real-time simulation provides the trainee with a unique visual acquaintance and familiarity before participating in or performing the surgical procedures. With the development of three-dimensional TV and VR (virtual reality) equipment, the stereoscopic models may be distributed to other centers and anatomy/surgical departments.

5 The Benefits

We discussed using the stereoscopic model for improving trainees' understanding of clinical anatomy. The model is CT/MRI image data based, and is personalized per different patient. By visualizing the anatomical structure through stereoscopic glass, it provides angles of views that simple computer model cannot. With these models, the trainee can potentially practice procedure on the model that specifically designed for the patient. The stereoscopic simulation training opens a new avenue for clinical trainees to improve their surgical methods and skills in their future clinical practice and reduce the risk of complications for real patients.

6 The Limitation

This review was limited to the skull and upper cervical spine based on a CT not an MRI. Segmentation of certain structures like trigeminal nerve, spinal cord, spinal roots are based on the combination of density of the tissue and grooves related to surrounding body structures. The studies of the review does not assess reproducibility of image segmentation techniques, nor directly assess trainee preference of success in learning.

7 Conclusion

The stereoscopic simulation training opens a new avenue for clinical trainees to improve their surgical methods and skills in their future clinical practice and reduce the risk of complications for real patients. The teaching facility owns the stereoscopic virtual models can set up a 3D simulation laboratory for clinical training. Each trainee can manipulate the models from any perspective before the surgical procedure or for routine practice. This provides personalized anatomy education for clinical trainees. With 3D glasses, this real-time simulation provides the trainee with a unique visual acquaintance and familiarity before participating in or performing the surgical procedures. With the development of

3D TV and VR (virtual reality), the 3D stereoscopic models may be distributed to other centers and anatomy/surgical departments. Future research will be more focused on evaluation of stereoscopic demonstration for surgical trainees.

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The Whole Picture: From Isolated to Global MRI Measures of Neurovascular and Neurodegenerative Disease

David Alexander Dickie, Terrance J. Quinn and Jesse Dawson

Abstract

Structural magnetic resonance imaging (MRI) has been used to characterise the appearance of the brain in cerebral small vessel disease (SVD), ischaemic stroke, cognitive impairment, and dementia. SVD is a major cause of stroke and dementia; features of SVD include white matter hyperintensities (WMH) of presumed vascular origin, lacunes of presumed vascular origin, microbleeds, and perivascular spaces. Cognitive impairment and dementia have traditionally been stratified into subtypes of varying origin, e.g., vascular dementia versus dementia of the Alzheimer's type (Alzheimer's disease; AD). Vascular dementia is caused by reduced blood flow in the brain, often as a result of SVD, and AD is thought to have its genesis in the accumulation of tau and amyloid-beta leading to brain atrophy. But after early seminal studies in the 1990s found neurovascular disease features in around 30% of AD patients, it is becoming recognised that so-called "mixed pathologies" (of vascular and neurodegenerative origin) exist in many more patients diagnosed with stroke, only one type of dementia, or cognitive impairment. On the back of these discoveries, attempts have recently been made to quantify the full extent of degenerative and vascular disease in the brain in vivo on MRI. The hope being that these "global" methods may one day lead to better diagnoses of disease and provide more sensitive measurements to detect treatment effects in clinical trials. Indeed, the "Total MRI burden of cerebral small vessel disease", the "Brain Health Index" (BHI), and "MRI measure of degenerative and cerebrovascular pathology in Alzheimer disease" have all been shown to have stronger associations with clinical and cognitive phenotypes than individual brain MRI features. This chapter will review individual structural brain MRI features commonly seen in SVD, stroke, and dementia. The relationship between these features and differing clinical and cognitive phenotypes will be discussed along with developments in their measurement and quantification. The chapter will go on to review emerging methods for quantifying the collective burden of structural brain MRI findings and how these "whole picture" methods may lead to better diagnoses of neurovascular and neurodegenerative disorders.

Keywords

Brain MRI · Neurodegeneration · Neurovascular disease · Stroke · Dementia

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1 Introduction and Caveats of Content

Preceding the application of magnetic resonance to observe the brain during life by over 125 years, descriptions of cerebral small vessel disease (SVD) date back to the 1800s (Virchow 1851; Robin 1859; Mansfield and Pykett 1978). Understanding of SVD was later greatly enhanced by the clinicopathological studies of CM Fisher from the 1960s onwards (Fisher 1982). Although profoundly important, these early studies, indeed all post-mortem pathology studies, cannot measure disease course through life. Understanding how diseases of the brain evolve in life is essential to providing effective treatments and this is done most effectively (and non-invasively) using in vivo imaging.

Magnetic resonance, the energy released from protons when they are placed within a magnet and exposed to a radio wave, was applied to detect the properties of water via a voltage oscillation screen in 1946 (Bloch 1946); this method was extended to directly visualise capillaries of water (H_2O) within a larger tube of heavy water (D_2O) in 1973 (Lauterbur 1973). Because the human body is largely made of water, Peter Mansfield and colleagues were able to apply this method to image a human finger in 1976 (Mansfield and Maudsley 1977). Since the first magnetic resonance image of the living human brain was published in 1980 (Holland et al. 1980), it has become widely used in clinical practice and research to describe features of brain degradation in SVD, stroke and dementia (Fazekas et al. 1987; Fox and Schott 2004; Wardlaw et al. 2013).

SVD is associated with cognitive impairment and gait disturbances, generally in the elderly but also in younger people with rare congenital conditions such as Cerebral Autosomal Dominant Arteriopathy with Sub-cortical Infarcts and Leukoencephalopathy (CADASIL), as a result of changes in the small perforating arteries, arterioles, venules, and veins of the brain. Advances in imaging technology have allowed the diagnosis of SVD to now be made routinely in the living rather than neuropathology at death providing cause of functional and cognitive deficits seen in life. Dementia, from the Latin for loss (de-) of mind (ment), is an umbrella term for diseases of the brain that result in progressive cognitive, functional, and behavioural decline, generally in people over 65 years. Stroke, referred to as a “brain attack” by the UK Stroke Association to illustrate the seriousness of the condition, occurs when the blood supply to part of the brain is cut off, either through haemorrhage (leaking of vessels) or ischaemia (blocking of vessels). It is important to differentiate these types of stroke so that appropriate treatment, e.g., clot (blockage) thinning for ischaemia, can be administered as soon as possible.

Computed tomography (CT) is still the most widely used imaging modality to identify cause of stroke, or to help ascertain whether stroke has occurred at all, in clinical practice. This is due to cost, time and contraindications to magnetic resonance imaging (MRI). However, although CT can be used to measure white matter features thought to reflect SVD (Dickie et al. 2017a), it is generally inferior to MRI at visualising the subtilties of SVD. Previous work provides more on the arguments for and against CT and MRI (Wardlaw 2007; Chalela et al. 2007; von Kummer and Dzialowski 2007); this chapter focuses solely on structural MRI. As well as structural MRI, positron emission tomography (PET), combined PET-MRI systems, and functional MRI are commonly used in dementia. But given the focus of this chapter, readers are directed to previous descriptions of these methods in Alzheimer’s disease (Jack et al. 2008; Buckner et al. 2009).

In 1906, Alois Alzheimer first described the cerebral and clinical hallmarks of the disease that was to be named after him by Emil Kraepelin (Maurer et al. 1997). This chapter does not intend to provide a thorough background in the definition, epidemiology, and treatment of Alzheimer’s disease (see, for example, Maurer et al. 1997; Selkoe 2013; Winblad et al. 2016; Scheltens et al. 2016), nor does it discuss other mainly neurodegenerative conditions such as Parkinson’s and multiple sclerosis (Marshall et al. 2018), but uses Alzheimer’s to highlight the importance of collectively assessing neurodegenerative processes, e.g., brain atrophy, and neurovascular disease on structural brain MRI.

2 Cerebral Small Vessel Disease

Cerebral SVD is a neurological disease of ageing characterised by a range of imaging findings thought to represent pathologies in the arteries, arterioles, veins, venules, and capillaries of the brain (Pantoni 2010; Shi and Wardlaw 2016). Many older people live normally in the community with brain MRI features of SVD but these features dramatically increase the risk for stroke, dementia, and death during follow-up (Debette and Markus 2010; Bos et al. 2018). The STandards for ReportIng Vascular changes on nEuroimaging (STRIVE) recently defined the MRI features of SVD to include lacunes of presumed vascular origin, cerebral microbleeds, perivascular spaces, and white matter hyperintensities of presumed vascular origin.

2.1 White Matter Hyperintensities of Presumed Vascular Origin

White matter hyperintensities (WMH) of presumed vascular origin, also known as leukoaraiosis, appear hyperintense on T2- and T2-fluid attenuated inversion recovery (FLAIR) weighted MRI and hypointense on T1 MRI (Fig. 1).

WMH were formally known as white matter lesions but the term hyperintensities of presumed vascular was adopted after it became apparent hyperintensities did not necessarily correspond to underlying lesions and to differentiate them from lesions seen in multiple sclerosis (Wardlaw et al. 2013, 2015). Predominantly found in periventricular and deep white matter, hyperintensities are also known to occur in the deep grey matter and infratentorial structures. WMH, deep grey matter, and infratentorial hyperintensities are collectively known as “subcortical hyperintensities” (Scheltens et al. 1993; Wardlaw et al. 2013).

Although referred to as “of presumed vascular origin”, vascular risk factors, including elevated blood pressure, smoking, cholesterol and diabetes, account for a very small percentage of the variance in cross-sectional WMH burden (Wardlaw et al. 2014; Wyss et al. 2019). Vascular risk factors have also been shown to account for limited variance in longitudinal progression of WMH (Dickie et al. 2016b). These counterintuitive results are all the more surprising when considering that WMH are seen in up to, if not more than, 90% of patients with ischaemic stroke (Fu et al. 2005; Wardlaw et al. 2014); where vascular risk factors are a main cause (O’Donnell et al. 2016). As well as tripling risk of stroke, WMH double risk of dementia and death during follow-up of two to twelve years (Debette and Markus 2010). Not limited to an increased risk for all cause dementia, WMH are associated with a specific increased risk of Alzheimer’s disease (Bos et al. 2018). Precise assessments of WMH burden are therefore crucially important for diagnoses and research into novel treatment for neurological disorders. Luckily, unlike other features of SVD, a large number of semiquantitative visual assessments and quantitative volumetric assessments have been developed for WMH.

2.1.1 Semiquantitative Visual Assessments of WMH

Semiquantitative visual assessments generally involve the structured recording of the size and number of WMH in different brain regions. There are at least 13 scales for semiquantitative visual assessment of WMH (Riitta et al. 1997; Kapeller et al. 2003). Two of the most commonly used are the Fazekas (Fazekas et al. 1987) and Scheltens (Scheltens et al. 1993) scales. The Fazekas scale is based on separate assessments of periventricular WMH, i.e., those contiguous with the lateral ventricles, and deep WMH, i.e., punctuated lesions in the deep white matter separate to the lateral ventricles, with a score of zero to three in each region; giving a total score of up to six (Fazekas et al. 1987). Example appearances of each score on FLAIR MRI are shown in Fig. 2.

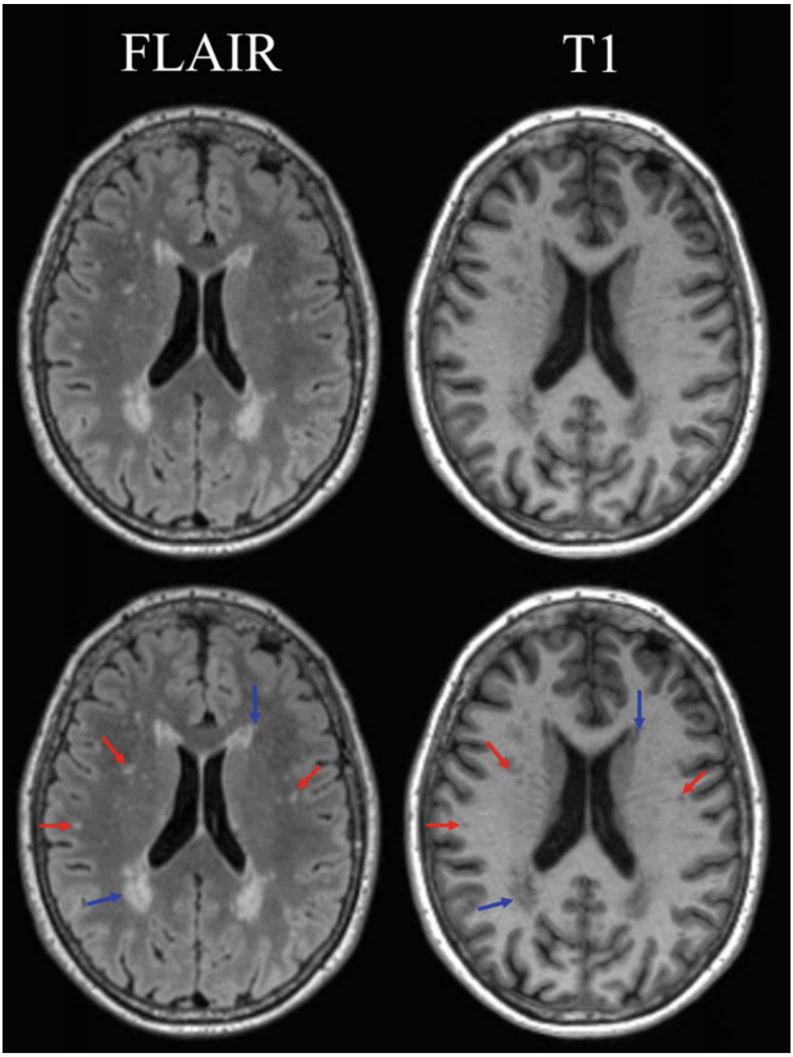

Fig. 1 White matter hyperintensities (WMH) of presumed vascular origin. Some of the periventricular WMH are highlighted with blue arrows and some of the deep WMH are highlighted with red arrows. Note the hypointense appearance of WMH on T1 (right) but relative limited clarity compared to the brightness of WMH on FLAIR (left)

Fazekas scale, although simple and quick to administer, has limited granularity and is prone to ceiling effects, e.g., it cannot detect longitudinal increases in patients who present with a score of 3, 3. The Scheltens scale sought to address these issues by assessing deep WMH burden separately in frontal, parietal, temporal, and occipital lobes (Fig. 3), the basal ganglia and thalamus, segments of the brainstem, and cerebellum on a scale with seven levels. Additionally, frontal, occipital and medial band periventricular burden were assessed on a scale with three levels (Scheltens et al. 1993). This allowed for increased granularity with a total score of 84 and limited ceiling effects. The downsides to Scheltens scale include increased complexity and time to administer. All semiquantitative scales are limited by inter-rater differences, i.e., visual perception of one rater differing to another leading to different scores for the same patient. Some of the limitations of semiquantitative scales may be addressed by quantitative volumetric assessments of WMH.

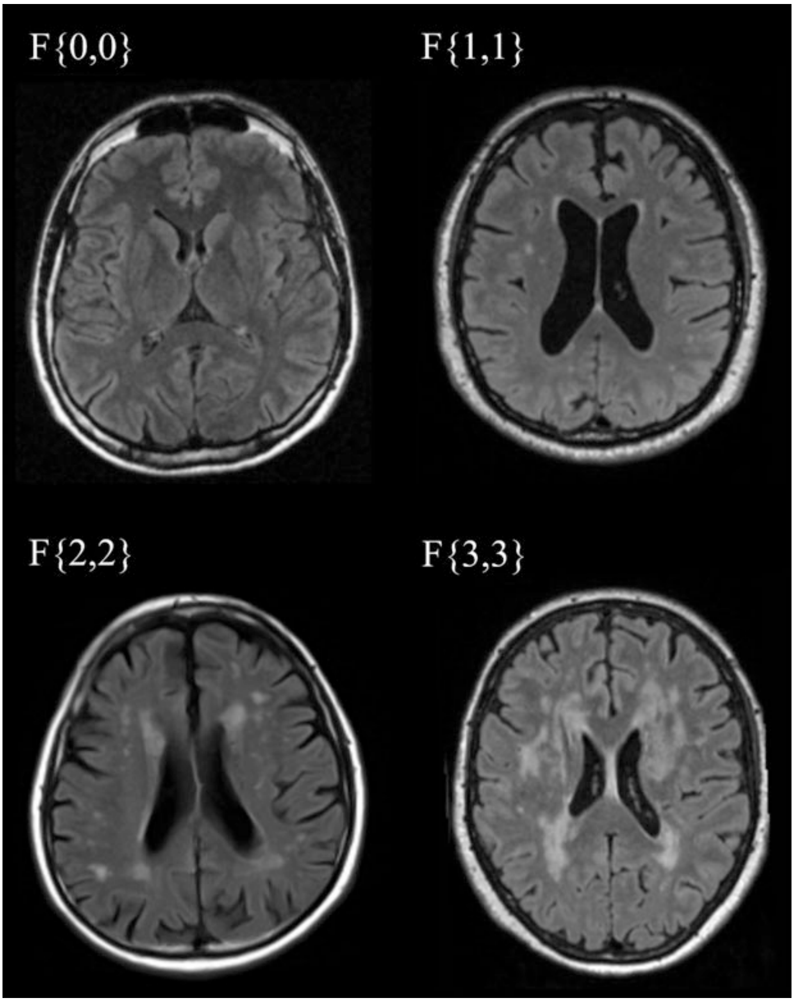

Fig. 2 Examples of Fazekas scores of periventricular 0, deep 0 (top left); periventricular 1, deep 1 (top right); periventricular 2, deep 2 (bottom left); and periventricular 3, deep 3 (bottom right). Note that differing combinations of scores are possible, e.g., periventricular 2, deep 1; periventricular 1, deep 2; periventricular 3, deep 1; and so on. These examples were selected to show all levels of score for both regions in as small a figure as possible (there are $8 * (8 - 1)/2 = 28$ possible combinations of periventricular and deep Fazekas scores). Scans are of different people

2.1.2 Quantitative Volumetric Assessments of WMH

Quantitative assessment of WMH is the process of calculating the volumetric burden of WMH in millimetres cubed (mm^3), centimetres cubed (cm^3), millilitres (ml), or as a proportion of intracranial volume (Fig. 4).

While 13 semiquantitative scales may have seemed excessive, it is bordering on scarce when considering the number of studies purporting to describe a "novel", "new", "reliable", "accurate", "reproduceable", or "precise" method for volumetric assessment of WMH. A systematic review in 2015 found 34 different methods for volumetric assessment of WMH (Caligiuri et al. 2015). Indeed, 24 different methods can be found via the first few pages of a search on Google, several of which were published after the 2015 review. This is not to mention that there were 20 entries submitted to the recent "WMH

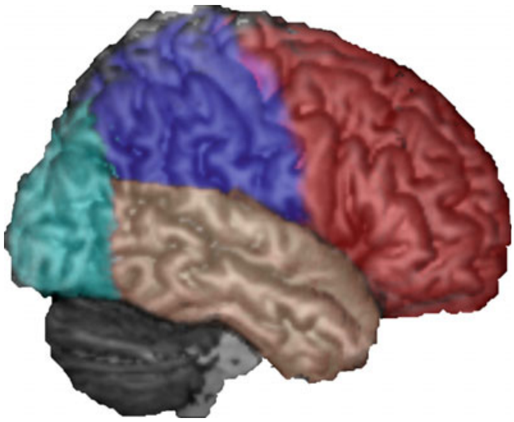

Fig. 3 Frontal (red), parietal (royal blue), temporal (bronze) and occipital (cyan) lobes of the brain according to a maximum probability "atlas" (Hammers et al. 2003) registered to an individual participant. Previous work describes the concept of a brain atlas (Dickie et al. 2017b)

Segmentation Challenge" at the Medical Image Computing and Computer Assisted Interventions Conference (MICCAI) 2017 (Kuijf et al. 2019). The wide variety of segmentation techniques used in such methods has recently been systematically reviewed (Frey et al. 2019). Hence the old proverb, "more than one way to segment a WMH". Segmentation methods have ranged from being entirely manual (i.e., WMH were delineated by hand) to "fully automatic". Despite computational advances and application of "machine learning" to the segmentation of WMH (Bowles et al. 2017) it is the authors experience, and that of many international experts in SVD imaging research (Wardlaw et al. 2013), that no computational method for WMH segmentation can be considered to be fully automatic. At the very least, visual checking of the computational output will always be required to identify the up to 20% of cases that fail pre-processing steps in volumetric assessments, including co-registration of sequences (Fig. 5) and skull stripping (Ducharme et al. 2016). In diseases such as stroke, dementia, and SVD it is likely that visual checking alone will not suffice as a reasonable proportion of cases will require manual editing of the automated output to exclude image artefacts (e.g., from patient motion), WMH mimics (e.g., fluid in the corticospinal tracts), and infarcts. So while quantitative assessments of WMH may provide limitless granularity and remove ceiling effects, they are limited by processing failures and manual quality control requirements.

2.1.3 Quantitative Versus Semiquantitative Assessments of WMH

The advantages and disadvantages of WMH assessment methods dictate that good practice is to perform quantitative and semiquantitative assessments. We present one such example here due to availability of data at hand however other more detailed comparisons are available (van Straaten et al. 2006). Fazekas and quantitative volumetric assessments of WMH have been performed in the publicly accessible Virtual International Stroke Trials Archive (VISTA; http://www.virtualtrialsarchives.org/vista/). VISTA holds brain imaging and clinical data from several completed clinical trials in stroke and transient ischaemic attack (Ali et al. 2007). In 307 patients (195 male, 112 female) from VISTA aged 65.96 ± 12.53 years, median total Fazekas score was 2; 25th percentile score was 1 and 75th percentile score was 4; mean WMH volume was 12.25 ± 12.54 ml (Dickie et al. 2019; Wyss et al. 2019). The method used to assess these volumes has been described previously (Dawson et al. 2018) and is illustrated in Fig. 5.

The Spearman correlation between total Fazekas score and WMH volume was 0.882 ($P < 0.0001$; Fig. 6). The large variation in WMH volumes among patients with the same total Fazekas score is exemplified by the cases shown in Fig. 7. The correlation between WMH volume and a global measure of cognition, Mini Mental State Examination was $\rho = -0.453$ ($P < 0.0001$) compared with $\rho = -0.426$ ($P < 0.0001$) when using total Fazekas score to assess WMH burden. The correlation between WMH volume and systolic blood pressure was $\rho = 0.292$ ($P < 0.0001$) compared with $\rho = 0.255$ ($P < 0.0001$) when using Fazekas score to assess WMH burden.

These examples show the slight strengthening of associations between WMH, vascular risk factors and cognition when using quantitative

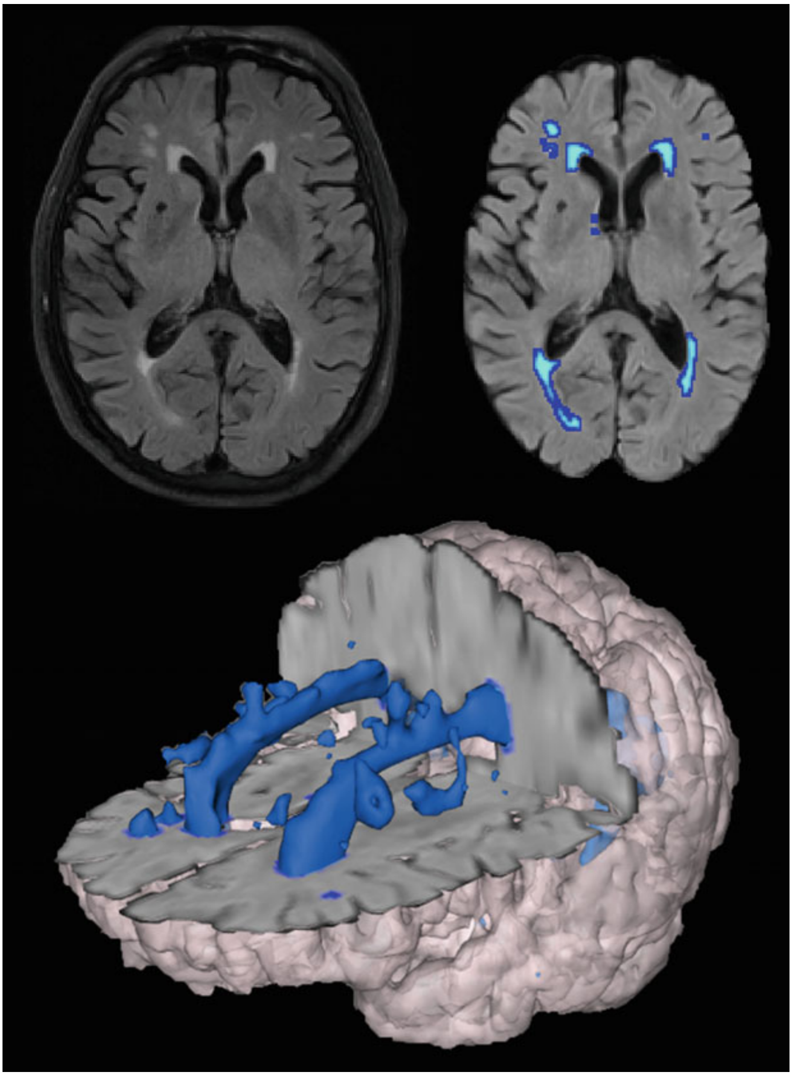

Fig. 4 Quantitative volumetric assessment (segmentation) of WMH from FLAIR MRI (top left panel) highlighted in blue in axial plane (top right panel) and in a 3D rendering (bottom panel)

volumetric assessments over semiqualitative visual assessments. This gain in statistical power may be subtle but this could be important when attempting to detect the effects of potential treatments and differences between normative ageing and disease which may be equally as subtle (Dufouil et al. 2005; Dickie et al. 2015a). The need for quantitative assessments is greater in populations with more severe WMH burden at the ceiling of visual scales at presentation, such as the growing number of people making it to very old age (Ritchie et al. 2018). As shown in Fig. 8, volumes of WMH can also be used to map the spatial distribution of WMH across a population (Dickie et al. 2016b, 2019; Ritchie et al. 2018).

However, as previously described and illustrated in Fig. 9, quantitative assessments require manual removal of artefacts and infarcts that mimic WMH. Hence the recommendation that both semiqualitative and quantitative assessments of WMH are performed. WMH mimics

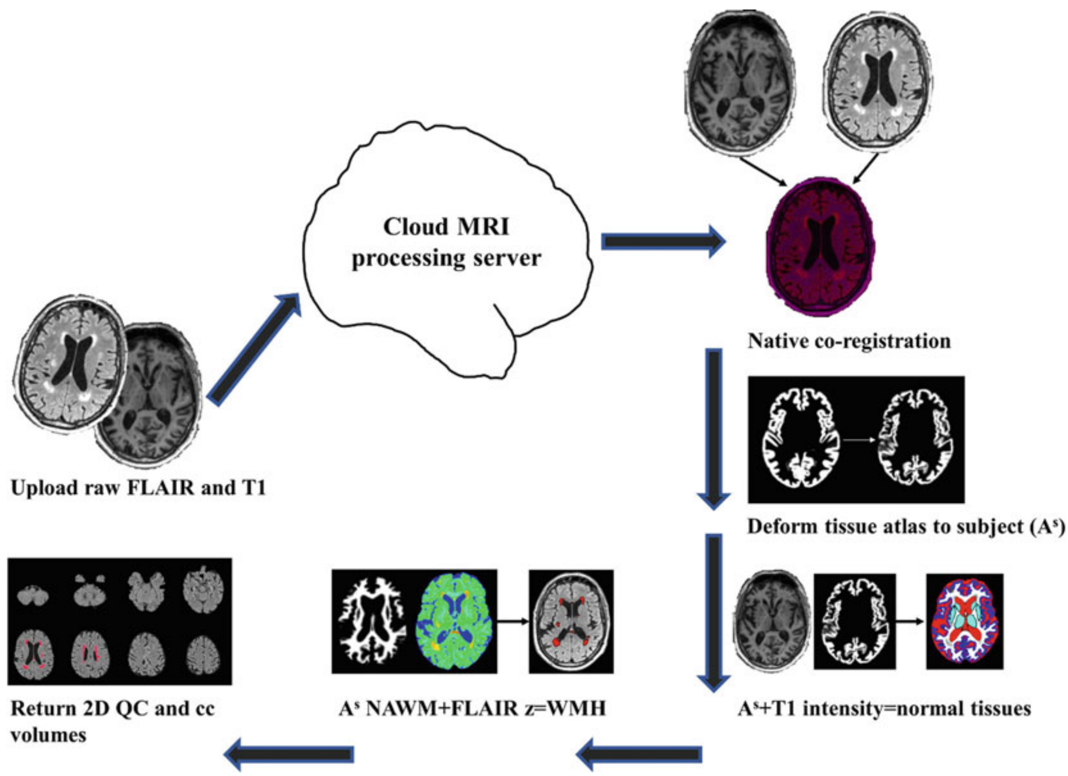

Fig. 5 Example of the main steps performed in quantitative volumetric assessment of WMH including co-registration of MRI sequences within subject, nonlinear deformation registration of an atlas of tissues to subject, statistical thresholding via a z-score image derived from FLAIR, and visual assessment of output. Full details of this method were described previously (Dawson et al. 2018)

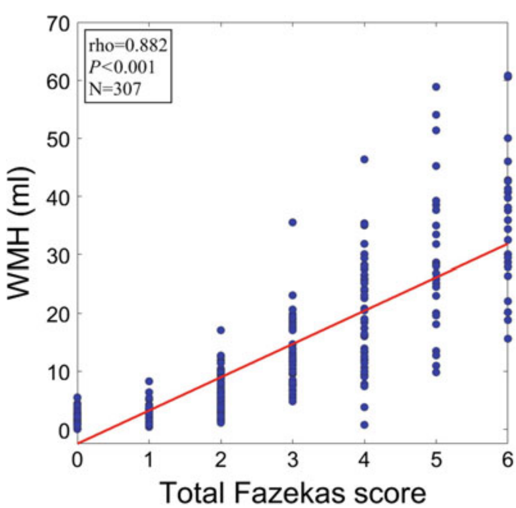

Fig. 6 Scatter plot of the association between WMH volume and total Fazekas score in 307 patients with ischaemic stroke and transient ischaemic attack

include another important feature of SVD, lacunes of presumed vascular origin which must be differentiated from WMH due to their differing pathophysiological and clinical profile.

2.2 Lacunes of Presumed Vascular Origin

Lacunes of presumed vascular origin are pitted cerebrospinal fluid filled spaces, or gaps as is the direct French translation, of 3–15 mm in diameter which often appear with a hyperintense rim in the basal ganglia or deep white matter (Figs. 9, 10; Wardlaw 2008; Wardlaw et al. 2013). Lacunes may form via subcortical infarction (subcortical ischaemic stroke), as identified with diffusion weighted imaging in the acute phase, or via deep haemorrhage that is identifiable from

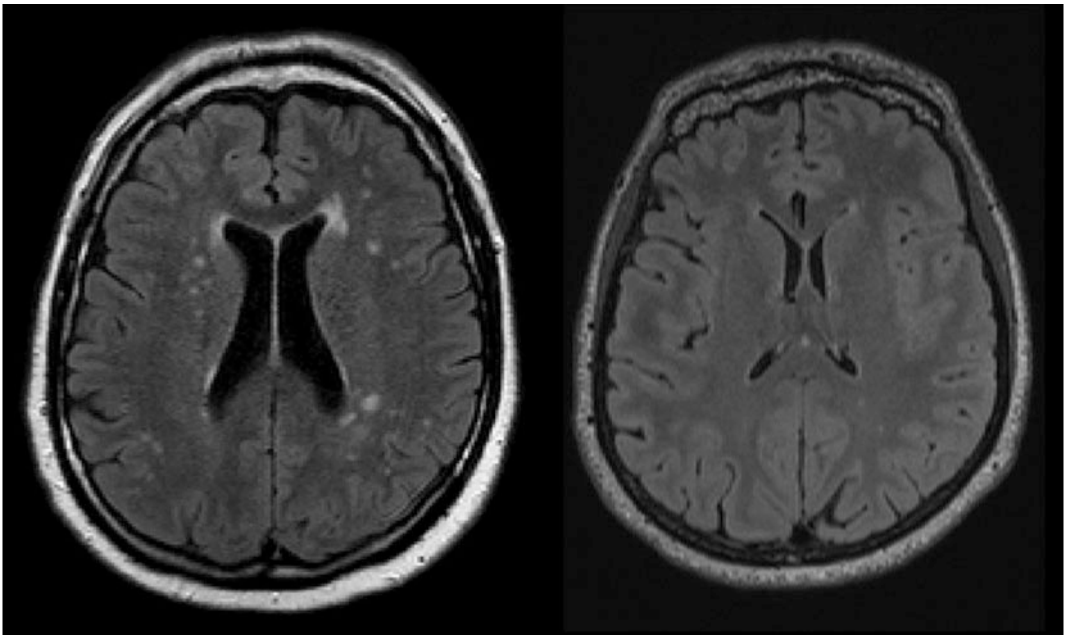

Fig. 7 Two different patients with periventricular and deep Fazekas scores of 1. Both patients met the criteria of caps or pencil thin lining for a periventricular score of 1 and punctuated deep hyperintensities that are not coalescing for a deep score of 1, but there are marked differences between the patients. The patient on the left has more pronouned periventricular hyperintensities and several more deep hyperintensities

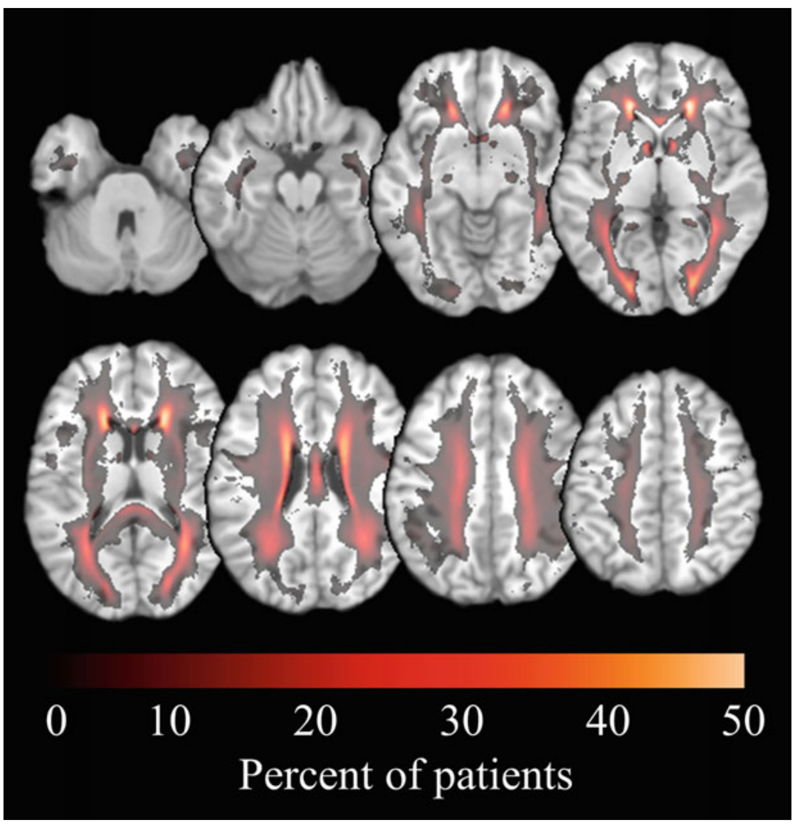

Fig. 8 Probability map of WMH from 307 patients with ischaemic stroke. WMH were quantitatively assessed in individual patients and then overlaid in the same anatomical space to produce a probability of WMH occurring in each voxel (point in the image). The probability map shows that a large proportion of patients ($\geq 50\%$) have periventricular WMH at the frontal horn of the lateral ventricles whereas deep WMH are distributed diffusely with no real concentration in any one region

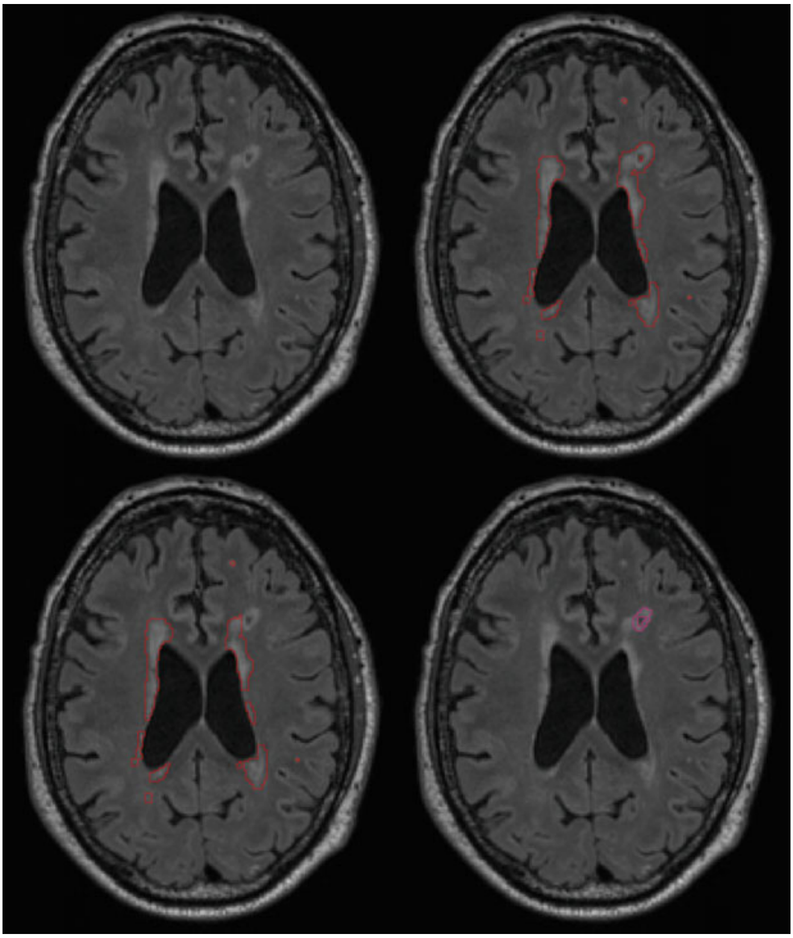

Fig. 9 FLAIR MRI from a patient with ischaemic stroke presenting with WMH and a lacune of presumed vascular origin (top left panel). Quantitative assessment initially defined the rim of the lacune as a WMH (red outline top right panel) based on it's location and intensity; this had to be removed manually (bottom left panel). The hyperintense rim of the lacune is delineated in the bottom right panel (magenta)

susceptibility-weighted imaging in the acute phase (Wardlaw et al. 2013).

But they do not necessarily result in clinically overt lacunar stroke syndrome, i.e., neurological deficits that lead to hospital admission; many lacunes develop "silently" without immediately noticeable neurological deficits (Potter et al. 2010). These silent lacunes are associated with hypertension and are commonly seen in healthy older people (Vermeer et al. 2007). However, consequences of lacunes, including cognitive impairment and dementia, may develop insidiously over time (Snowdon et al. 1997; Vermeer et al. 2003; Shi and Wardlaw 2016).

How long-term cognitive symptoms of lacunes manifest is currently unclear: some (Vermeer et al. 2003), but not others (Jokinen et al. 2011), have found a negative association between appearance of lacunes and global cognitive function decline. While not all have found associations with global cognitive decline, poorer executive function and motor control were negatively associated with presence of lacunes (Jokinen et al. 2011). Differences between legacy studies may have been due to the myriad definitions of lacunes prior to standardised lexicon being developed in 2013 through STRIVE (Potter et al. 2011; Wardlaw et al. 2013; Shi and

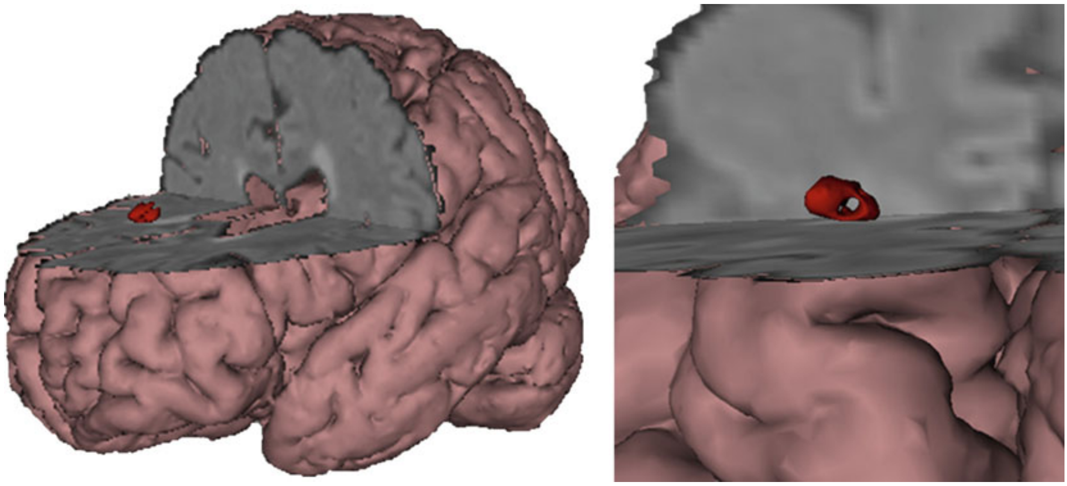

Fig. 10 Three-dimensional rendering of a FLAIR MRI and segmented lacune (red). The panel on the left shows how small lacunes may be relative to the brain and the significant neurological impairment they may cause. The panel on the right provides a zoomed in view to appreciate the cavernous nature of the lacune in 3D

Wardlaw 2016). The nature of long-term lacunar cognitive impairment may not become clear until more studies are conducted using these newly published standards.

Regardless of the nomenclature used, the burden of lacunes was generally defined by manually counting the location, size and number of individual lesions (Vermeer et al. 2003; Wardlaw et al. 2013) but semi-automatic (Hervé et al. 2009) and "automatic" (Ghafoorian et al. 2017) methods have recently been proposed. The similar appearances and locations of WMH and lacunes on structural MRI mean that these methods require visual checking at the very least and, more likely than not, manual editing. Hyperintensities on T2 may correspond to the majority of SVD features but hypointensities on T2-gradient echo (GRE), including cerebral microbleeds, are also thought to represent underlying SVD.

2.3 Cerebral Microbleeds

Cerebral microbleeds are small foci (2–5 mm) of blood products in the tissue of the brain that are visible as hypointensities on magnetic sensitivity sequences including T2-GRE (Fig. 11) and susceptibility-weighted scans (Greenberg et al. 2009; Wardlaw et al. 2013). They occur in 15–20% of people over 60 years and more commonly in people over 80 years (Vernooij et al. 2008; van Es et al. 2011) or with SVD (Staals et al. 2014). The risk of cognitive decline and dementia is increased in those with cerebral microbleeds (Staals et al. 2014; Akoudad et al. 2016; Gorelick and Farooq 2016). Visual ratings are generally used to measure burden of cerebral microbleeds in cortical junctions, subcortical areas, and infratentorial structures (Charlotte et al. 2009; Gregoire et al. 2009). Some efforts have been made to automate this process in a limited number of participants (Seghier et al. 2011; Morrison et al. 2018). But the small size of cerebral microbleeds and large number of mimics and artefacts in magnetic-sensitivity MRI sequences, e.g., cross-sectional cuts of vessels on SWI; air, bone, and iron deposits on T2-GRE, mean that significant manual intervention may still be required to accurately quantify their burden (Seghier et al. 2011).

While measurements of cerebral microbleeds provide an indication of small vessel haemorrhagic pathology (Fazekas et al. 1999), measurements of the spaces around vessels are potential markers of differing small vessel pathology.

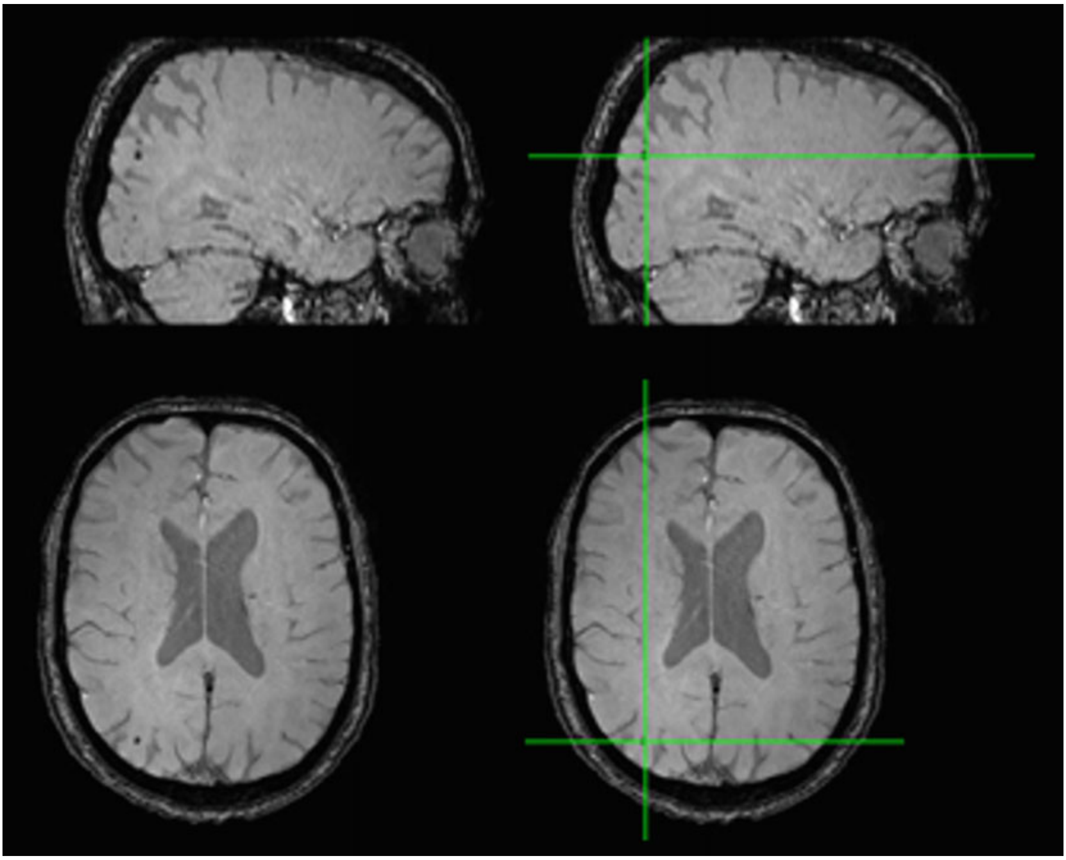

Fig. 11 Cerebral microbleed in the caudal area of the inferior parietal lobe highlighted by crosshairs on the right panels

2.4 Perivascular Spaces

Perivascular spaces, often referred to as Virchow-Robin spaces after their 19th century discoverers, surround the arteries, arterioles, veins, and venules that course from the sub-arachnoid space through the brain parenchyma (Kwee and Kwee 2007). They form part of the brain's extracellular fluid drainage system and are important for clearance of waste products, namely amyloid-beta (Weller et al. 2008; Bakker et al. 2016). Visible as ovoid or linear hyperintensities on T2 MRI (Fig. 12), perivascular spaces are generally found in the mesencephalon, hippocampus, basal ganglia, and centrum semiovale in all age groups but become more visible and frequent with higher blood pressure, advancing age, and other features of SVD (Zhu et al. 2010).

Some have found that larger perivascular spaces are associated with dementia (Patankar et al. 2005) and worse cognitive function (MacLullich et al. 2004). One hypothesis is that perivascular spaces become dilated from build-up of amyloid-beta. This build up is thought to occur via age-related sclerosis of the small vessels resulting in reduced pulsations that drive the force of extracellular fluid motion (Weller et al. 2008). Much like a shower with low pressure will struggle to wash away mud down the drain, reduced extracellular fluid motion will struggle to wash away amyloid-beta. Accumulation of amyloid-beta in the brain is thought to be an initiating factor in Alzheimer's disease (Selkoe and Hardy 2016). However, a recent meta-analysis of over 3500 people found that perivascular spaces were not associated with cognitive dysfunction in the general population

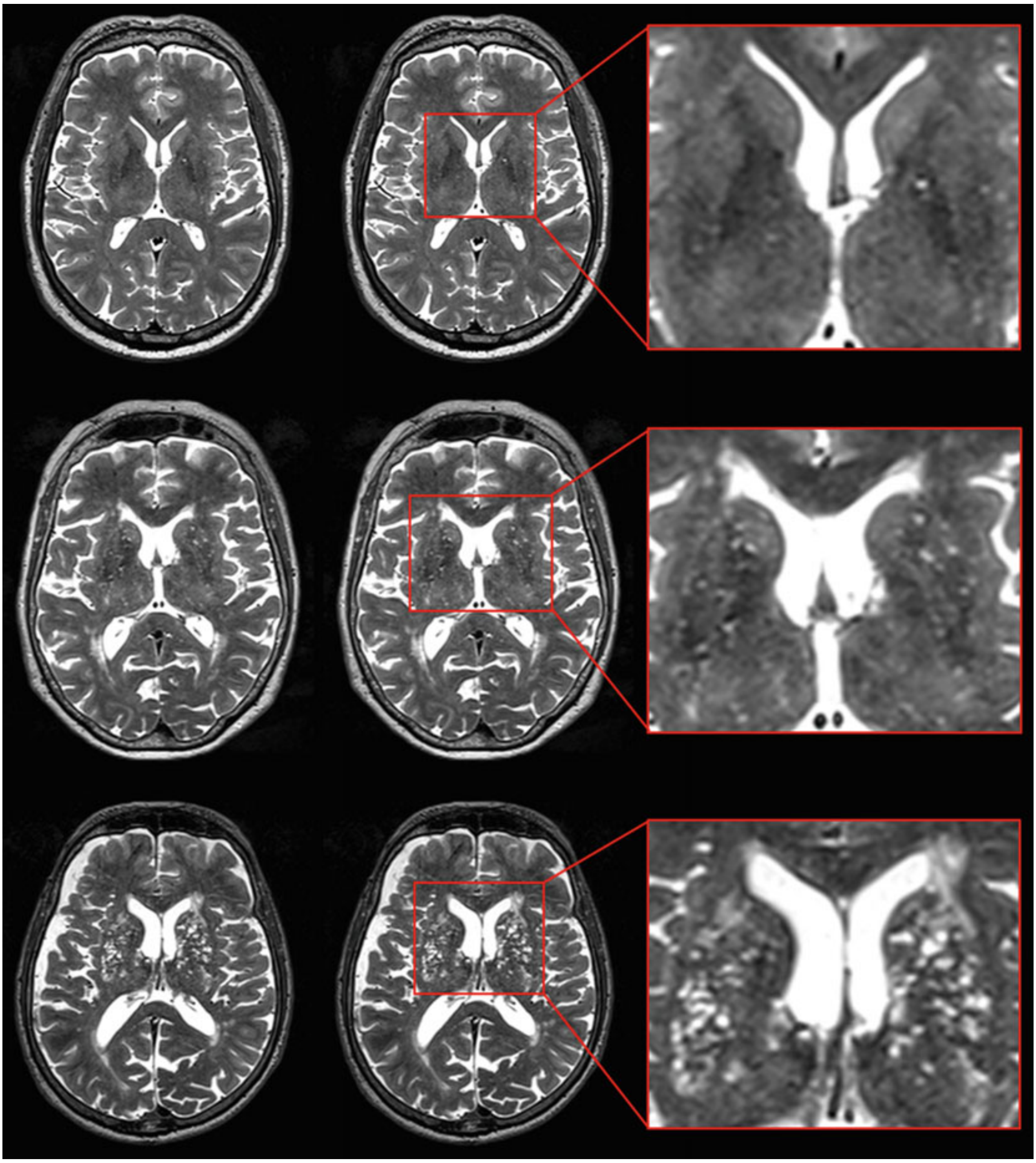

Fig. 12 Examples of mild (top panel), moderate (middle panel), and severe (bottom panel) perivascular spaces in three different ischaemic stroke patients. Note similar hyperintensity of perivascular spaces and cerebrospinal fluid

(Hilal et al. 2018). With the clinical significance of perivascular spaces still up for debate, they should not be classified as lesions (Wardlaw et al. 2013).

Despite this, their association with other features of SVD (Zhu et al. 2010) means that perivascular space measurement is still clearly important. Perivascular spaces are generally measured by counting their number in the mesencephalon, hippocampus, basal ganglia, and centrum semiovale but recent attempts have been made to automate this process using these semiquantitative assessments to train quantitative computational classifiers (Ballerini et al. 2018;

Dubost et al. 2019). This work to better characterise and understand the significance of perivascular spaces, and indeed all features of SVD, remains ongoing.

2.5 Summary of Features of SVD

White matter hyperintensities of presumed vascular origin, lacunes of presumed vascular origin, cerebral microbleeds, and perivascular spaces are imaging features thought to represent damage to the small vessels in the brain. They generally appear as hyper or hypointense on structural brain MRI. Although the array of developments discussed in this chapter represent fantastic progress in research, even fairly simple to apply assessments such as Fazekas scale are not universally applied in clinical practice. This may be due to pressures in radiological reporting or because many older people live normally in the community with these features (Ritchie et al. 2015; Dickie et al. 2016b). However, as we have seen, the presence of these features has been linked to stroke, vascular cognitive impairment and dementia; and as we will now see, an increasingly complicit role in severity of Alzheimer's disease.

3 Alzheimer's Disease

Alzheimer's disease (AD), first described by Alois Alzheimer in 1906 (Maurer et al. 1997), is characterised by progressive build-up of amyloid-beta (into plaques) and tau (into neurofibrillary tangles) that are thought to lead to brain atrophy and eventually progressive cognitive, behavioural, and functional decline (Reisberg et al. 1987; Gauthier and Gauthier 1990; Trinh et al. 2003; Fox and Schott 2004; Serrano-Pozo et al. 2011; Selkoe and Hardy 2016; Scheltens et al. 2016). Alzheimer first identified this "serious disease of the cerebral cortex" in the patient known as "Auguste D.", who presented with memory loss, disorientation, hallucinations, and an untimely death in her fifties. As well as the cascade of neurofibrillary tangles and cortical thinning, the cause of August D.'s death was also attributed to "arteriosclerosis of the small cerebral vessels" (Maurer et al. 1997).

Despite over 100 years of study and several advances in imaging and other biomarker assessments (Jack et al. 2018), there are currently no clinical interventions that can halt or reverse these pathological processes (Winblad et al. 2016). Processes that can develop insidiously decades prior to clinical symptoms of AD becoming apparent (Sperling et al. 2011; Selkoe and Hardy 2016). The current National Institute on Aging—Alzheimer's Association (NIA-AA) Research Framework diagnosis of Alzheimer's in the living is not based on the clinical symptoms, e.g., memory loss, but by biological constructs, i.e., biomarkers, of the underlying pathology. These biomarkers are grouped by amyloid-beta, aggregated tau, and neurodegenerative injury. Although there is scope for its future inclusion, there is not currently a vascular component in the group of biomarkers used to diagnose AD during life (Jack et al. 2018). Post-mortem neuropathological diagnosis of AD, the only method to currently provide a definitive diagnosis of AD (Jellinger and Attems 2015), is still based on visualisation of amyloid-beta plaques and neurofibrillary tangles (Schneider et al. 2009; James et al. 2016) and brain atrophy has been the focus of many in vivo MRI studies in AD (Thompson et al. 2003).

3.1 Brain Atrophy and the Rise of Mixed Pathologies

Brain atrophy is the process of neuronal and synaptic decay. It can be measured using MRI in a variety of ways. Semiquantitative visual (Farrell et al. 2009) and quantitative volumetric (Courchesne et al. 2000; Thompson et al. 2003; Fotenos et al. 2005; Dickie et al. 2012, 2015b; Job et al. 2016) assessments of grey and white matter, and cerebrospinal fluid volume (Fig. 13), and cortical grey matter thickness (Fig. 14; Tustison et al. 2014; Lewis et al. 2018) are commonly reported. Cerebrospinal fluid appears

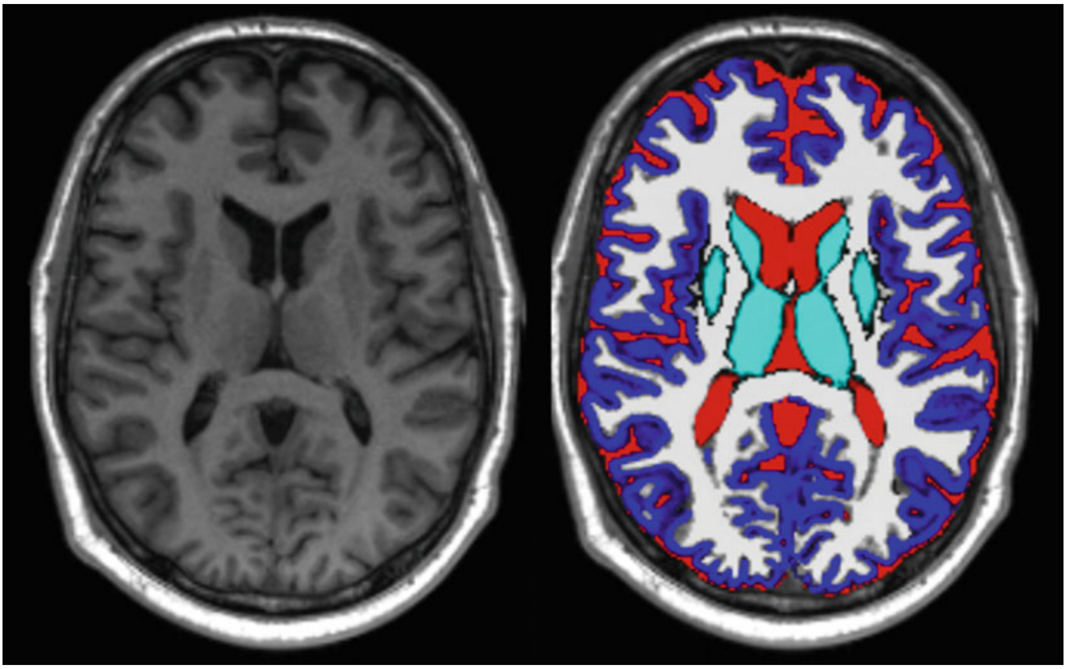

Fig. 13 Cerebrospinal fluid (red), cortical grey matter (royal blue), subcortical grey matter (cyan), and normal appearing white matter (white) volume segmentations from T1 MRI (left panel)

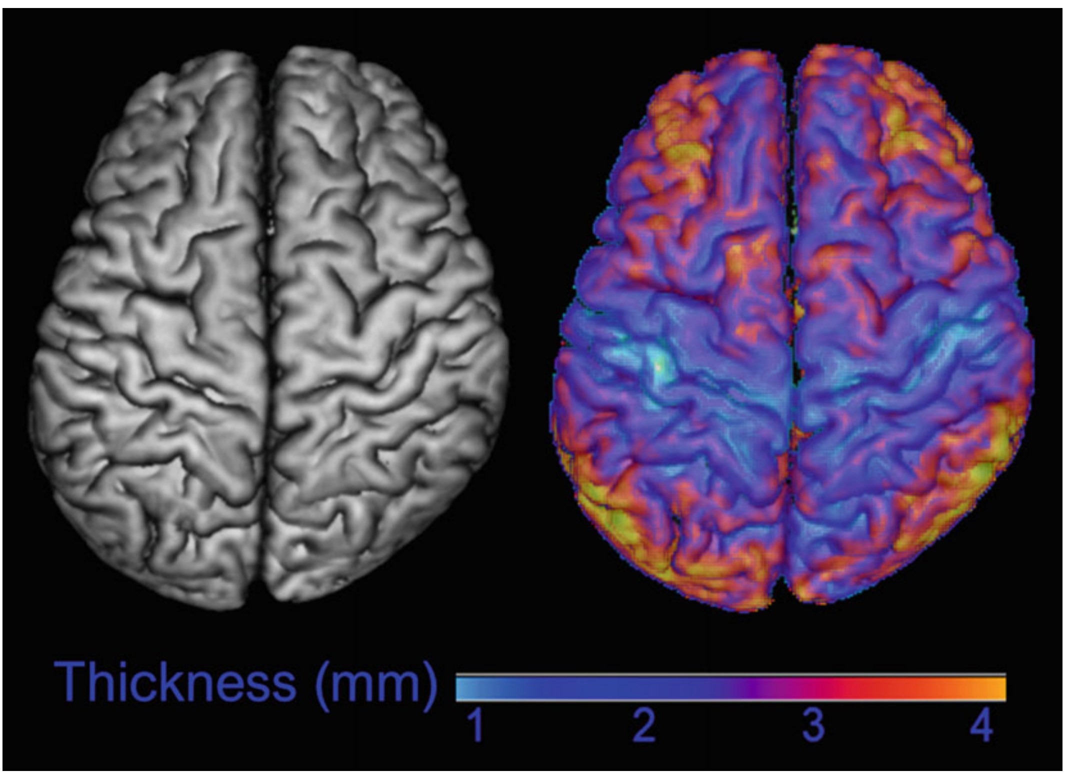

Fig. 14 Cortical thickness (right panel) measured from T1 MRI (left panel) showing a characteristically thinner cortex at the vertex around the central sulcus versus thicker cortex in inferior frontal and occipital regions

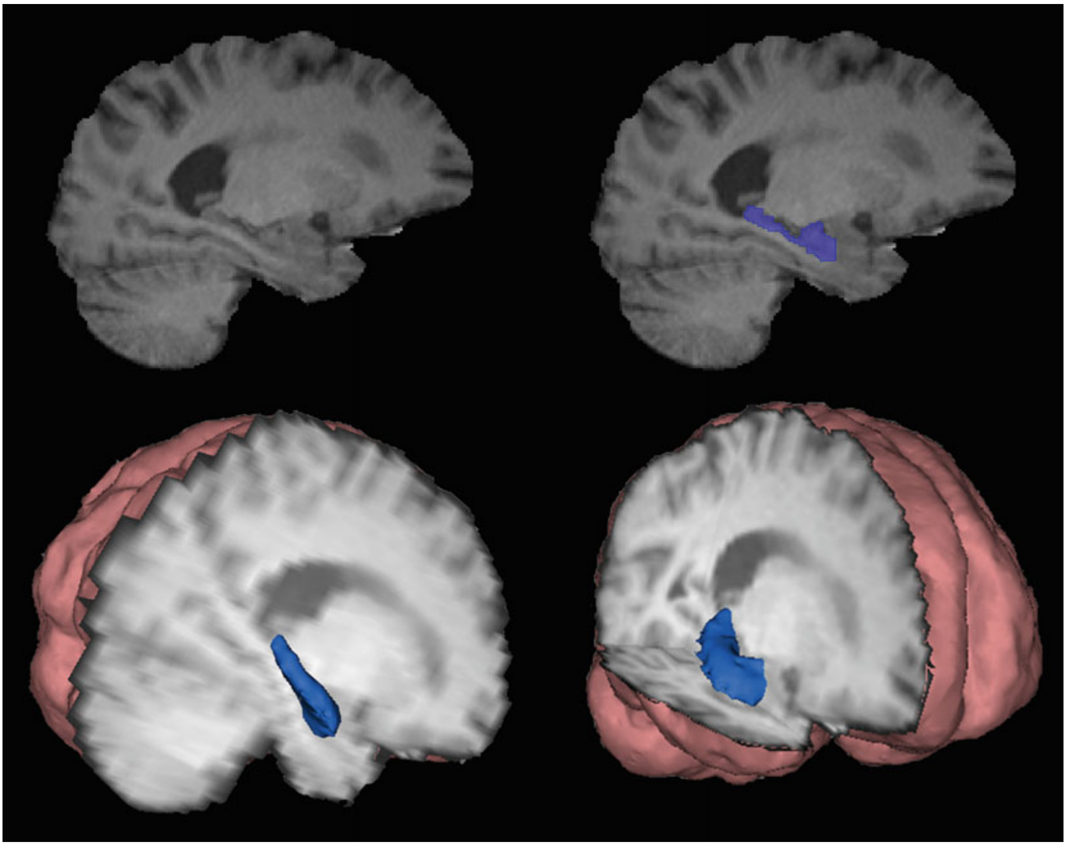

Fig. 15 Segmentation of the hippocampus (in blue) from T1 MRI (top panel) using FreeSurfer tools (Fischl et al. 2002). The 3D renderings (bottom panel) are designed to show the "seahorse" like structure of the hippocampus from where the name is derived; "hippos" being the Greek for "horse" and "kampos" meaning "sea monster"

hypointense on T1 (Fig. 13) and FLAIR (Fig. 9) MRI and hyperintense on T2 sequences without fluid signal suppression (Fig. 12), compared to the relative isointensity of grey and white matter. Volumes of regional structures, e.g., subcortical grey matter (Fig. 13) and the hippocampus (Fig. 15), have also become commonly reported measures of atrophy (Fischl et al. 2002; Miller et al. 2016). Whichever method is used it can only be deemed a true measure of brain atrophy in longitudinal study, i.e., in cross-sectional "snap-shot" studies it cannot be known for sure whether people with smaller brain volumes were always this way or once had larger brain volumes. However, although it is true that decay can only be directly measured over time, it has been demonstrated that cross-sectional differences in brain volume between age groups are reasonable estimates of actual atrophic change (Fotenos et al. 2005).

While MRI provides the best method for visualising changes in brain tissue in vivo, computerised brain volumetry may be confounded by physiological variations such as dehydration. Dehydration may lead to an apparent reduction in brain volume, that resolves following rehydration (Duning et al. 2005), and therefore may confound assessments of true pathological processes, e.g., neuronal loss. Brain MRI volumetry may be further confounded with the use of parametric statistical analysis methods that assume volumes are distributed statistically normal when they are not (Dickie et al. 2013, 2015a). The use of these statistical methods may artificially inflate differences between those clinically diagnosed with AD and

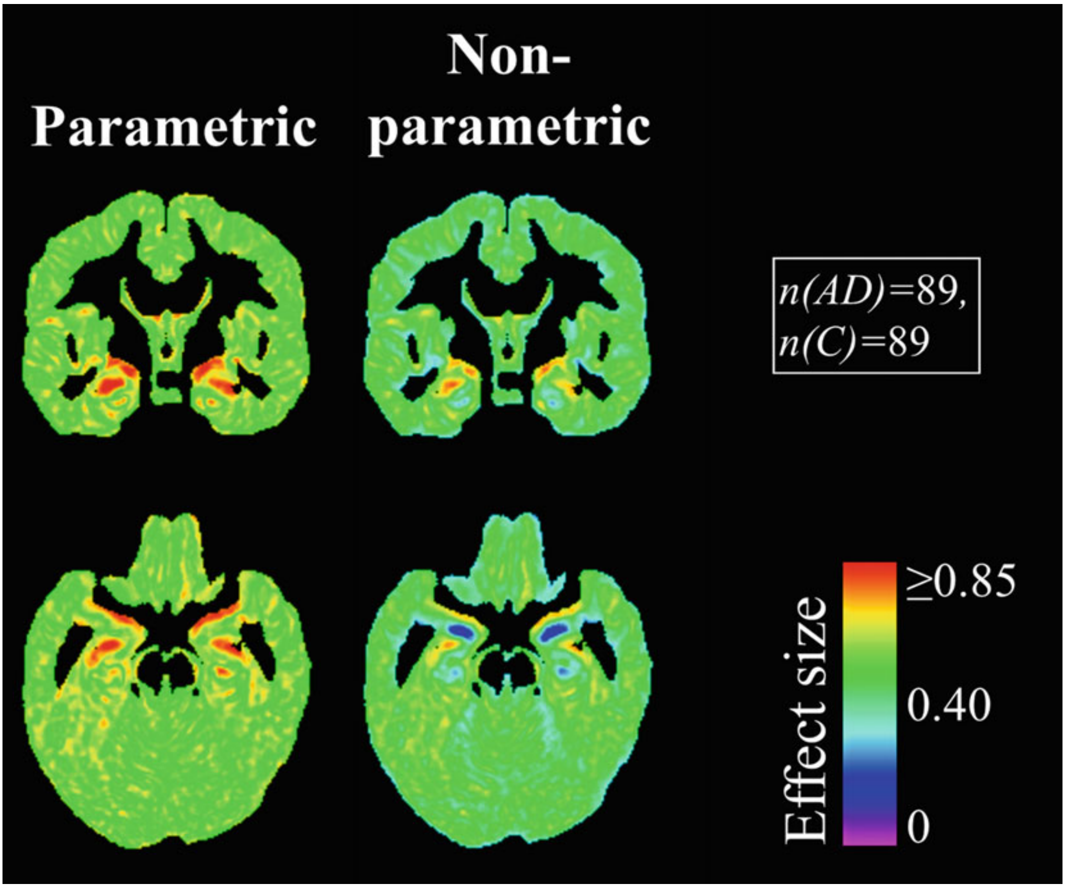

Fig. 16 Parametric and nonparametric comparisons of voxel-wise grey matter probabilities in N = 89 healthy controls (C) and N = 89 people diagnosed with Alzheimer's disease (AD). The nonparametric common language effect size (CLES)—which makes no assumptions regarding distribution of GM probabilities—shows that parametric CLES artificially inflated differences between the groups; suggesting people diagnosed with AD had much lower probabilities of GM in the hippocampal area than they actually did have (due to non-Gaussian distributions of grey matter probabilities within voxels). Although there were differences between controls and AD, with generally lower GM probabilities in AD compared to control, these differences were much more subtle than suggested by the parametric analysis. The non-Gaussian distributions are due to a minority of extremes within each group, e.g., people diagnosed with AD with very low probabilities of grey matter versus a small number of "super-normal" controls with very high probabilities

those without this diagnosis (Fig. 16). These inflated differences can be detected when comparing parametric effect sizes with nonparametric methods that directly compare groups rather than assuming normal distributions (McGraw and Wong 1992; Coe 2002).

Furthermore, the standard MRI sequence used to quantify brain tissue volumes is T1. WMH and grey matter appear similar in intensity on T1 MRI. This means that, without manual editing of computational outputs or inclusion of other sequences that better differentiate WMH and grey matter (e.g., FLAIR), the presence of WMH in many older people (Ritchie et al. 2015; Dickie et al. 2016b) may lead to artificially high grey matter volumes being calculated from T1 scans (Fig. 17). This in turn could limit the diagnostic utility of brain volumetry by confounding associations with clinical and cognitive phenotypes.

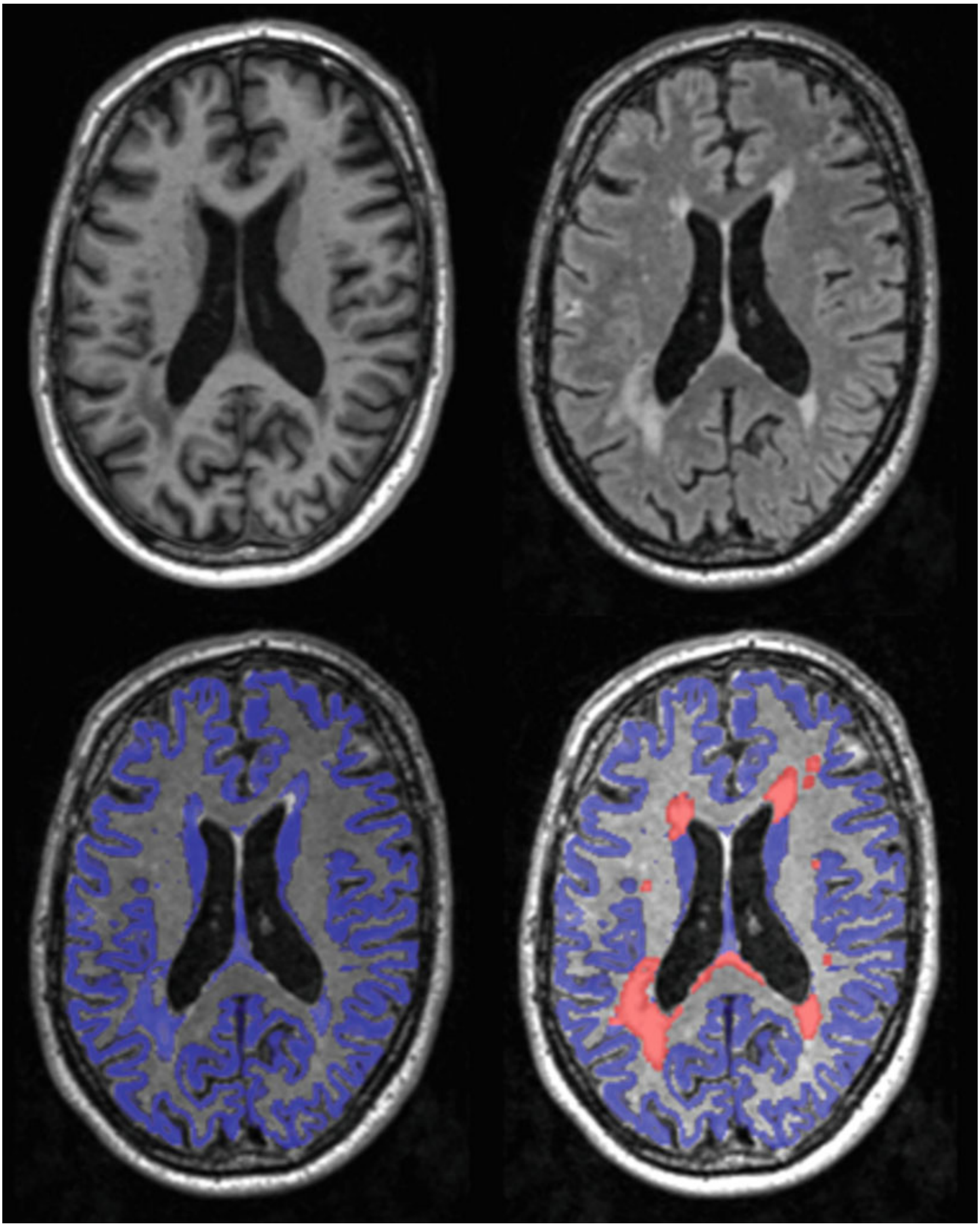

Fig. 17 Segmentation of grey matter from T1 MRI (top left) using FMRIB's Automated Segmentation Tool (FAST). White matter hyperintensities (WMH) are present on the FLAIR scan (top right) and the bottom left panel shows how FAST misclassifies these as GM. The WMH are highlighted in red in the bottom right panel

Casual observations of the co-existence of higher WMH and lower grey matter volumes in older people and in people with stroke have been confirmed in cross-sectional studies finding that those with higher WMH burden had lower brain volumes and thinner cortices (Aribisala et al.

2012; Tuladhar et al. 2015; Dickie et al. 2016a, 2019). Increased rates of brain atrophy were associated with WMH progression in those with lacunar stroke syndrome and WMH burden of Fazekas $\geq$ 2 (Lambert et al. 2016) but a longitudinal relationship between cortical thinning and WMH progression was not found in community dwelling older adults (Dickie et al. 2016a). So while a direct mechanism between WMH progression and brain atrophy may exist in some populations but not others, there is overwhelming evidence that, whatever their underlying mechanism(s), neurovascular and neurodegenerative disease often co-exist in ageing, SVD, stroke, and dementia populations (Wen et al. 2006; Rossi et al. 2006; Godin et al. 2009; Aribisala et al. 2012; Raji et al. 2012; Jellinger and Attems 2015; Knopman et al. 2015; The IST-3 Collaborative Group 2015; Tuladhar et al. 2015; Dickie et al. 2016a; Lambert et al. 2016).

The discovery that mixed neurodegenerative and neurovascular pathologies exist in patients diagnosed with AD is not new (Aronson et al. 1991; Snowdon et al. 1997). But while these early studies found evidence of vascular pathology in approximately 30–40% of patients with a diagnosis of AD, a recent study found that less than ten percent of patients diagnosed with AD have "pure pathological AD", i.e., brain atrophy associated with the accumulation of amyloid into plaques and tau into neurofibrillary tangles (Serrano-Pozo et al. 2011; James et al. 2016). Over 50% of AD patients had infarcts and approximately 35% histological small vessel pathology (James et al. 2016). There is therefore a clear need to quantify aggregates of neurovascular and neurodegenerative pathologies to determine whether these "global" measures can identify potential therapeutic targets and better predict cognitive, behavioural, and functional decline before it occurs. Somewhat poetically, this will see us come full circle to Alzheimer and his colleagues who attributed the death of Auguste D. to both neurodegenerative and neurovascular processes.

4 Global Measures of Neurovascular and Neurodegenerative Disease

Previous sections have described that features of SVD and brain atrophy are individually associated with cognitive dysfunction. However, these findings have either not been consistently replicated across studies or associations between individual features and cognition have been weak (Ritchie et al. 2015). Without specifically defining a measure of global neurodegenerative and neurovascular disease, early investigations found that those with AD pathology and brain infarcts had poorer cognitive function than those without infarcts (Snowdon et al. 1997; Petrovitch et al. 2005). Global measures of health have been developed in other areas of medicine; the "Clinical Frailty Scale" was shown to better predict risk of early death than measures of cognition, function, or co-morbidity (Rockwood et al. 2005). And efforts are now being made to strengthen associations between potential causes and features of brain degradation so to identify novel targets for treatment, and provide stronger predictors of future outcome. These efforts have been based on calculating global measures of neurovascular and neurodegenerative disease on structural MRI.

4.1 Total MRI Burden of Cerebral Small Vessel Disease

The "total MRI burden of cerebral small vessel disease" is based on stratification and summation of four semiquantitative visual rating scales for measuring WMH, lacunes, perivascular spaces, and microbleeds (Huijts et al. 2013; Klarenbeek et al. 2013; Staals et al. 2014). WMH are scored according to Fazekas (Fazekas et al. 1987), lacunes and microbleeds are counted according to international consensus definitions (Wardlaw et al. 2013), and perivascular spaces are scored as follows, 0: no perivascular spaces; 1: <10 perivascular spaces; 2: 10–20 perivascular spaces; 3: 21–40 perivascular spaces; and 4: >40 perivascular spaces (MacLullich et al. 2004). These individual scores are then stratified and summed to provide a total MRI burden of SVD as follows: one point for periventricular Fazekas score of three and/or deep Fazekas score of two or three; one point for one or more lacune; one point for one or more microbleed; and one point for perivascular spaces of grades two to four. This provides a total SVD score out of four.

The associations between this score and vascular risk factors are stronger than with individual SVD features and the score was associated with cognition in two separate studies including hypertensive, stroke, and community-dwelling ageing cohorts (Huijts et al. 2013; Staals et al. 2014, 2015). Despite these strengths the score is restricted by the limitations inherent in semi-quantitative visual ratings previously described, e.g., ceiling effects, limited granularity (Sects. 2.1.1–2.1.3). In addition, the total MRI burden of SVD does not include brain atrophy as, although it is a major correlate and risk factor for cognitive and functional decline (Fox and Schott 2004; The IST-3 Collaborative Group 2015), no strong case for including it in the score was found (Staals et al. 2014). This may have been due to the visual scoring methods used and, as with individual features, quantitative methods may provide a solution to the limitations of semiquantitative visual ratings of total brain degradation.

4.2 MRI Measure of Degenerative and Cerebrovascular Pathology in Alzheimer Disease

The "MRI measure of degenerative and cerebrovascular pathology in Alzheimer disease" is derived from the linear combination of WMH volume, presence of infarcts, hippocampus volume, and cortical thickness (Brickman et al. 2018). Infarcts were assessed using semiquantitative visual assessment and coded as either present or absent, the other features were derived quantitatively. The multiple linear regression association between all four features as independent variables and episodic memory as the dependent variable provided the beta coefficients for an equation to estimate the quantitative MRI measure of degenerative and cerebrovascular pathology. Higher values of the MRI measure were associated with better episodic memory, lower neurofibrillary tangle and cerebral infarction burden at autopsy, higher CSF amyloid beta (higher values of amyloid beta in CSF indicate that it is being cleared from the brain, see Sect. 2.4), lower tau, and lower positron emission tomography (PET) derived amyloid (Brickman et al. 2018). Additionally, the MRI measure differentiated healthy controls, patients with mild cognitive impairment (MCI), those with clinically diagnosed AD, and predicted conversion to MCI and clinical AD in healthy controls. However, associations between the combined MRI measure and clinical assessments were similar to those obtained with individual measures (Brickman et al. 2018).

Although a promising early development that may limit the need for a spinal tap or PET scan, this combined marker does not appear to provide significant added value over individual markers of pathology (Bennett 2018). More direct, rather than linear regression-based, assessments of global neurovascular and neurodegenerative disease may provide this added value and the Brain Health Index family of methods represent such direct assessments.

4.3 The Brain Health Index

The Brain Health Index (BHI) family of global measures of neurodegenerative and neurovascular disease was stumbled upon in 2013. While attempting to develop quantitative tissue classification methods more appropriate for older people, e.g., see Fig. 17, it was observed in a four-dimensional cluster analysis of FLAIR, T1, T2, and T2* MRI that isointense voxels clustered together while and hypo- and hyperintense voxels formed another cluster. As described in Sects. 2 and 3, individual features of SVD and

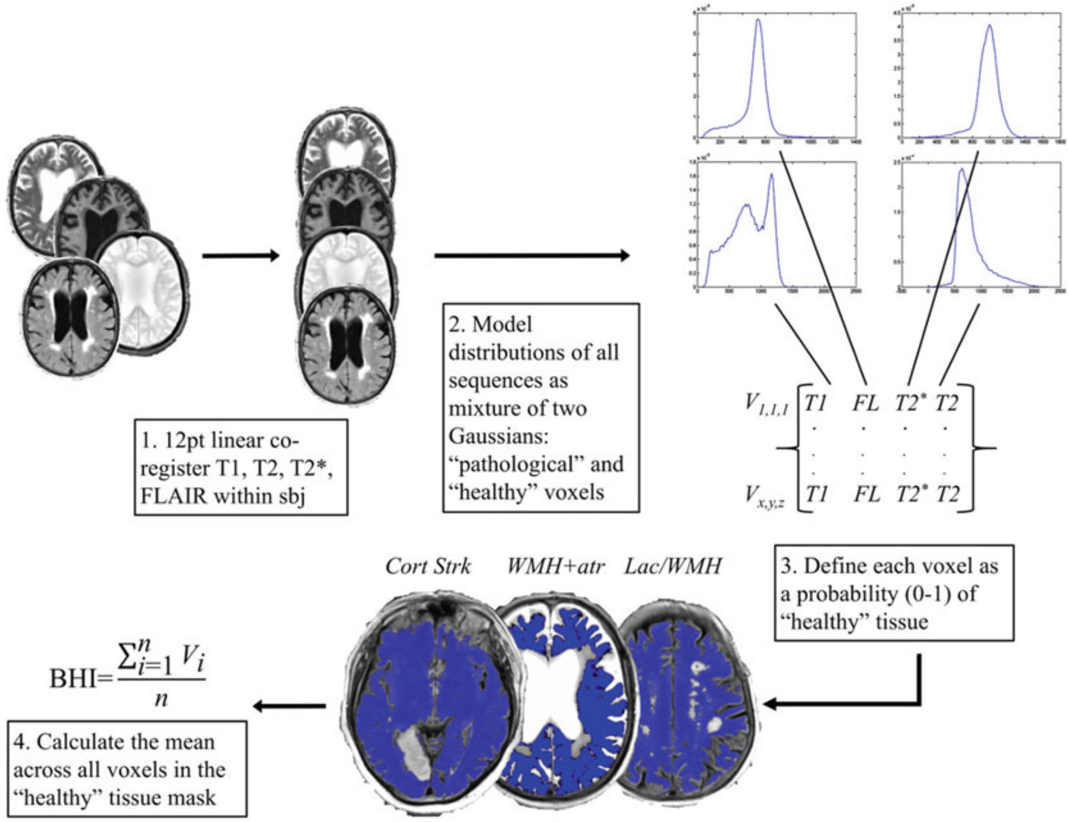

Fig. 18 Illustration of the steps performed to calculate the brain health index (BHI) from T1, T2, T2*, and FLAIR MRI. Blue areas in the "healthy" tissue masks (middle bottom panel) indicate probable normal/"healthy" appearing tissue, areas without overlay colour are more likely features of SVD or cerebrospinal fluid. BHI masks are from three separate subjects showing exclusion of cortical stroke (Cort Strk—left mask), white matter hyperintensities (WMH) and atrophy (WMH + atr—middle mask), and a lacune/WMH (Lac/WMH—right mask) from "healthy tissue". FLAIR/FL: fluid attenuated inversion recovery; sbj: subject; V: voxel in BHI mask; n: number of voxels in BHI mask; i: voxel at a given location x, y, z in BHI mask

tissue atrophy generally have either hypo- or hyperintense appearances across FLAIR, T1, T2, and T2*, while normal appearing tissue is generally isointense in comparison (Wardlaw et al. 2013). Although interesting, the results of the cluster analysis were quickly dismissed as the principle aim of the overarching project was to measure whole brain volume (that included features of SVD within the parenchyma) and WMH changes in the eighth decade of life (Ritchie et al. 2015; Dickie et al. 2016b). For two years or so the cluster analysis code remained archived and largely forgotten until the potential of measures of global brain health became clear (Staals et al. 2014). Following the success of the total SVD score, Wardlaw and colleagues were awarded funding by the Innovate UK Technology Strategy Board to further investigate quantitative markers of global neurovascular and neurodegenerative burden. As part of this investigation the four-dimensional cluster analysis code would eventually become the BHI.

The steps involved in calculating BHI are illustrated in Fig. 18 and were described in detail previously (Dickie et al. 2018). Higher values of BHI indicate a "healthier" brain in contrast to the total MRI burden of cerebral small vessel disease where a higher value indicates a less healthy brain (Staals et al. 2014). The BHI was moderately correlated with the total SVD score

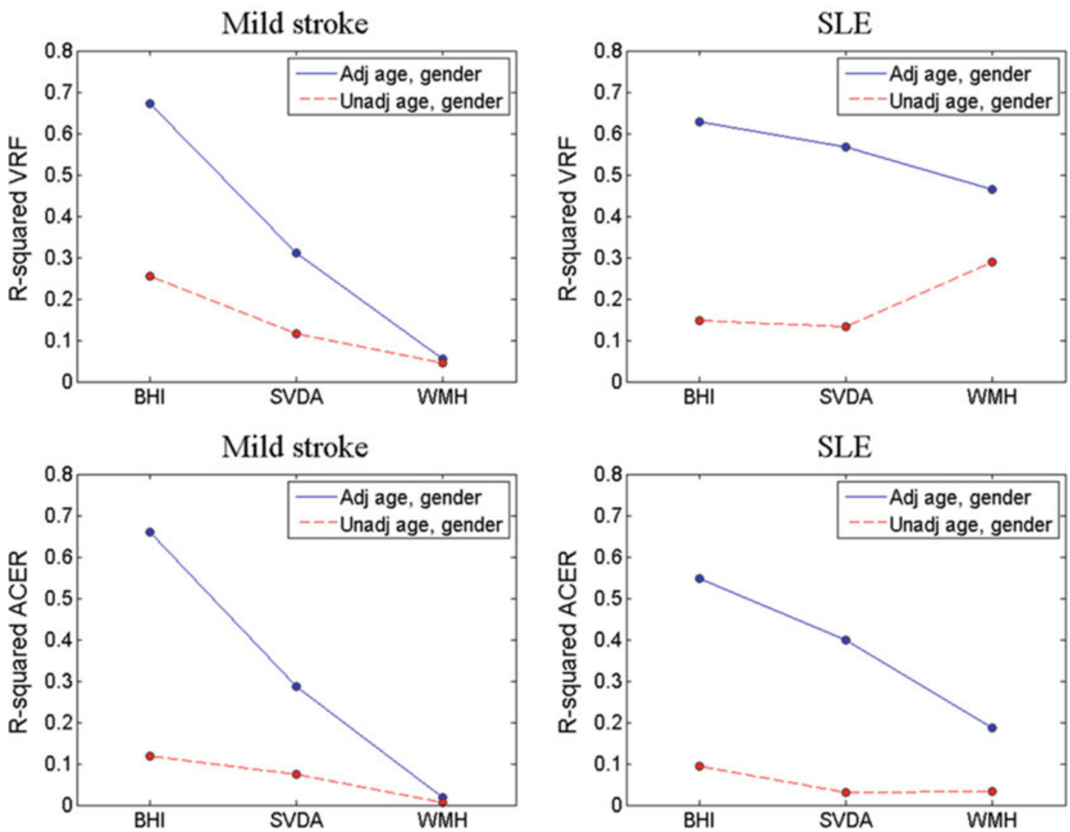

Fig. 19 Proportion of variance explained (R^2) in the brain health index (BHI), total small vessel disease score including atrophy (SVDA), and white matter hyperintensities (WMH) volume by vascular risk factors in mild stroke (left panel) and systemic lupus erythematosus (SLE; right panel) patients (Dickie et al. 2018)

($\rho = -0.38$, $P < 0.001$). The moderateness of this correlation was explained by the total SVD score not including a component of brain atrophy (whereas atrophy is a large component of the BHI); the correlation became higher when summing visually graded brain atrophy and the total SVD score. Vascular risk factors explained a greater proportion of the variance in BHI than WMH volume and SVD score in 157 patients with mild stroke and 51 with systemic lupus erythematosus (SLE; Fig. 19).

Further, the BHI (standard beta = 0.20–0.59, $P < 0.05$) was significantly and more strongly associated with Addenbrooke's Cognitive Exam Revised, including at one year follow-up, than WMH volume (standard beta = 0.04–0.08, $P > 0.05$) and total SVD score (standard beta = 0.02–0.27, $P > 0.05$) in mild stroke and SLE patients. Furthermore, the BHI (standard beta = 0.57–0.59, $P < 0.05$) was more strongly associated with reaction time than normal appearing grey and white matter (standard beta = 0.04–0.13, $P > 0.05$) in 80 healthy people (Dickie et al. 2018).

Although the BHI may provide added value over individual features of brain atrophy and SVD, it is nothing more than an early step towards global, clinically applicable, measurements of neurovascular and neurodegenerative disease. It requires high resolution T1, T2, T2*, and FLAIR MRI to capture the full burden of brain atrophy and SVD. Such high-resolution sequences are not always acquired in clinical settings due to time constraints, e.g., thick slab T1 are often acquired for quick visual assessments of atrophy and T2* sequences may not be collected at all. Early investigations have shown that T1 and FLAIR may be sufficient to capture the majority of brain atrophy and SVD burden, but this requires further testing. In addition, the four-sequence method itself requires testing in much larger and diverse cohorts to determine its wider applicability and whether or not it could be introduced into clinical scanning environments that see a wide range of patients and neurological conditions.

Following realisation that BHI may not be suitable with many clinically obtained MRI, other approaches to develop global measures of neurovascular and neurodegenerative disease were investigated. A very simple approach, borne out of the success of the summation of clinical visual rating scores, was to add the proportion of WMH and cerebrospinal fluid (CSF) within the intracranial volume (Wyss et al. 2019). Although this metric could not be considered global (it only included two features out of at least six) it still represented a measure of combined neurovascular (WMH) and neurodegenerative (CSF) disease burden.

Vascular risk factors accounted for more variance (12%) in the combined volume than either WMH (7%) or CSF (11%) alone (all $P < 0.001$) in 317 people with ischaemic stroke or transient ischaemic attack. The association between baseline combined volume and six-month follow-up Mini-Mental State Examination (MMSE) score (standard beta = −0.442, standard error (SE) = 0.07, $P < 0.0001$) was 32% greater than WMH (standard beta = −0.302, SE = 0.06, $P < 0.0001$) and 12% greater than CSF (standard beta = −0.391, SE = 0.07, $P < 0.0001$) alone. The combined volume required between 207 and 3305 (20%) fewer patients per arm than WMH alone to detect reductions of 10–40% in volume progression over two years.

These results, from the VISTA Prevention database (Wyss et al. 2019), show that the simple addition of WMH and CSF volumes normalised by intracranial volume provided added value over either volume alone. However, careful checking and, in many participants, editing of these volumes was required because of the diverse range of acquisition parameters in VISTA. There are often no standard MRI parameters applied within individual hospitals never mind different hospitals, regions, and countries so the example of VISTA represents “real world” challenges any quantitative measure of neurovascular and neurodegenerative will face. This again emphasises that, although the BHI family of methods represent promising early forays, much work is required to develop clinically robust global measures of neurovascular and neurodegenerative disease.

5 Future Directions

This chapter has shown that much progress has been made in SVD, stroke and dementia neuroimaging research. From early development of clinical visual rating scales that have proven robust enough to mirror modern “state-of-the-art” quantitative assessments (Fazekas et al. 1987; Dickie et al. 2019) to development of international consensus definitions of diagnostic criteria and MRI analysis (Sperling et al. 2011; Wardlaw et al. 2013; Thompson et al. 2014). But there is still much work to do. While there are several directions for research to take, a principle aim must be the translation of these methods into the United Kingdom National Health Service where the simplest of semi-quantitative scales, e.g., Fazekas for WMH, are still not routinely used in radiological reporting. Without clinical translation these methods provide nothing more than interesting things to write about and pretty pictures in a book rather than the improvements to diagnosis and treatment of SVD, AD, and other neurological disorders that they promise.

Although WMH, lacunes, microbleeds, and perivascular spaces are thought to characterise damage to the small vessels in the brain, they are not direct measurements of vessel damage and may only represent “the tip of the iceberg” (Banerjee et al. 2016). So the etiology and pathogenesis of these features are still not entirely understood. For example, WMH could be due to altered interstitial fluid movement

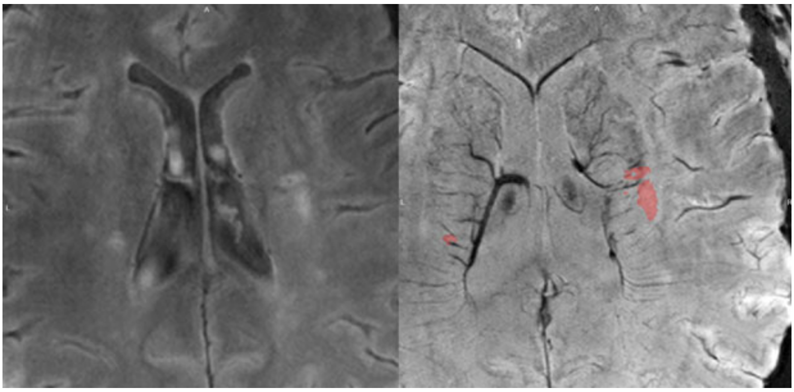

Fig. 20 7 T FLAIR (left panel) and SWI (right panel) MRI of a patient with ischaemic stroke. FLAIR hyperintensites were superimposed onto SWI to show the interaction between features thought to represent SVD and the small vessels themselves. It is just one image slice in one patient but shows that vessels on SWI do not appear visible within hyperintense regions potentially indicating small vessel ischaemia or other pathology. This work remains ongoing

and content, demyelination, axonal damage, inflammatory response, and/or ischaemia via thickening and tortuosity of the small vessels (Wardlaw et al. 2015). Ongoing work using ultra-high field, 7 T, MRI may allow for non-invasive high-resolution visualisation of the cerebral small vessels and aid understanding of the pathogenesis of SVD (Fig. 20).

There is growing evidence for and recognition of the range of pathological processes that cause cognitive impairment in a large majority of patients rather than it being due to any one cause (Snowdon et al. 1997; Staals et al. 2014; Jellinger and Attems 2015; James et al. 2016; Dickie et al. 2018; Brickman et al. 2018; Wyss et al. 2019). However, pathological diagnosis of AD is still based on visualisation of amyloid-beta plaques and neurofibrillary tangles (Schneider et al. 2009; James et al. 2016) and clinical trials mainly focus on individual features of either SVD or brain atrophy (Dufouil et al. 2005; Weber et al. 2012; Douaud et al. 2013; Cash et al. 2014; Bath and Wardlaw 2015; Dawson et al. 2018). In a recent systematic review it was shown that some AD trials adopting volumetric MRI as an endpoint used multiple brain atrophy metrics, e.g., hippocampal and ventricular volumes, but none included neurovascular disease features individually or as part of a global metric (Cash et al. 2014).

The recent finding that as few as <10% of patients diagnosed with AD have "pure pathological AD" (James et al. 2016) may be a significant contributary factor to the inability of treatments to halt or reverse established AD (Winblad et al. 2016). In other words, while treatments for AD generally focus on preventing brain atrophy (Cash et al. 2014), it is likely that neurovascular disease is also contributing to the clinical and cognitive symptoms of the disease (Jellinger and Attems 2015). Meanwhile, trials designed to treat individual features of SVD with a view to limiting cognitive decline have fared similarly (Dufouil et al. 2005; Weber et al. 2012; Pearce et al. 2014; Bath and Wardlaw 2015). As well as being used for potentially more sensitive clinical trial endpoints, methods such as BHI could be used to stratify patients based on degree of cerebrovascular disease at trial entry where those with more advanced disease may increase event rates and allow detection of response to vascular treatments that were found to be neutral in preventing dementia in unselected community-dwelling older people (van Charante et al. 2016).

And so it may be that re-stratification of diagnostic criteria and/or global outcome measures of total neurodegenerative and neurovascular disease burden provide the best hope for the development of disease-modifying treatments in SVD, stroke, and dementia.

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Three-Dimensional Geometry of Phalanges as a Proxy for Pair-Matching: Mesh Comparison Using an ICP Algorithm

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Abstract

Forensic anthropologists are frequently faced with the challenge of individualizing and sorting commingled remains in a variety of scenarios. A number of protocols have been proposed to standardize the methodological approach to individuating commingled remains, some of which are focused on pair-matching. A recent study by Karell et al. (2016) proposed a virtual method for pair-matching humeri using a semi-automatic procedure that gave encouraging results. With regards to the phalanges, there are only a handful of studies focusing on identifying and siding phalanges, as well as exploring their directional and functional asymmetry. Yet, they are still as important as every other bone when sorting commingled human remains in various situations, such as archaeological common burials and mass graves, commingled decomposed remains resulting from atrocities, accidents or natural disasters. This study investigates a new method for pair-matching, a common individualization technique, using digital three-dimensional models of bone: mesh-to-mesh value comparison (MVC) as proposed by Karell et al. (2016). The MVC method digitally compares the entire three-dimensional geometry of two bones using an iterative closest point (ICP) algorithm to produce a single value as a proxy for their similarity. The method is automated with the use of Viewbox software 4.1 *beta* for a simultaneous comparison of all possible pairs. For this study, 515 phalanges from 24 individuals of mixed ancestry were digitized using CT scans and the 3D modeling program AMIRA 5.3.3. The models were also hollowed (internal information of compact and trabecular bone removed) to test the method with simulated surface scan models. The subsequent data—over 73,000 comparisons—were assessed using sensitivity and specificity rates via ROC analysis to indicate how well the automated version of MVC pair-matched phalanges. The best bone in terms of pair-matching was the proximal phalanx of Digit 3 with 87.5% sensitivity and 92.4% specificity rates at a threshold value of 0.488 for the unhollowed bones. The specificity drops slightly (91.1%) when the hollowed

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models are compared. To compare the performance of the method in all phalanges, the specificity was set to 95%—allowing for a 5% acceptable error—and the adjusted sensitivity was compared. The highest sensitivity, namely 68.8%, was noted for Digit 2 proximal phalanx for both unhollowed and hollowed models. Thus far, our preliminary results indicate that the MVC method performs well when pair-matching phalanges, though it is less accurate than pair-matching other types of bones. The introduction of 95% specificity threshold allows for rejecting pairs in great confidence, which could, for instance, significantly reduce the number of DNA comparisons required for the remaining possible matches. In addition, the similar results obtained from hollowed and unhollowed models indicate that the internal information included in the unhollowed models adds little to the identification of true pairs. This means that if a CT scan is not available, the method could be applied to surface models produced by light and laser scanners as well. While additional work needs to be done to verify these preliminary results, this research has the potential to expand the repertoire of individualization methods.

Keywords

Forensic anthropology · Pair-matching · Hand phalanges · 3D models · Mesh-to-mesh value comparison · 3D pattern recognition · ICP

1 Introduction

The adult human skeleton consists of 206 bones, and each one of them has proven to be of extreme importance for the exploration of evolutionary, bioarchaeological and forensic questions. Some skeletal elements, like the skull and the pelvis, have received special attention, mainly due to their ability to elucidate issues such as herit¢ability and locomotion in modern and past populations (Martínez-Abadías et al. 2009; Gruss et al. 2015), while others, like the small hand and feet bones, have been comparatively neglected. This can be attributed to the poor preservation of such small bones in the archaeological and fossil record and the potential problems of identification and siding. Nevertheless, they are still as important as every other skeletal element in forensic investigations, for extracting biological information, that can lead to identification (e.g. unique conditions, handedness) (Danforth and Thompson 2008a; Varas and Thompson 2011) and/or provide evidence of violent events (e.g. defence cut marks, healed fractures) (Saukko and Knight 2016). The current study focuses on the morphological variation of phalanges in an effort to develop a pair-matching method applicable in commingled contexts.

Pair-matching techniques have been developed to improve the sorting of commingled human remains in various situations, such as, archaeological common burials, and mass graves, commingled decomposed remains produced by human atrocities, accidents or natural disasters (Garrido Varas and Intriago Leiva 2012; Karell et al. 2016). Such techniques can be based on visual assessment, osteometric sorting (Adams and Byrd 2006; Thomas et al. 2013) and/or more complicated methods of pattern comparisons such as geometric-morphometrics (Garrido-Varas et al. 2015) and point cloud comparison (Karell et al. 2016). For the purpose of developing pair-matching approaches, both virtual models and physical measurements have been used to develop methods for the scapula, the calcaneus and the metatarsals (Thomas et al. 2013; Garrido-Varas et al. 2015; Karell et al. 2016; Lynch 2017). Some individualisation techniques have successfully explored matching articulations based on metrics and regression analysis, but these are limited to large articulations of the lower limbs (Anastopoulou et al. 2018a, b). There is lack of methodological approaches for sorting smaller bones, such as the wrist bones, tarsal bones and phalanges.

Phalanges, in particular, pose a challenge for pair matching due to the fact that phalanges from different digits of the hand can be easily mixed and confused when sorted with the naked eye, which complicates identification. There is no study to date that presents a clear methodology on how to pair-match phalanges belonging to the same individual accurately and reliably. Thus, the aim of this study was to develop a methodology of pair-matching phalanges based on 3D models from reconstructions of Computed Tomography scans following a similar methodology as Karell et al. (2016) developed for the humerus.

2 Materials and Methods

2.1 Materials

The current study employed a sample of 515 phalanges from 41 hands (18 right and 23 left) belonging to 24 individuals. Proximal (PP), middle (MP) and distal (DP) phalanges from every available digit were used. A detail list of the available samples for each digit can be found in Table 1.

The material of the study derived from individuals that were submitted to postmortem CT as part of a different project (Virtopsy.GR). The Virtopsy.GR is a research project that explores the validity of postmortem computed tomography (PMCT) as an additional technique to the autopsy findings in forensic investigations of death on the island of Crete (Kranioti et al. 2017). Each individual had undergone PMCT just a few hours after death. The CT scan data were anonymized and each case was given an identification number with basic demographic data (age and sex). The project was approved by the Ethics Committee of the University Hospital of Heraklion in Crete in June 2016.

2.2 Methods

2.2.1 Scanning Protocol

The CT scans were acquired by the General University Hospital of Heraklion in Crete, using a Revolution GSI system (General Electric Medical Systems, USA). This system provides up to 128 slices per tube rotation and offers more than 15 applications for routine use in cardiac, oncology, neurology, spine, urology, musculoskeletal and more. In the GSI mode the system switches the tube potential from 80 to 140 kVp at

Table 1 Number of bones modelled from 24 individuals

Phalanges	Right	Left	Pairs
Digit 1 PP	17	23	16
Digit 1 DP	17	23	16
Digit 2 PP	16	22	15
Digit 2 MP	16	22	15
Digit 2 DP	17	22	16
Digit 3 PP	15	22	14
Digit 3 MP	17	22	16
Digit 3 DP	17	22	16
Digit 4 PP	15	22	14
Digit 4 MP	17	22	16
Digit 4 DP	16	22	15
Digit 5 PP	17	21	15
Digit 5 MP	16	22	15
Digit 5 DP	15	22	14
Total	228	287	213

a fast rate of up to 4.8 kHz. Thus, it allows the reconstruction of spectral images in the range from 40 to 140 keV. GE's Smart Spectral tools, such as GSI Assist and GSI Viewer 3D, enable one-click workflow on the console. GSI ASiR delivers dose neutral Spectral CT protocols. The scanning protocol for the Virtopsy.GR project uses a tube current of 50 mA, tube voltage of 120 kV, slice thickness of 0.625 mm and slice increment of 0.5 mm. Scans with a field of view of 250 × 250 mm (matrix 512 × 512) were made in the coronal (transverse) plane. Voxel size was 0.5 × 0.5 × 0.5 mm. Data were saved as a Digital Imaging and Communications in Medicine (DICOM) format and then converted to a High Dynamic Range file. So, only the CT scan data (the HDR files) were used for the purpose of this study.

2.2.2 Scanning Method and Segmentation

Following the completion of these scans, each scan was "cropped" using Amira 6.0 software, so as to include only the hands. Each hand was loaded on Amira 6.0 software and each phalanx was manually segmented using the "brush" tool. This procedure resulted in 515 three-dimensional phalange models which were extracted as stereolithography (.stl) and wavefront [.obj] format and were then randomized prior to analysis.

2.2.3 Model Manipulation

For the purposes of this paper two datasets were analyzed. D1 included the original 3D models created from the segmentation of the CT scans and D2 the models, in which the internal material (compact and trabecular bone) was removed, maintaining only the surface. D2 models were created using a function of Viewbox 4.1 *beta* software.

2.2.4 Mesh-to-Mesh Value Comparison (MVC) Method

All right phalange models were mirror-imaged using the free software NetFabb basic and were named as mirror-imaged right models (MIR). Two folders containing all left (L) and MIR models were compared automatically using Viewbox 4*beta* software following the guidelines set by Karell and colleagues (Karell et al. 2016). The software uses a trimmed ICP algorithm (Besl and McKay 1992; Chetverikov et al. 2002) to compare all homologous points between two models (meshes) and computes a single value which expresses the similarity between the shapes of the two models. The single value is called mesh-to mesh value (MTMV) and is expressed in mm. The software runs simultaneously all possible comparisons between the two folders using the following settings: The estimated overlap for the scan is set to 100%, whereas the number of initial positions for rough alignment was set at 20. This alignment used the nearest neighbor search "Approximate fast", with a point sampling of 1%, so that it matched point to point with one hundred iterations. On the other hand, the fine alignment used the nearest neighbor search "Exact with normal compatibility", with a point sampling of 100%, which matched point to plane with one hundred iterations. Finally, completing the mesh-to-mesh comparison, the program automatically creates an Excel spreadsheet of all the MTMV for analysis. The lowest MTMV are hypothesized to belong to true pairs, meaning the left and mirror-right phalanges belong to the same individual.

2.2.5 ROC Analysis

MedCalc software was used to conduct a Receiver Operating Characteristics (ROC) Analysis on the MTMV values. ROC Analysis is currently used to evaluate medical tests (Bewick et al. 2004), such as whether a person is positive or negative for a medical condition, as for instance, the presence of a virus. Here, ROC curves were employed in the evaluation of MTMV between potential pairs of bones as effective predictors of true pairs (belonging to the same individual). The hypothesis tested was whether a pair (L-MIR phalanx) is a correct match (positive) or not (negative). If both diagnosis (true match) and test (predicted match) are positive, the result is called true positive (TP), whereas if diagnosis is positive and the test is negative, the result is called false positive (FP). Similarly, a negative diagnosis with a negative test is called true negative (TN) and a negative diagnosis with a positive test is called false positive (FP). The quality of the test can be measured with sensitivity and specificity (Kranioti and Tzanakis 2015). Sensitivity (true positive probability) is the proportion of true matches that are correctly identified by the test, while specificity (true negative probability) is the percentage of non-pairs that are correctly identified by the test. Predictive value of a positive test is defined as: $PVP = TP/(TP + FP)$ and predictive value of a negative test is defined as: $PVN = TN/(TN + FN)$ (Bewick et al. 2004; Kranioti and Tzanakis 2015). To help decide whether a pair is a match or not, a cut-off point of the MTMVs is chosen. ROC curve is widely accepted as a method for selecting an optimal cut-off point for a test and to make comparisons between tests (Akobeng 2007). The ROC curve is created by calculating sensitivity and specificity and creating a plot with $y = sensitivity$ and $x = 1 - specificity$ for the entire range of cut-off points (Kranioti and Tzanakis 2015). A large area under the curve (AUC) reflects good performance of the test (Bewick et al. 2004; Akobeng 2007).

3 Results

A total of 73,000 comparisons were automatically conducted, MTMVs were calculated and then analyzed using ROC analysis. Sensitivity, specificity, area under the curve (AUC) and cut-off points were calculated for datasets D1 and D2 and compared. For example, for D1 for Digit 2 proximal phalanx sensitivity was 71.4%, specificity was 98.0% and the threshold was set to 0.434 mm (Table 1). For intermediate and distal phalanges, sensitivity was 86.7% and 62.5%, while specificity was 62.9% and 72.1%, respectively. The threshold for the intermediate models was 0.588 mm and for the distal ones 0.511 mm. For D2 Digit 1 distal phalanx sensitivity was 100.0% and specificity 63.7%, and for Digit 3 proximal phalanx 85.7% and 92.4% respectively. As indicated in Table 2, there was no significant difference in the performance of the two datasets.

ROC analysis results in a cut-off value which combines the best prediction of true pairs with best rejection of non-pairs. It is possible though to calculate, using thousands of simulations, the

Table 2 Sensitivity, specificity, cut-off points and AUC for each paired phalanges

	D1				D2			
	SENS	SPEC	Criterion	AUC	SENS	SPEC	Criterion	AUC
Digit 1 PP	75	96	0.515	0.89	75	94.4	0.514	0.892
Digit 1 DP	93.8	66.1	0.588	0.853	100	63.7	0.586	0.876
Digit 2 PP	71.4	98	0.434	0.842	66.7	95.3	0.435	0.854
Digit 2 MP	86.7	62.9	0.588	0.786	86.7	60.8	0.593	0.781
Digit 2 DP	62.5	72.1	0.511	0.736	43.8	89.1	0.427	0.652
Digit 3 PP	*85.7*	*91.1*	*0.497*	*0.932*	*85.7*	*92.4*	*0.488*	*0.928*
Digit 3 MP	75	91.9	0.443	0.906	68.75	93.02	0.438	0.803
Digit 3 DP	50	98.3	0.386	0.718	56.3	91.6	0.434	0.715
Digit 4 PP	75	81.6	0.526	0.838	78.6	78.2	0.545	0.842
Digit 4 MP	81.3	77.4	0.544	0.84	81.3	74.3	0.54	0.833
Digit 4 DP	81.3	69.3	0.547	0.798	53.3	93.8	0.424	0.764
Digit 5 PP	86.7	68.2	0.619	0.839	73.3	80.4	0.543	0.806
Digit 5 MP	60	89.9	0.51	0.775	53.3	91.7	0.471	0.764
Digit 5 DP	50	81.7	0.521	0.67	42.9	91.5	0.449	0.647

values for different thresholds of specificity and sensitivity and the corresponding cut-off points. Tables 3 and 4 illustrate the adjusted values for a fixed sensitivity of 80, 90, 95, 97.5 and 99% (Table 3) and fixed specificity of 80, 90, 95, 97.5 and 99% (Table 4) for D1 and D2 in an effort to predict the highest number of true pairs and to reject the highest number of non-pairs.

The MTMVs for true pairs were analysed for D1 and D2. Table 5 illustrates mean, standard deviation, minimum and maximum values for both groups. A Wilcoxon paired test was performed using 10.000 Monte Carlo simulations to test whether there were differences between the means of the MTMVs of the true pairs and this test produced negative results.

Interpretation of the results and potential application of the method

To better explain the results of the analysis we will showcase an example using the Digit 3 PP subsample. We analysed 22 left and 15 right Digit 3 PP that can be combined in 330 possible pairs, of which only 14 are true pairs. ROC analysis results in AUC = 0.932 (Fig. 1) with sensitivity 87.5% and specificity 91.1% for D1 and similar results for D2-87.5% and 92.4% respectively (see Table 4). We will assume that bones were scanned with a CT scanner and we will use D1 for the purpose of this exercise.

For a threshold value of 0.497 mm, all MTMVs equal or less than 0.497 mm will indicate a true pair. In our data this resulted in 40 pairs of which 12 are true pairs. The method correctly identified 12/14 pairs resulting in 85.7% accuracy, but it also identified 26 pairs that are not correct. Similarly, from the remaining 290 comparisons (MTMV > 0.497), all but two do not belong together, thus the method rejects two true pairs and 288 non-pairs (91.1%). To identify all pairs, one must fix specificity to 99% (Table 3), which will raise the MTM threshold value to 0.588 mm. This will result in identifying 95 pairs as matches, even though only 14 are true pairs. At the same time 235 pairs will be rejected. It is worth mentioning that 11 of the 14 true pairs showed the lowest MTMV when compared to each other in contrast with all other comparisons. Mean MTMV for true pairs was 0.4399 ± 0.0853 SD. MTMV values >0.4399 + 2SD = 0.610 are excluding

Table 3 Specificity, threshold values and 95% confidence intervals for fixed sensitivity at 80, 90, 95, 97.5 and 99% for D1 and D2

			Sensitivity %				
			80	90	95	97.5	99
Digit 1 PP	D1	Specificity %	84.8	58.13	58.13	32.27	32.27
		95% CI a	80.8–88.3	53.0–63.2	53.0–63.2	27.6–37.3	27.6–37.3
		Threshold	0.588	0.722	0.722	0.889	0.891
	D2	Specificity %	75.2	65.87	65.87	33.33	33.33
		95% CI a	70.5–79.5	60.8–70.7	60.8–70.7	28.6–38.4	28.6–38.4
		Threshold	0.628	0.680	0.681	0.898	0.900
Digit 1 DP	D1	Specificity %	78.13	66.13	66.13	41.87	41.87
		95% CI a	73.6—82.2	61.1–70.9	61.1–70.9	36.8–47.0	36.8–47.0
		Threshold	0.542	0.588	0.588	0.678	0.680
	D2	Specificity %	77.07	68	68	63.73	63.73
		95% CI a	72.5–81.2	63.0–72.7	63.0–72.7	58.6–68.6	58.6–68.6
		Threshold	0.539	0.571	0.571	0.586	0.586

(continued)

Table 3 (continued)

			Sensitivity %				
			80	90	95	97.5	99
Digit 2 PP	D1	Specificity %	66.47	41.84	35.31	35.31	0
		95% CI a	61.2–71.5	36.5–47.3	30.2–40.7	30.2–40.7	0.0–1.1
		Threshold	0.604	0.716	0.753	0.754	1.599
	D2	Specificity %	76.26	42.14	27.89	27.89	27.89
		95% CI a	71.4–80.7	36.8–47.6	23.2–33.0	23.2–33.0	23.2–33.1
		Threshold	0.548	0.714	0.809	0.818	0.818
Digit 2 MP	D1	Specificity %	68.25	46.29	46.29	13.06	13.06
		95% CI a	63.0–73.2	40.9–51.8	40.9–51.8	9.6–17.1	9.6–17.1
		Threshold	0.570	0.645	0.645	0.858	0.861
	D2	Specificity %	64.69	37.09	16.02	16.02	16.02
		95% CI a	59.3–69.8	31.9–42.5	12.3–20.4	12.3–20.4	12.3–20.5
		Threshold	0.572	0.694	0.806	0.806	0.811
Digit 2 DP	D1	Specificity %	57.26	27.37	27.37	3.07	3.07
		95% CI a	52.0–62.4	22.8–32.3	22.8–32.3	1.5–5.4	1.5–5.4
		Threshold	0.556	0.698	0.699	1.485	1.583
	D2	Specificity %	31.01	18.16	18.16	3.63	3.63
		95% CI a	26.2–36.1	14.3–22.5	14.3–22.5	1.9–6.1	1.9–6.2
		Threshold	0.685	0.799	0.808	1.299	1.328
Digit 3 PP	D1	Specificity %	91.14	91.14	76.27	74.37	74.37
		95% CI a	87.4–94.0	87.4–94.0	71.2–80.8	69.2–79.1	69.2–79.1
		Threshold	0.494	0.497	*0.588*	0.595	0.597
	D2	Specificity %	92.41	77.22	77.22	71.2	72.2
		95% CI a	88.9–95.1	72.2–81.7	72.2–81.7	65.9–76.1	65.9–76.2
		Threshold	0.488	0.574	0.578	0.604	0.604
Digit 3MP	D1	Specificity %	82.96	61.17	61.17	55.03	55.03
		95% CI a	78.7–86.7	55.9–66.3	55.9–66.3	49.7–60.3	49.7–60.3
		Threshold	0.500	0.609	0.609	0.644	0.647
	D2	Specificity %	64.25	20.67	20.67	2.79	3.79
		95% CI a	59.0–69.2	16.6–25.2	16.6–25.2	1.3–5.1	1.3–5.2
		Threshold	0.611	1.005	1.011	1.93221123	1.978
Digit 3 DP	D1	Specificity %	32.68	24.02	24.02	10.61	10.61
		95% CI a	27.8–37.8	19.7–28.8	19.7–28.8	7.6–14.3	7.6–14.3
		Threshold	0.644	0.727	0.727	0.896	0.924
	D2	Specificity %	31.84	22.63	22.63	11.45	11.45
		95% CI a	27.0–36.9	18.4–27.3	18.4–27.3	8.3–15.2	8.3–15.2
		Threshold	0.660	0.751	0.752	0.91583532	0.926

(continued)

Table 3 (continued)

			Sensitivity %				
			80	90	95	97.5	99
Digit 4 PP	D1	Specificity %	68.44	55.59	55.59	18.72	18.72
		95% CI a	63.3–73.2	50.3–60.8	50.3—60.8	14.8–23.1	14.8–23.1
		Threshold	0.606	0.662	0.664	0.914	0.915
	D2	Specificity %	77.93	56.7	56.7	22.35	23.35
		95% CI a	73.3–82.1	51.4–61.9	51.4–61.9	18.1–27.0	18.1–27.1
		Threshold	0.545	0.660	0.660	0.896	0.898
Digit 4 MP	D1	Specificity %	77.37	53.91	53.91	23.18	23.18
		95% CI a	72.7–81.6	48.6–59.2	48.6–59.2	18.9–27.9	18.9–27.9
		Threshold	0.544	0.640	0.640	0.823	0.824
	D2	Specificity %	74.3	54.19	54.19	24.02	24.02
		95% CI a	69.4–78.8	48.9–59.4	48.9–59.4	19.7–28.8	19.7–28.8
		Threshold	0.540	0.629	0.631	0.812	0.813
Digit 4 DP	D1	Specificity %	69.27	53.63	53.63	12.85	12.85
		95% CI a	64.2–74.0	48.3–58.9	48.3–58.9	9.6–16.8	9.6–16.8
		Threshold	0.547	0.607	0.608	0.898	0.905
	D2	Specificity %	47.21	46.09	46.09	40.78	40.78
		95% CI a	41.9–52.5	40.8–51.4	40.8–51.4	35.6–46.1	35.6–46.1
		Threshold	0.617	0.622	0.622	0.647	0.648
Digit 5 PP	D1	Specificity %	73.68	68.71	**68.71**	38.3	38.3
		95% CI a	68.7–78.3	63.5–73.6	63.5–73.6	33.1–43.7	33.1–43.7
		Threshold	0.578	0.611	0.619	0.778	0.779
	D2	Specificity %	69.59	38.6	38.6	27.19	27.19
		95% CI a	64.4–74.4	33.4–44.0	33.4–44.0	22.5–32.2	22.5–32.2
		Threshold	0.599	0.768	0.770	0.839	0.839
Digit 5 MP	D1	Specificity %	53.41	41.25	41.25	20.18	20.18
		95% CI a	47.9–58.8	35.9–46.7	35.9–46.7	16.0–24.9	16.0–24.9
		Threshold	0.701	0.763	0.764	0.901	0.902
	D2	Specificity %	55.79	42.43	42.43	5.64	5.64
		95% CI a	50.3–61.2	37.1–47.9	37.1–47.9	3.4–8.7	3.4–8.7
		Threshold	0.664	0.740	0.741	1.079	1.079
Digit 5 DP	D1	Specificity %	44.62	31.01	1.27	1.27	0
		95% CI a	39.1–50.3	26.0–36.4	0.3–3.2	0.3–3.2	0.0–1.2
		Threshold	0.699	0.759	1.120	1.151	1.246
	D2	Specificity %	31.96	14.24	5.38	5.38	0
		95% CI a	26.9–37.4	10.6–18.6	3.2–8.5	3.2–8.5	0.0–1.2
		Threshold	0.731	0.881	1.033	1.040	1.417

Table 4 Sensitivity, threshold values and 95% confidence intervals for fixed specificity at 80, 90, 95, 97.5 and 99% for D1 and D2

			Specificity %				
			80	90	95	97.5	99
Digit 1 PP	D1	Sensitivity %	81.25	75	75	50	43.75
		95% CI a	54.4–96.0	47.6–92.7	47.6–92.7	24.7–75.3	19.8–70.1
		Threshold	0.588	0.586	0.515	0.472	0.454
	D2	Sensitivity %	75	75	68.75	50	50
		95% CI a	47.6–92.7	47.6–92.7	41.3–89.0	24.7–75.3	24.7–75.3
		Threshold	0.627	0.514	0.497	0.488	0.458
Digit 1 DP	D1	Sensitivity %	50	50	43.75	37.5	12.5
		95% CI a	24.7–75.3	24.7–75.3	19.8–70.1	15.2–64.6	1.6–38.3
		Threshold	0.514	0.483	0.431	0.428	0.365
	D2	Sensitivity %	75	43.75	43.75	37.5	6.25
		95% CI a	47.6–92.7	19.8–70.1	19.8–70.1	15.2–64.6	0.2–30.2
		Threshold	0.514	0.473	0.433	0.402	0.366
Digit 2 PP	D1	Sensitivity %	73.33	66.67	66.67	60	53.33
		95% CI a	44.9–92.2	38.4–88.2	38.4–88.2	32.3–83.7	26.6–78.7
		Threshold	0.495	0.488	0.434	0.413	0.406
	D2	Sensitivity %	73.33	73.33	66.67	53.33	26.67
		95% CI a	44.9–92.2	44.9–92.2	38.4–88.2	26.6–78.7	7.8–55.1
		Threshold	0.545	0.503	0.435	0.406	0.330
Digit 2 MP	D1	Sensitivity %	60	40	33.33	26.67	20
		95% CI a	32.3–83.7	16.3–67.7	11.8–61.6	7.8–55.1	4.3–48.1
		Threshold	0.477	0.437	0.415	0.386	0.351
	D2	Sensitivity %	60	46.67	33.33	26.67	13.33
		95% CI a	32.3–83.7	21.3–73.4	11.8–61.6	7.8–55.1	1.7–40.5
		Threshold	0.512	0.440	0.411	0.381	0.354
Digit 2 DP	D1	Sensitivity %	50	43.75	31.25	18.75	18.75
		95% CI a	24.7–75.3	19.8–70.1	11.0–58.7	4.0–45.6	4.0–45.6
		Threshold	0.496	0.429	0.390	0.376	0.357
	D2	Sensitivity %	43.75	43.75	25	12.5	12.5
		95% CI a	19.8–70.1	19.8–70.1	7.3–52.4	1.6–38.3	1.6–38.4
		Threshold	0.502	0.427	0.387	0.380	0.332
Digit 3 PP	D1	Sensitivity %	85.71	85.71	50	35.71	21.43
		95% CI a	57.2–98.2	57.2–98.2	23.0–77.0	12.8–64.9	4.7–50.8
		Threshold	0.585	0.497	0.438	0.396	0.377
	D2	Sensitivity %	85.71	86.71	50	21.43	14.29
		95% CI a	57.2–98.2	57.2–98.3	23.0–77.0	4.7–50.8	1.8–42.8
		Threshold	0.574	0.488	0.428	0.392	0.381

(continued)

Table 4 (continued)

			Specificity %				
			80	90	95	97.5	99
Digit 3MP	D1	Sensitivity %	75	75	56.25	50	50
		95% CI a	47.6–92.7	47.6–92.7	29.9–80.2	24.7–75.3	24.7–75.3
		Threshold	0.498	0.443	0.420	0.401	0.377
	D2	Sensitivity %	68.75	62.5	50	43.75	31.25
		95% CI a	41.3–89.0	35.4–84.8	24.7–75.3	19.8–70.1	11.0–58.7
		Threshold	0.438	0.438	0.417	0.376	0.366
Digit 3 DP	D1	Sensitivity %	62.5	56.25	50	50	25
		95% CI a	35.4–84.8	29.9–80.2	24.7–75.3	24.7–75.3	7.3–52.4
		Threshold	0.469	0.461	0.461	0.386	0.360
	D2	Sensitivity %	56.25	50	50	43.75	37.5
		95% CI a	29.9–80.2	24.7–75.3	24.7–75.3	19.8–70.1	15.2–64.6
		Threshold	0.434	0.433	0.411	0.382	0.360
Digit 4 PP	D1	Sensitivity %	75	56.25	43.75	31.25	25
		95% CI a	47.6–92.7	29.9–80.2	19.8–70.1	11.0–58.7	7.3–52.4
		Threshold	0.526	0.471	0.415	0.402	0.377
	D2	Sensitivity %	75	62.5	37.5	25	12.5
		95% CI a	47.6–92.7	35.4–84.8	15.2–64.6	7.3–52.4	1.6–38.3
		Threshold	0.518	0.460	0.428	0.384	0.320
Digit 4 MP	D1	Sensitivity %	75	56.25	43.75	25	25
		95% CI a	47.6–92.7	29.9–80.2	19.8–70.1	7.3–52.4	7.3–52.4
		Threshold	0.520	0.481	0.428	0.407	0.336
	D2	Sensitivity %	62.5	56.25	37.5	25	18.75
		95% CI a	35.4–84.8	29.9–80.2	15.2–64.6	7.3–52.4	4.0–45.6
		Threshold	0.515	0.469	0.421	0.343	0.335
Digit 4 DP	D1	Sensitivity %	56.25	50	43.75	31.25	12.5
		95% CI a	29.9–80.2	24.7–75.3	19.8–70.1	11.0–58.7	1.6–38.3
		Threshold	0.480	0.443	0.415	0.401	0.327
	D2	Sensitivity %	56.25	50	31.25	18.75	12.5
		95% CI a	29.9–80.2	24.7–75.3	11.0–58.7	4.0–45.6	1.6–38.3
		Threshold	0.480	0.424	0.407	0.382	0.353
Digit 5 PP	D1	Sensitivity %	66.67	53.33	26.67	20	13.33
		95% CI a	38.4–88.2	26.6–78.7	7.8–55.1	4.3–48.1	1.7–40.5
		Threshold	0.527	0.483	0.412	0.378	0.328
	D2	Sensitivity %	73.33	46.67	33.33	26.67	26.67
		95% CI a	44.9–92.2	21.3–73.4	11.8–61.6	7.8–55.1	7.8–55.1
		Threshold	0.543	0.476	0.407	0.399	0.354

(continued)

Table 4 (continued)

			Specificity %				
			80	90	95	97.5	99
Digit 5 MP	D1	Sensitivity %	60	60	46.67	13.33	13.33
		95% CI a	32.3–83.7	32.3–83.7	21.3–73.4	1.7–40.5	1.7–40.5
		Threshold	0.627	0.510	0.470	0.419	0.358
	D2	Sensitivity %	60	53.33	33.33	26.67	20
		95% CI a	32.3–83.7	26.6–78.7	11.8–61.6	7.8–55.1	4.3–48.1
		Threshold	0.535	0.471	0.429	0.417	0.343
Digit 5 DP	D1	Sensitivity %	50	28.57	28.57	14.29	7.14
		95% CI a	23.0–77.0	8.4–58.1	8.4–58.1	1.8–42.8	0.2–33.9
		Threshold	0.521	0.482	0.419	0.404	0.333
	D2	Sensitivity %	50	42.86	35.71	14.29	7.14
		95% CI a	23.0–77.0	17.7–71.1	12.8–64.9	1.8–42.8	0.2–33.9
		Threshold	0.520	0.449	0.417	0.392	0.308

Table 5 Minimum, maximum, mean and standard deviation of MTMVs for true pairs and Wilcoxon z-scores for paired differences between D1 and D2

	N	D1				D2				Wilcoxon Z-value	p-value
		Min	Max	Mean	SD	Min	Max	Mean	SD		
Digit 1 PP	16	0.2854	0.8913	0.5038	0.1564	0.2808	0.9003	0.4998	0.1528	−0.414	0.688
Digit 1 DP	16	0.3222	0.6796	0.4768	0.0984	0.3248	0.5863	0.4628	0.0797	−0.414	0.688
Digit 2 PP	15	0.2756	0.7538	0.4602	0.1619	0.2397	0.8178	0.4514	0.1618	−0.170b	0.879
Digit 2 MP	15	0.2807	0.8606	0.4882	0.1474	0.2878	0.8114	0.4848	0.1446	−0.568	0.577
Digit 2 DP	16	0.2914	1.5827	0.5327	0.2999	0.2943	1.3277	0.5603	0.2551	−0.879	0.387
Digit 3 PP	14	0.2942	0.5966	0.4399	0.0853	0.2950	0.6044	0.4408	0.0836	−0.659	0.526
Digit 3 MP	16	0.2636	0.6465	0.4180	0.1088	0.2528	1.9784	0.5551	0.4235	−0.776	0.445
Digit 3 DP	16	0.2948	0.9239	0.4991	0.1791	0.2880	0.9257	0.5022	0.1867	−0.310	0.770
Digit 4 PP	16	0.3055	0.9151	0.4850	0.1588	0.3056	0.8983	0.4858	0.1470	−0.103	0.933
Digit 4 MP	16	0.2652	0.8241	0.4701	0.1389	0.2837	0.8132	0.4706	0.1328	−0.103	0.933
Digit 4 DP	16	0.3071	0.9055	0.4875	0.1435	0.2992	0.6476	0.4781	0.1184	−0.569	0.579
Digit 5 PP	15	0.2990	0.7785	0.4999	0.1217	0.2989	0.8394	0.5096	0.1547	−0.114	0.922
Digit 5 MP	15	0.3375	0.9017	0.5500	0.1672	0.3350	1.0793	0.5442	0.1993	−0.114	0.922
Digit 5 DP	14	0.3326	1.1509	0.5950	0.2076	0.3080	1.0397	0.5823	0.2084	−0.157	0.895

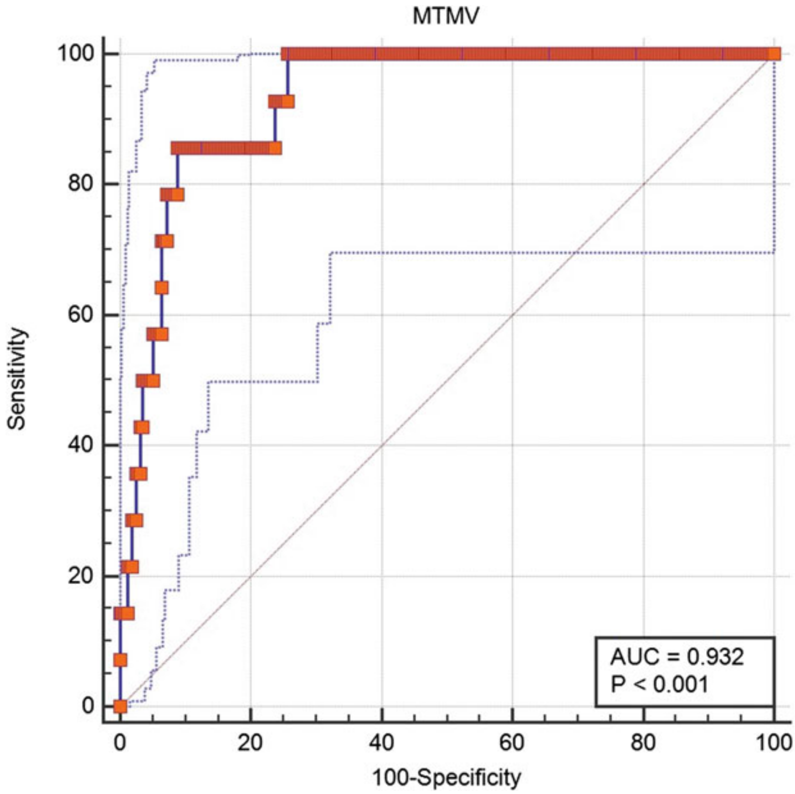

Fig. 1 Area under the curve for Digit 3 proximal phalanx

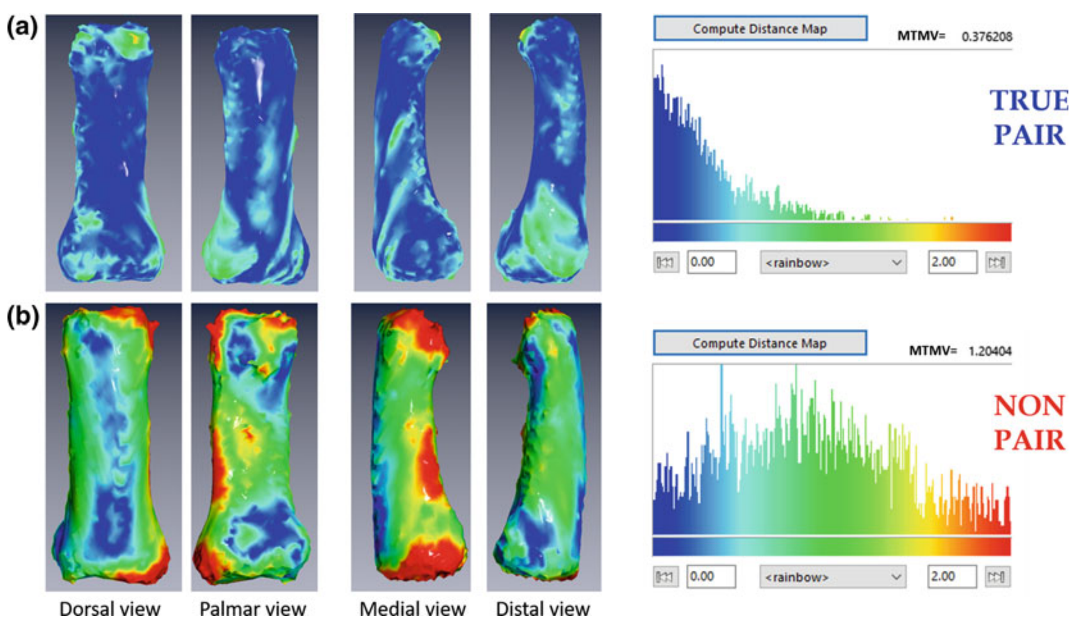

Fig. 2 A colored distance map applied to two possible pairs of Digit 3 proximal phalanges created with Viewbox 4.1 *beta*, **a** true pair with MTMV = 0.376 and **b** non pair with MTMV = 1.201

correctly 227 non-pairs. MTMV values >0.4399 + 3SD = 0.6958 are classified as non-pairs with great confidence.

Figure 2 illustrates an example of a true match (a, MTMV = 0.376 mm) and of a non match (b, MTVT = 1.201 mm). A colored distance map has been applied in both cases to show true distances between homologous points on the two models. Blue indicates point distances close to zero and red values close to 2 mm.

Thus, one can conclude:

1. MTMV values >0.610 mm are highly indicative of non-pairs in Digit 3 proximal phalanges while >0.700 mm safely indicates non-pairs.
2. Lowest MTMV for a pair of Digit 3 proximal phalanges indicates high possibility of bones to belong together.

Naturally these results need to be confirmed with an independent sample.

4 Discussion

Phalanges are probably the most neglected bones of the human skeleton due to their small size. They have been previously studied for the purpose of creating biometric standards for sex (Smith 1991, 2000; Scheuer and Elkington 1993; Case and Ross 2007; El Morsi and Al Hawary 2013; Mahakkanukrauh et al. 2013), stature (Habib and Kamal 2010) and age estimation (Gilsanz and Ratib 2005) based on both classical osteometry and virtual methods. Yet, there is a substantial lack of population specific standards compared to other bones that are more likely to be recovered in forensic or archaeological settings, such as the skull or long bones. Nevertheless, there are a number of studies examining the hand morphology of modern humans, primates and fossils from an evolutionary and functional perspective (Deane and Begun 2008; Tocheri et al. 2008; Mednikova 2011, 2013; Ward et al. 2014; Almécija et al. 2015; Lorenzo et al. 2015), whereas a few others have examined hand plasticity in relation to activity (Karakostis et al. 2016). In addition, a few studies focused on providing a detailed methodology for identifying and siding phalanges and exploring directional and functional asymmetry (Case and Heilman 2006; Danforth and Thompson 2008b; Christensen 2009; Garrido Varas and Thompson 2011). To date, no other study has explored potential pair-matching techniques for sorting phalanges in commingled situations.

The current study used 515 hand phalanges belonging to 24 individuals to explore the potential value of the symmetry in these bones in sorting pairs. Left and right bones were CT scanned, modelled and compared to each other using a series of software combining both manual, semi-automated and automated procedures. A single value was used to compare the overall shape similarity between two models (L and MIR) and was then used to differentiate between pairs and non-pairs with the aid of ROC curves. Different threshold values were calculated in order to facilitate either the inclusion of all pairs (99% sensitivity) or the safe exclusion of non-pairs (99% specificity). These calculations allow an interactive use of the ROC curve by the user, depending on the circumstances of the case under investigation. For example, excluding possible matches may be as crucial to a forensic investigation as identifying true matches. In fact, the results of this study indicate that MTMVs > 0.61 for Digit 3 PP (which coincides with 2SD from the mean) is highly indicative of a non-match. This is in agreement with a previous study using the humerus, where all but one true pair were identified using a threshold of the mean plus two standard deviations (Karell et al. 2016). By selecting a threshold of 3 standard deviations from the mean, it is almost certain that one can safely identify non-pairs (see example of Digit 3 PP). This information is very important in a commingled situation as it would reduce significantly the number of DNA comparisons necessary to ascribe the skeletal element to the correct missing person.

The current method is the first semiautomatic 3-dimensional method that attempts to pair-match phalanges. The method was developed in a mixed ancestry and sex sample and these factors do not seem to affect the performance of the method in accordance with previous studies using MTMVs (Karell et al. 2016). Naturally, the sample needs to be further expanded in size, including surface scans and bones in different taphonomic conditions, so that the preliminary findings presented here can be validated. Nevertheless, the results appear very promising, especially if one takes into account the fact that, although phalanges are the least anatomically complex skeletal elements of the human body, the current method achieves notable success in rejecting a substantial number of possible pairs.

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Multimodal Learning in Health Sciences and Medicine: Merging Technologies to Enhance Student Learning and Communication

Christian Moro, Jessica Smith and Zane Stromberga

Abstract

Advances in consumer-level educational technologies show great promise for enhancing the learning experiences of students in health and medicine. There are particular benefits to using a combination of various devices and technologies when teaching challenging concepts. These include augmented reality-enabled devices enriched with accompanying 3D printed models, or virtual reality sessions coupled with online quizzes or revision activities. Tablet applications can also be integrated while students engage concurrently in desktop-based online learning. This mixing and merging of different technologies can allow educators to focus on the strengths of each device, while mitigating limitations arising from a single mode's stand-alone use. This chapter describes a series of options to integrate multiple digital modes when educating health science and medical students using technology. It also presents the opportunity for health professional program graduates to be trained in teaching using technology, as their future careers can be enhanced by an ability to educate effectively, or from the skills developed when incorporating innovations such as serious games into a health curriculum. With the dynamic and ever-changing nature of health and medical education, educators can find great benefits when introducing multimodal digital learning into their respective courses.

Keywords

Multimodal education · Mixed-mode learning · Augmented reality · Educational technology · 3D printing · Medical education · Serious games

1 Multimodal Learning in Higher Education

Technology is being introduced in universities at ever-increasing rates. Students arrive at tertiary institutions from secondary schools where combining two or more modes of education is daily practice in their curriculum (Mills 2010), and as such, would expect the same interactivity in a modern university course. Integrating e-books, videos, animations, blogs, web pages, and digital games are the new ways of demonstrating literacy that involve clever combinations of teaching

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and learning modes. In digital platforms, text is most often accompanied by illustrations, interactivity, pop-ups, hyperlinks, and audio files to create meaning that extends beyond the possibilities of solely-written works such as essays (Unsworth 2001). This is becoming a core component of school education, where more than 200 learning outcomes in the Australian School Curriculum address this type of literacy, right from foundation (prep) to year 12. Nearly half (44%) of current jobs are at high risk of being digitally disrupted in the next 20 years (Moro and Mills 2019), and as such, incorporating technology into university curriculum is not only beneficial to learning, but can also be vital to students' ability to work effectively in their future careers. The incorporation of technology into teaching practices at universities has also resulted in academics moving away from the traditional didactic-style lectures and into more digitally-enhanced group-based (Moro and McLean 2017), self-directed (Murad et al. 2010) or online modes of learning (Clark and Mayer 2016). However, the next step is to integrate multiple forms of technology in learning. This can involve mixing 3D printing with cadaveric practicals, or textbooks with smartphone or tablet applications. The merging of multiple devices allows educators to engage students using the strengths of various modes, which can be particularly beneficial in disciplines such as anatomy or general health care education (Estai and Bunt 2016).

Mobile devices, such as smartphones and tablets, have the potential to aid teaching in health sciences and medicine. These devices can not only be used for communication and entertainment purposes but also aid in providing easy access to a wide variety of electronic resources to support learning, such as interactive 3-dimensional (3D) models. Pimmer et al. (2016) review of past studies utilising mobile devices in higher education revealed that health and medicine were the dominant areas in which mobile learning was used. Furthermore, the authors showed that the multimodal representation of study material helped facilitate personalised and more frequent study practice and aid in improved learning outcomes. These conclusions were also supported in Klímová (2018) review of 10 randomised controlled trials of the use of mobile learning in medical and healthcare professional education, where it was found to be a beneficial tool in the acquisition of new knowledge and skills and an appropriate supplement to accompany traditional learning tools.

There are several other interactive technologies capable of displaying high-quality 3D models that can be incorporated into modern health sciences and medicine curricula. For example, when using virtual reality (VR) devices (Fig. 1, *left*), the user's senses (sight, hearing, and motion) are fully immersed in a synthetic environment that mimics the properties of the real world through high resolution, high refresh rate head-mounted displays, stereo headphones and

Fig. 1 *Left* an educator assists a student utilising a Samsung Gear VR device for 3D visualisations. *Right* a biomedical science student utilising the Microsoft HoloLens to augment available 3D skeleton models by adding muscle layers over the top

motion-tracking systems (Kuehn 2018; Moro et al. 2017a, b). This technology has a multitude of applications and has previously been used to enhance learning and skill acquisition across different disciplines in education (Jensen and Konradsen 2018), aid patient rehabilitation with cognitive impairment (De Luca et al. 2018) and assist in anxiety reduction (Camara and Hicks 2019). A more accessible technology to the general consumer is augmented reality (AR) which utilises a camera and screen (i.e. smartphone or tablet) to display 3D models superimposed into the real-world. The user is then able to interact with both the real and virtual elements of their surrounding environment (Birt et al. 2018). Due to its easy accessibility, this technology has been widely used to assist in STEM education (Ibáñez and Delgado-Kloos 2018), online retailing (Bonetti et al. 2018), gaming experience (Hamari et al. 2019) and tourism (tom Dieck and Jung 2018) to name a few. Lastly, mixed reality (MR) is a merging of AR and VR environments, with real and virtual words superimposed through head-mounted displays allowing for life-like renders of 3D models in real-time using devices like Microsoft HoloLens 2 (Fig. 1, *right*). This mixed reality technology is still in development stages and not yet widely available and affordable for the general consumer.

2 Merging Printed Text and Hand-Held Interactive 3D Visualisation Devices

Using traditional methods of learning, such as attending didactic lectures and using printed resources, has caused an over-reliance on simple memorisation as the predominant study tactic (Cai et al. 2018), which is classified as the lowest order of learning by Bloom's taxonomy (Krathwohl 2002). Comprehensive understanding of a concept is considered as the highest order of learning in Bloom's taxonomy, which extends beyond simply recognising a structure and remembering its clinical significance. Science and medical students often experience difficulty obtaining spatial understanding of 3D structures from two-dimensional (2D) illustrations, such as those in found in science textbooks (Berney et al. 2015). By using these traditional methods of learning, students are required to mentally manipulate and rotate static, 2D illustrations. While textbook learning resources provide invaluable factual knowledge about different scientific concepts, students who have difficulties mentally perceiving and rotating 3D models consequently perform worse in tests evaluating spatial knowledge. However, the interactive 3D applications alone do not provide the depth necessary to fully grasp the concepts surrounding the structure in question. Using printed text in conjunction with digital 3D visualisation methods may help learners acquire information and build mental representations of anatomical or physiological structures, or provide educators with an opportunity to adapt their education tools to the different types of learning styles. The use of this integrated teaching is achievable through a range of devices, including the Microsoft HoloLens and various Virtual Reality head-mounted displays (Fig. 1).

Indeed, based on findings from a systematic review comparing various digital 3D visualisation methods to traditional teaching methods such as textbook learning concluded that not only medical students preferred to use 3D models over 2D images to learn anatomy, they also reported a higher knowledge gain and better results in knowledge-recall tests (Triepels et al. 2019). In an original research study, Nicholson et al. (2006) reconstructed a fully interactive 3D model of the middle and inner ear from a magnetic resonance imaging scan. In their study, medical students (n = 28) completed a tutorial on ear anatomy with an interactive 3D model, while the control group (n = 29) completed the tutorial without the exposure to the model. Based on knowledge quiz results, the 3D model group achieved a significantly higher mean score of 83% compared to 65% in the control group. In a more recent Ng et al. (2015) study, graduating medical students (n = 72) were randomised into two groups to study the anatomy of the middle ear: (1) 3D model and printed reading materials on the epitympanum anatomy and (2) printed reading materials with 2D illustrations of the epitympanum anatomy. The researchers found that using 3D models was not only the student preferred learning tool, but also 3D group fared significantly better in the anatomy quiz, achieving a mean score of 65.1% compared to 32.4% in the 2D group. Fields such as oncology or pharmacology are also becoming increasingly difficult to comprehend, with increasing numbers of medications and receptors discovered each year. As research into areas such as these continue to uncover additional actions of pharmaceuticals or receptor targets (Moro et al. 2016; Stromberga et al. 2019), the use of 3D devices can greatly assist the student when identifying these complex interactions. Thereby, combining the advantages of using printed materials together with interactive 3D visualisations presents as a promising approach to enhancing the learner's experience in health and medical education.

2.1 3D Printing in Health and Medicine Education

In recent years, 3D printed specimens have become an alternative teaching tool in health sciences and medical education (Drake and Pawlina 2014). Prior to implementing this technology in teaching, it has been typically used for preoperative assessment and presurgical planning in an industry setting (Faur et al. 2013). These 3D printed models have been recognised as a great alternative to teaching involving cadavers, as the printed models are similar to cadaveric specimens and highly accurate when compared to the original specimen (McMenamin et al. 2014). Additionally, 3D printed models are more durable, are easy to reproduce in large quantities and are also more cost-effective than cadavers (Smith and Jones 2018). Using MRI and CT scans obtained from different patients and using 3D printing technology to reproduce these models can also help show anatomical variation that the students would not typically be exposed to if they solely used textbooks, anatomical

Fig. 2 *Left* educators working with 3D printed models alongside cadaveric material to describe physiological concepts within a medical anatomical laboratory. *Right* students utilising 3D Printing to incorporate hearts, lungs and other anatomical structures into the traditional laboratory-based skeletons

atlases (either printed or 3D) or cadaveric specimens (Fig. 2). While there are numerous advantages of incorporating this technology in teaching, it is also important to consider limitations. For example, these models are unable to accurately reflect the dynamic spatial relationships and movements between the anatomical structures, which are important in order for the students to understand functional anatomy. This limitation was addressed in Cai et al. (2018) study where the authors had 3D printed a dynamic knee joint simulator. The authors compared the traditional didactic lecture learning in medical students to using the knee joint simulator and found that students in the simulator group obtained significantly better results in a knowledge-based quiz when compared to the traditional learning group.

3 Serious Games and Gamification in Higher Education

The development in computer technology over the last two decades and the accessibility of the internet has given a rise in the use of games in a higher education setting. Serious games are interactive and entertaining digital software that serve an educational purpose. In health science and medicine, there is potential benefit when introducing gamified learning approaches, as long as they are supplementary in nature, and do not attempt to replace traditional medical teaching tools (Gorbanev et al. 2018). The number of serious games in health sciences and medicine is growing rapidly, and the educator's implementation strategies are vital to the success of these applications to learning (Wang et al. 2016). Some games may also assist with surgical skills training, and other hands-on applied technical skills (Chon et al. 2019; Graafland et al. 2012). One appealing aspect of educators creating their own games, is the possibility of linking multiple modes into one device. Text-based tablet applications, websites, visual stimulus, hyperlinks and interactive components can all be packaged in a way that can assist learning. This is evident in serious games for health science and medical anatomy and physiology education, such as the tertiary-level game, *The King's Request: Anatomy and Physiology Revision Game* (Fig. 3). These types of completely free games, accessible to all students, are able to engage and excite student learning in traditionally dry or

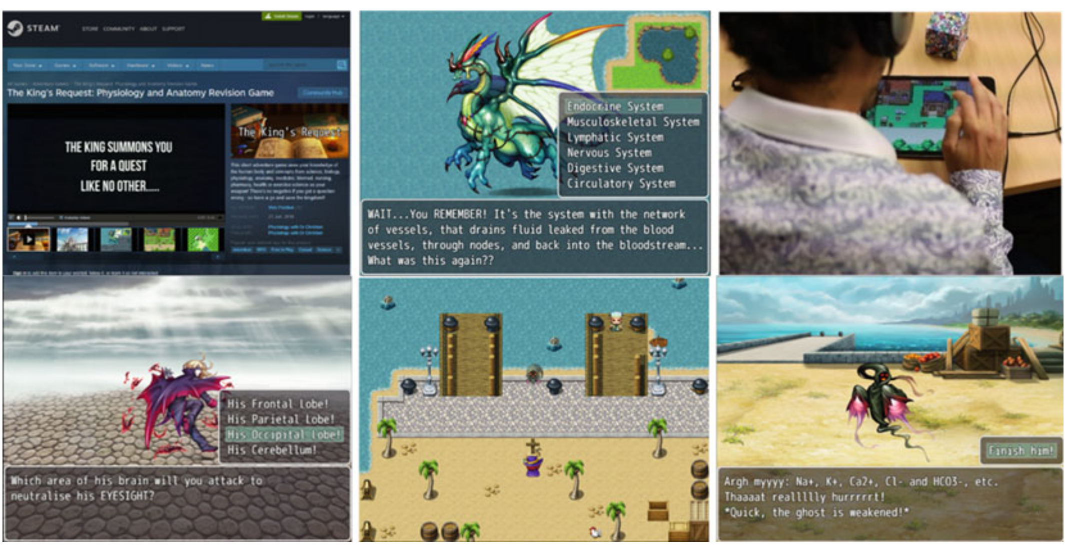

Fig. 3 The king's request: anatomy and physiology revision game. One of the available free games to engage students while revising health science content

difficult subjects. These multimodal applications also bring the class content in-line with student's self-learning strategies, as the majority of students consistently report using a variety of e-learning tools alongside the textbook (Wynter et al. 2019). There is also the additional benefit of training students skills with games, which may in the future form part of the health careers. For example, serious games can be effectively utilised in the clinical environment for activities such as motor rehabilitation (Taut et al. 2017).

4 Health Communication: Teaching Health Sciences and Medical Students to Use Technology in Patient Education

One role of students graduating from health sciences and medicine will be educating their patients, clients and members of the community about their health. Most pursuits of the health system, whether it be physiotherapy, pharmacy, nursing, medicine or others involve the clinician explaining health concepts. As such, educating health science or medical students how to teach can be a great benefit to their future careers. This is particularly important when communicating with the general community, as many people will have difficulties with health literacy, or hold a limited ability to comprehend health information. Education in health is outlined as an essential constituent in the prevention of disease and promotion of health maintenance (Nutbeam 2000), where health professionals can increase patient health literacy through both formal and informal modes of education. Furthermore, epidemiological studies in the U.S. have revealed a link between health, socioeconomic status and educational attainment, where populations with lower educational achievement are more likely to have higher rates of morbidity and mortality as a result of chronic disease (Pamuk et al. 1998). Thus, by integrating education and communication training into a health science curriculum, tertiary institutions can further support students in their future careers.

Some challenges faced by modern graduates in the health industry involve improving the health literacy of their patients and clients, many of whom may have infrequent interactions with the health system. This type of additional expectation often leads medical students with concerns that they are not prepared for practice, and have not fully obtained all the required skills to be workplace-ready (Moro et al. 2019). For example, many teens with chronic illnesses, such as diabetes mellitus, use the internet to gather information relating to the management of their illness. As such, healthcare professionals need to be aware of what content is available online and expect this prior knowledge into their consultations. Young adults, in particular, can be difficult to educate, and this age group often feels as though they cannot comprehend information related to the maintenance of their health (Lindau et al. 2002). As such, universities need to anticipate these clinical difficulties and assist with promoting tertiary students' knowledge of health literacy (Ivanitskaya et al. 2006), the variability between population's education (van der Heide et al. 2013) and the quality of deliverance (Baker et al. 2000; Furnham et al. 2011). This further raises the question as to how health literacy can be improved, consistently and effectively, for young adults attending tertiary institutions. Many studies are now looking into the feasibility of augmented reality as an interactive educational intervention as there has been a recent shift from passive, teacher-centred learning towards active, student-centred learning (Moro et al. 2017a, b).

5 Conclusion

The modern health science and medical educator is no longer restrained to one singular mode of teaching. Instead, multiple devices, modes, formats and technologies can be utilised simultaneously to enhance student engagement and learning as well as achieving a greater level of interactivity. Using multiple modes of content delivery allows the educator to maximise the strengths of each device, whilst minimising the limitations exhibited from relying on a single mode for learning.

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Dissecting Art: Developing Object-Based Teaching Using Historical Collections

Emma Black and Ourania Varsou

Abstract

This book chapter draws on the arts and humanities to discuss how object-based teaching using historical collections can be re-birthed, re-developed, and implemented in higher education settings for the exploration of challenging topics, including medical ethics, within the context of anatomical sciences. Although the authors have focused on the above discipline, the chapter showcases its versatility and adaptability to other areas including vocational degrees such as medicine, dentistry, and nursing. A model lesson plan has been discussed in detail based on 'objects' related to three separate but strongly linked themes: Women as Academics, Women as Artists, and Women as Portrayed as the Subjects of Dissection in Anatomical Art. This is a novel approach that discusses how the combination of existing collections of rare books, rich in anatomical illustrations, and museum artefacts can be used in a meaningful and structured way to encourage conversations amongst learners while promoting awareness about sensitive topics and increasing confidence in communication. The authors have drawn from personal past experience and the current literature to discuss the above aims and critically explore logistical issues that may be associated with the identification of suitable 'objects'. The authors' ultimate goal is to introduce a concise and easy to adapt 'how to guide' for educationalists who have an interest in the integration of arts and humanities in vocational and science curricula.

Keywords

Anatomy · Arts · Medical humanities · Medicine · Museum and gallery studies

1 Introduction

The word 'anatomy' originates from ancient Greek and over time, with influences from Latin and Old French language, it morphed into its modern version that we are accustomed to nowadays. The original Greek word was ανατομία (pronounced as anatomia) and when this is divided into its two main constituent parts, the true meaning of the word becomes apparent. *Ανα-* (pronounced as ana) meaning 'up' and the

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verb *τέμνειν* (pronounced as temnein) meaning 'to cut'. The origin of the word implies an active process involving two entities (i.e. the person who 'cuts' and the structure being 'cut up') and relying on visuospatial skills with the visual aspect being a rather strong element. The roughness of the word *τέμνειν* also sheds further light into the ethics of how the human form may have been studied in ancient times.

But, what does the word 'anatomy' really mean for modern day academics? When consulting the Merriam Webster Dictionary, there are two striking definitions for anatomy; "the art of separating the parts of an organism in order to ascertain their position, relations, structure, and function" and "a treatise on anatomical science or art" (Merriam-Webster Online Dictionary 2019). From these definitions, it is immediately apparent that 'anatomy' and 'art' are used interchangeably. The common theme, spanning from antiquity up to the present day, is that anatomy as the science of examining the human body and art with its visual component have evolved together in a strongly linked symbiotic relationship perhaps needing and complementing each other.

The aim of this chapter is to bring anatomy, art, and ethics together due to their common themes. Specifically, the chapter will explore how object-based teaching using historical anatomical/medical collections can be re-developed in higher education settings for the exploration of challenging topics, including medical ethics, within the context of anatomical sciences. The authors' ultimate goal is to introduce a concise and easy to adapt 'how to guide' for educationalists who have an interest in the integration of arts and humanities in vocational and science curricula.

2 Historical Anatomical Context

Dissection is an important element for the study of anatomy with a rich history, straddling many centuries, which would require more than a book chapter to discuss in detail. In this section, the authors have explored specific historical parts that were deemed to be most relevant for unravelling the anatomy-art relationship with pertinent ethical dilemmas.

Anatomy started long before Herophilus of Chalcedon, but he is referred to as the 'Father of Anatomy' and has been accredited as the first to conduct both human and animal dissections (Klenerman 2015). Herophilus, along with Erasistratus of Ceos, were the first physicians to carry out systematic human dissections in Alexandria during 300 BC (Ghosh 2015). Herophilus recognised the brain as an organ of the nervous system and distinguished it from the cardiovascular system (Klenerman 2015; Panegyres and Panegyres 2016). Specifically, Herophilus consolidated the view of the human brain as the seat of our intelligence responsible for our thoughts, reasoning, and senses (Klenerman 2015). Consequently, Herophilus and Erasistratus introduced the encephalocentric theory (Pearce 2016). This was very much in contrast to the prevailing Aristotelian cardiocentric concept that was holding the heart as the organ of intelligence (Pearce 2016), emotions, and feelings with its origins dating back to the ancient Egyptians (Hajar 2011). It was most likely the direct, but also systematic, study and exploration of the human body that allowed Herophilus and Erasistratus to make such observations, paving the way for future physicians in relation to systematic enquiry. Alas, there were no anatomical illustrations, sketches or 'objects' to accompany their observations. It is important to keep in mind, however, that the above is a mere speculation as their records were destroyed and we rely on accounts from later physicians. Another intriguing aspect is to consider the prompts or motivators that empowered and in a way enabled Herophilus and Erasistratus to go against the societal, cultural, and moral beliefs of their time and perform human, rather than solely focus on animal, dissections. As Ghosh et al. discusses, royal patronage must have played a crucial role especially as there was a focus of establishing Alexandria as a "centre of literary and scientific learning" (2015). The bodies of executed criminals were dissected (Ghosh 2015) perhaps alongside vivisections (Pearce 2016) or experimentation on the living (Hajar 2000), this poses many ethical dilemmas. Turning Tertullian's cynical quote into a question raises several predicaments for the mind; was "Herophilus the physician or that butcher who cut up hundreds of human beings so that he could study nature"? (Hajar 2000). This is not straightforward to answer and, for academics nowadays, it is important to examine historical accounts, such as these, keeping in mind the era when the actions took place and utilising the records to appreciate and discuss ethics by making links to modern day medicine. It is vital to acknowledge the past and learn from it for the present and future.

Galen of Pergamon, a physician of Ancient Rome, has been known as the 'Father of Medicine' (Klenerman 2015). Galen produced extensive and detailed written accounts in relation to the human body without conducting human dissections. One of his well-known quotes is "though he sees the truth, he does not use it" referring to followers of opposing schools of thought (Hajar 2011). This is ironic, as in his own records there are many erroneous descriptions of human anatomy (Hajar 2011). As Hajar et al. proposes this might be due to the lack of anatomical illustrations, sketches or 'objects' in his descriptions (2011).

During the Renaissance, Andreas Vesalius debunked many medical myths by identifying such errors in Galen's texts and shifting the focus back to human cadaveric dissection to ensure anatomical accuracy (Dominiczak 2013). Vesalius studied the human body using empirical observation (Dominiczak 2013; Klenerman 2015) combining text with anatomical illustrations which was a rather innovative approach for his time (Dominiczak 2013). In his most famous work, *De humani corporis fabrica libri septem*, several hundreds of exquisite anatomical engravings are accompanied by descriptive text (Fig. 1) depicting the human anatomy (Dominiczak 2013). An important collaborator of his, who tends to be forgotten, was the artist Jan van Calcar who produced the drawings for Vesalius' printed works including most likely the illustrations for the *Fabrica* (Zampieri et al. 2015).

Apart from illustrations, models and specimens have also played an important role in the field of anatomical sciences. Historical models, nowadays considered as museum artefacts, were produced using a variety of different materials including wax (Fig. 2), plaster (Fig. 3), and papier-mâché adhesives offering an alternative to dissection (Hopwood 2008). Scientific wax modelling peaked particularly around the 18th century for teaching and research purposes (Hopwood 2008; Shteir 2007) starting from Italy and then gradually spreading to other European places (Hopwood 2008). At that time, human corpses were becoming scarce and the readily available wax models were a useful teaching adjunct for anatomy (Hopwood 2008).

During the 19th century, Adolf Ziegler and his son Fredrich had one of the largest ateliers in Germany, manufacturing permanent forms of anatomical wax models with these being frequently encountered in modern anatomical/medical collections (Hopwood 2008). Their main area of expertise was the development of magnified embryos and they worked in close partnership with academics for the production of their models (Hopwood 2008). One of the main purposes of these models was for students to recognise and familiarise themselves with the various microscopic stages of human embryogenesis (Dietrich 2002; Shteir 2007). On the other hand, the work of Paul Zeiller from the same era is a rather rare find nowadays that might be due to his preference of working alone or perhaps due to a fall out that he experienced with the anatomists (Hopwood 2008). Such historical models, are invaluable teaching resources, as they mirror the trends and norms of different eras allowing us to learn about anatomical tradition and the history of medicine.

The above notes discuss not only the evolution of dissection and hence how anatomy was studied, but also provide us with an insight into the anatomy-art relationship and the importance of visual aids in the field of anatomical sciences. By its very nature, anatomy is a highly visual and perhaps tactile subject. It seems that to fully understand the intrigued inner workings of the human form, visualisation is an essential adjunct

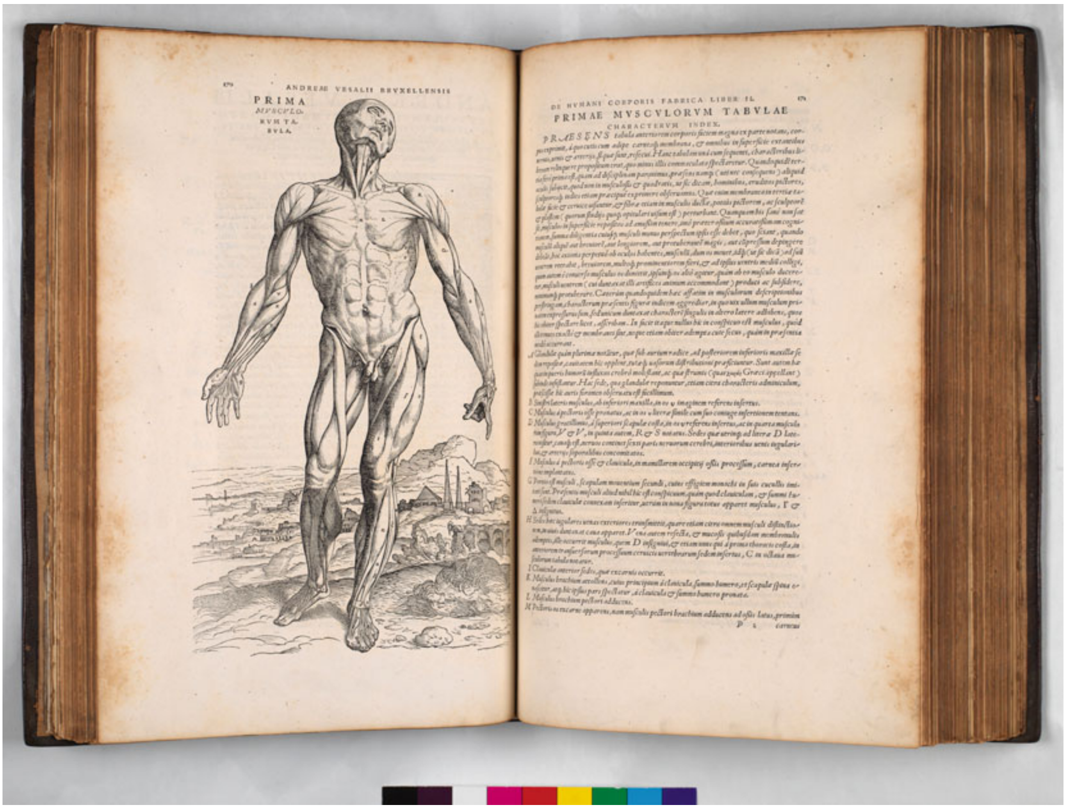

Fig. 1 Anatomical illustration from De humani corporis fabrica by Andreas Vesalius, 1543. Reproduced courtesy of the University of Glasgow Library Archives and Special Collections [Hunterian Z.1.8]

Fig. 2 Wax anatomical model of a half dissected human face (left side) manufactured by the Tramond atelier around the 1900s in France. Reproduced courtesy of the University of St. Andrews Museum Collections [MSAM2]

Fig. 3 Plaster anatomical model of the human abdomen manufactured around the 1900s (manufacturer unknown). Reproduced courtesy of the University of St. Andrews Musseum Collections [MSAM40]

be it in the form of anatomical illustrations, museum artefacts, or anatomy specimens that can be more broadly referred to as 'objects'. Let us not forget that medical instruments also provide us with an indirect understanding of the human body and allow us to appreciate the history of medicine and medical ethics.

3 Preparation for Teaching

The aim of the proposed lesson plan is to encourage the use of medical humanities in 'science' teaching, to increase awareness of and accessibility to associated 'objects', and to explore the role of women in anatomical art. For this lesson, we have used three iconic 'objects' to show how, through a targeted selection of artefacts, medical humanities can be used to elicit powerful discussions on the diverse roles of women in medicine and science. Similarly, to keep the session easy to replicate, we have provided key pieces of information on each 'object', rather than a potted and sanitised history. If you have access to a collection within your institution, these themes can be adapted to suit your 'objects'. However, access to a collection is not necessary to replicate this session as study cards and images are provided within the chapter.

For this session we have chosen a workshop setting to encourage open discussion, drawing from personal experience of how formal lecture settings can often stifle debate and peer interaction. During the workshop we would encourage you to focus on ethics and the individual(s) associated with your 'objects', considering how social constructions of women have led to narrow views of females in science and art in the past. Through our methodology, we aimed to deconstruct traditional learning structures adopting the following: "active learning exercises, such as teamwork, debates, self-reflection, and case studies, that prompt students' engagement and reflection, encouraging them to explore attitudes and values, while fostering their motivation to acquire knowledge and enhance skills" (Mclaughlin et al. 2014).

4 Considerations

An important part of the lesson design is to consider how to give enough background information to encourage robust debate around the 'objects', but also allow your audience to form and express their own opinions. Recent object-based studies have deliberated the level and amount of 'object' interpretation to give learners prior to their engagement with collections. Dudley et al. discuss the positives and negatives of providing little or no information, positively showing how new creative processes can be opened up by interaction with 'objects' on a pre-cognitive, sensory or material level (2012). Dudley et al. also acknowledges the negatives of presenting museum 'objects' without background and shows the potential to frustrate learners. The author's point is especially relevant to the Dissecting Art lessons, which have the commonality of aiming to use 'objects' to stimulate empathy for and imagination of other people's lives (Dudley 2012). Hence, through this session we would suggest that you focus on a small number of 'objects' to ensure depth of engagement with materials and the subject area. However, negotiating this middle ground with anatomical/medical collections can be challenging and the contents bring several complexities, relating broadly to three major concerns as discussed below. The first two points relate to both object-based and image-based learning, and the third to object-based learning only.

(1) Intellectual access: Fundamentally, there can be a lack of knowledge regarding what is anatomical/medical art and how it was created. When using such material for discussions, it would be inappropriate and self-defeating, not to provide the audience with a transparent and unbiased history of how such art was formed through the process of dissection.
(2) Emotional access: The material we used for the lesson plan shows depictions of dissection, human remains, and foetal mortality that can be distressing if presented without context or sufficient warning. However, with appropriate background information, this material has great potential to develop emotional skills in medical and scientific practice partly by stimulating in-depth ethical discussions and a deeper insight into such matters.
(3) Physical access: The fragility of material must be fully understood before contact with these 'objects' is permitted. There may also be concerns regarding damage and loss of irreplaceable 'objects'.

4.1 Intellectual Access, Medical Humanities

When working to contextualise 'objects' and images relating to this session, it is important to consider the different learning styles and cultural backgrounds of the audience, as the resources we have chosen for the proposed lesson relate predominantly to European medicine. To make this lesson accessible to audiences and learners from around the world, it is important to establish a starting point of knowledge and provide a comprehensive, but brief, history of European medicine and anatomical art, including relevant ethical concerns. The historical anatomical context from this chapter can be adapted accordingly to suit the learning needs of your audience. Thinking ahead to how this introduction will impact on the development of observational skills and discussion, it is important that learners understand the environments and era when this type of anatomical/medical art was created along with the legal and moral codes of practice.

Therefore, it is advisable to begin this lesson by delivering key points of information relating to the history of dissection and the legal acts surrounding the procurement of bodies from 1505 to 2004. Provision of unbiased historical information will enable learners to appreciate each 'object' within each time period allowing them to formulate their own thoughts and emotions.

To balance the introduction, you can also introduce your audience to the concept of the sourcing of human remains for medical research and art through four points in a historical timeline, including the moments in time when bodies were sourced without formal consent processes and dissection was perceived as punitive or discriminatory (Patrizio and Kemp 2006). This means demonstrating how law had disproportionately affected those seen as 'lower class' with limited access to legal defence and at most risk of offending or ill health due to impoverished circumstances and living in areas of higher risk behaviours (Bryant and Peck 2009). This introduction has to be provided, in a supportive and 'safe' teaching environment, with the cultural background of the audience in mind, sufficient reassurance that learners vocalise their uneasiness at any point of the session, and that the experts are available for 'emotional debriefing' sessions at the end of the lesson.

- 1505: The first dissection act in Scotland was the 1505 Seal of Cause granted to The Barber Surgeons of Edinburgh, later known as The Royal College of Surgeons of Edinburgh. In Edinburgh from 1505, the body of "ane condampnit man efter he be deid". In England, from 1540, four bodies a year were granted to the Company of Barber-Surgeons, later known as the Royal College of Surgeons of England (Patrizio and Kemp 2006).
- 1752: The Murder Act 1752 was implemented as a deterrent to prevent the act of murder through fear of dissection. The criminal justice system was the main legal source of bodies for dissection until the Anatomy Act of 1832.
- 1832: The Anatomy Act of 1832 aimed to put a stop to grave robbing and the illegal trade of human bodies by increasing access to cadavers. By the time this was passed, 'dissection' and 'anatomisation', as the legal process of opening and disarticulating the human body for teaching and research, was already associated with a social stigma and was often an exploitative process (Searle 1998). Importantly, the 1832 Anatomy Act shifted the source of bodies from the criminal justice system to the poorhouse (Richardson 1987).
- 2004: The Human Tissue Act 2004 (England, Wales, Northern Ireland) and 2006 (Scotland) consolidated the legislation of the Anatomy Act 1984 while introducing a regulating framework for all human tissue, including retention and public display matters, ensuring good practice. Nowadays, in the UK, body donation is a most generous decision, not associated with stigma, for which anatomy teachers and researchers are extremely grateful.

By presenting this background information, anatomical/medical art can be understood and debated as a developing process reflecting the evolving depiction of dissection ('anatomical examination') in Europe; although this began as exploitative and non-consensual taking the lives of some of the society's most vulnerable people, it has evolved nowadays into a legally regulated and ethical process in the UK. This introduction will set the scene for a series of ethical dilemmas that your audience will be asked to consider during the session providing a truly deep, but also unbiased, discussion.

4.2 Emotional Access, Medical Teaching

Medical/anatomical collections, from the past, hold stories relating to the lives and deaths of those who were abused by historic medical practices and these narratives can be used to explore emotional intelligence in current practice. The ‘objects’ and images for this session have also been selected to highlight the personal stories of women, who through inequality, somehow ‘lost’ their rightful place in the history of medicine. In previous years of working to develop this particular session, we observed that the more intimate environment of viewing ‘objects’ and images in small groups allowed for in-depth discussion and enabled closer facilitation when exploring potentially emotive areas including congenital difference, dissection without consent, and infant mortality, which arise when looking at the works of various anatomists from the past. In their discussion on emotional intelligence and emotional regulation in medical competency, Hodges and Lingard differentiate between “doing the right thing” and “being the right thing” (2012). Accepting this point of view, we designed a lesson plan that gives learners the space to consider how the development of emotional intelligence and communication can bring obvious advantages in situations such as delivering unwelcome or shocking news (Hodges and Lingard 2012). Additionally, the lesson considers how emotional regulation such as “detached concern” is rightly seen as a sign of competency in situations of trauma (Hodges and Lingard 2012). During the development of this lesson, we wanted to explore how students can learn to regulate emotions in situations where they may hold negative or judgemental views. The material used has been selected to challenge unknown or known prejudices, and the links between women, empathy, and ethics were particularly relevant to these sessions.

In addition to the more obvious areas discussed above, developing physician empathy has been shown to have many more benefits including “improved patient satisfaction, greater adherence to therapy, better clinical outcomes, and lower malpractice liability” (Batt-Rawden et al. 2013). The opportunity to use medical humanities to create more collaborative and contemplative environments has been positively received in undergraduate programmes where “art-based interventions have been suggested to enhance medical students’ self-reflection, communication and collaboration with colleagues, and understanding of physician-society relationships” (Muszkat et al. 2010). Here, we wanted to draw upon the development of professional and interpersonal skills, by allowing learners to consider codes of practice and ethics in relation to patients who faced discrimination. This meant we gave our audiences enough information to comprehend issues in inequality and to explore their own levels of empathy.

4.3 Physical Access, Museum Concerns

The ‘objects’ used as examples in the suggested lesson plan are from two, often, very different environments. Physically, due to storage and handling conditions, illustrated historical books are classified as ‘rare’ books held in library archives under the supervision and care of professionals with expertise in paper conservation and collection care. The anatomical models, some of which were produced as counterparts to illustrations and dissection, often remain within medical settings (e.g. dissection rooms, anatomy museums, etc.) under the supervision and care of curators. When handling such ‘objects’ for teaching, it is vital to work with experts to ensure proper standards are met. These tend to include, but are not limited to, the following: clean and dry teaching settings, the exclusion of pens and liquids that could irreversible damage ‘objects’, clean hands or gloves for active handling (please note that this point varies depending on the curator’s advice), and agreed photographic permissions. Every collection will have its own procedures, and the safest and most courteous way to proceed with any teaching session is to work with the experts responsible for the collection who can also provide your audience with a brief specialist-led introduction enriching your session.

5 Lesson Plan and Resources

In Table 1 we have provided a summary of the required resources and general teaching considerations, while in Table 2 we have outlined a more detailed lesson plan that could be adapted depending on availability of existing collections in your own institution. In this section, we have also included 3 study question cards (Card 1, 2, 3) that contain relevant information on the 'objects' we have chosen for our suggested lesson plan.

Card 1 Women as academics in anatomical art.

Professor Florence Rena Sabin (1871–1953) made significant contributions to the scientific community. Amongst her many achievements, Professor Sabin was the first women to hold a full professorship at Johns Hopkins School of Medicine during an era when equality between sexes in the medical profession was only starting to be explored. Professor Sabin spent several weeks with the manufacturer creating a realistic prototype of this model based on her book *An atlas of the medulla and midbrain*. Although the model and its accompanying atlas were used for a long time in several medical schools around the world for teaching purposes, not many people are aware nowadays of its links with Professor Sabin even in departments with surviving models.

Professor Florence Rena Sabin has been an inspirational role model for women in science. How should we acknowledge nowadays the contribution of the many unsung women scientists of the past?

Does it matter that Professor Sabin's contribution to this model is not immediately apparent?

Why do you think Professor Sabin's manual has remained hidden amongst the myriads of other atlases?

What obstacles do you think Professor Sabin might have encountered during her academic career?

Would it have been different, if Professor Sabin was starting her career in the 21st century? (Fig. 4)

Table 1 Resources and considerations for setting up a dissecting art session

Location	Seminar room or anatomy laboratory, if anatomical/pathology specimens are to be used Please be mindful to the rules and regulations of your own institution/department and country of origin in relation to the transfer and display of anatomical/pathology specimens It may be prudent to have discussions with the most senior anatomist and your curator, prior to embarking on such a session, to ensure good code of practice
Staff	3 experts ideally consisting of 1 anatomist, 1 collections specialist, and 1 ethicist
Duration	2 h for the workshop 1 h for preparation 1 h for debriefing
Class size	Suitable for 6+ participants
Resources	Study cards alongside chosen 'objects', if available, and stationary such as pencils and paper. Additional stationary for feedback, if needed (e.g. post-it notes, recording device, etc.)
Considerations	Physical, emotional, and intellectual accessibility of 'objects' and settings. Wider considerations including institutional rules and regulations along with recommended codes of conduct from relevant regulatory bodies

Table 2 Suggested lesson plan for a dissecting art session

Topic	Duration
Introduction to relevant history	15 min
Small group discussions *Spilt the audience into three equally numbered groups, each with a study question card and its relevant 'object' if available. The sub-groups have 45 min to discuss, with the help of a facilitator, the questions related to each 'object'. The facilitator is there to promote discussion and not to impose their own views; they should be trained to remain unbiased at all times and know when and how to manage difficult situations/discussions that may be putting learners at an uncomfortable position* **Group one: Women as academics in anatomical art** **Group two: Women as portrayed as the subjects of dissection in anatomical art** **Group Three: Women as artists in anatomical art**	45 min
Whole group discussions *Reconvene as one large group to discuss the main topic(s) of each study question card and its relevant 'object', if available, under one overarching theme. It is of paramount importance to allow the learners to express their own views with the facilitator providing prompts to stimulate discussions, but generally remaining unattached to the discussions. The purpose of the facilitator, again, is to know when and how to manage difficult situations/discussions* **Place of women in anatomical and medical art** Whether disempowered through social class, or empowered by wealth or education, each woman in our discussion has somehow been side-lined in medical history. How do you feel about the following points? Professor Florence Rena Sabin typically remains uncredited on the accompanying record card for the model she designed. What is our (academic) duty in relation to ensuring historic women are credited for their work within our institutions? Following dissection, the Unknown Woman's body would have remained without a formal burial and a named resting place. How can we pay respect nowadays to those women whose bodies advanced medicine in the past? Frederik Ruysch overshadowed his daughter Rachel who was an acclaimed still life botanical artist. What historic and modern views of 'women's roles' might have contributed to this? **Final questions** What have we learnt from the past? (Have we?) What can we do for the future?	45 min (15 min for each group)
Closing remarks *Final closing statements from facilitator, who should still remain unbiased, along with signposting of available staff for 'emotional debriefing' sessions including office hours for any learners who would prefer privacy to discuss any topics that may have stimulated emotional thoughts*	15 min

Card 2 Women as portrayed as the subjects of dissection in anatomical art.

When William Hunter published his studies on the gravid uterus, entitled *Anatomia uteri humani gravidi tabulis illustrata* in 1774, it was common practice for anatomists to acquire bodies for dissection from the wards where they worked without formal records of consent to dissection. However, at that time, the only legally viable dissection subjects would have been bodies of convicted criminals procured via the Murder Act 1752. This method of obtaining cadavers meant that more male bodies were available and that the female

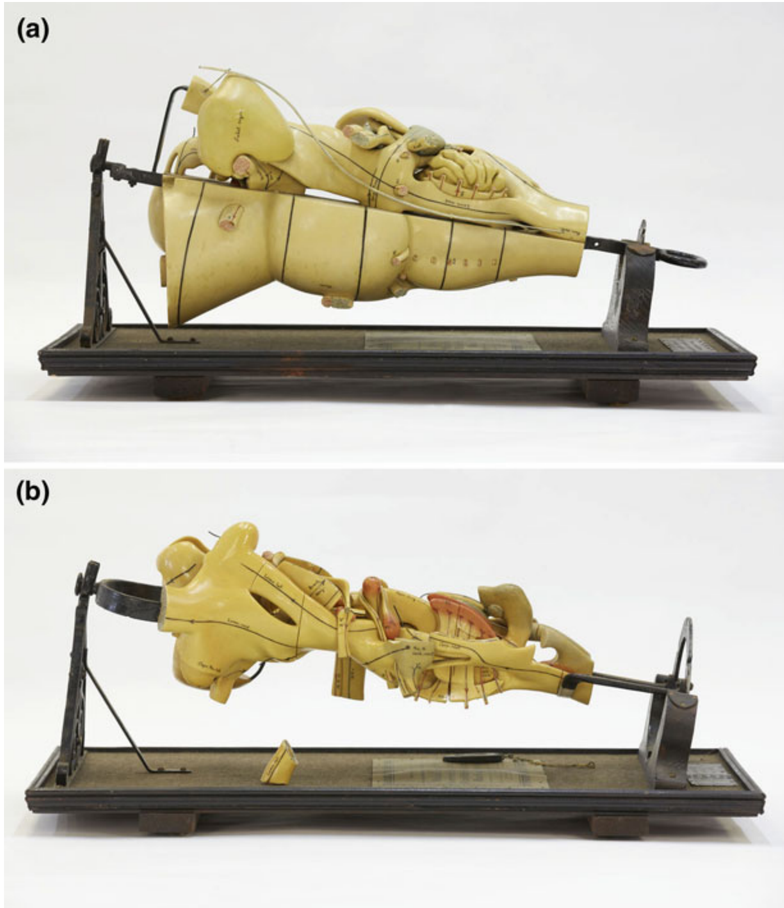

Fig. 4 Wax anatomical model of the medulla, pons and midbrain of a newborn baby manufactured by the Ziegler atelier around the 1900s in Germany. Reproduced courtesy of the University of St. Andrews Museum Collections [MSAM6 and MSAM7]

body was often missing or misrepresented in medical teaching. In particular, studies on the gravid uterus (pregnant womb) were underrepresented. As a result of his research, William Hunter published many original studies that advanced medicine on subjects such as the dangers of forceps deliveries, the transverse womb, and puerperium care.

The contributions of William Hunter advanced the field of midwifery and obstetrics. How should we pay respect to the women whose bodies contributed to such medical advancements in the past?

How would you argue the case for dissection in this example?

What would be your reasons for refusing dissection under these circumstances?

How do you feel about the anatomical dissection and the representation (or lack of) the Unknown Woman in this illustration?

How else could research have advanced medical knowledge of the female body during this era? (Fig. 5)

Fig. 5 Drawing for plate XIII by Jan van Rymsdyk, 1750. Reproduced courtesy of the University of Glasgow Library Archives and Special Collections [Hunterian Az.1.4]

Card 3 Women as artists in anatomical art.

Rachel Ruysch (c. 1643–1706) was the daughter of surgeon anatomist Frederik and a prominent botanical still life artist. Her father procured foetal specimens through his position as the Praelector of the Amsterdam Guild of Surgeons and chief instructor of midwives and used them for anatomical displays and illustrations. Ruysch's *Opera omnia anatomico-medico-chirurgico* remains one of the most influential and visually stunning works in the history of medical illustration. Rachel worked in collaboration with her father preparing specimens and developing the artistic arrangement of human remains by adding lace cuffs to limbs along with flowers and shells to tableaux to enhance themes of transient beauty and to hide scars caused by dissection. Rachel officially began her career as an artist at the age of 15

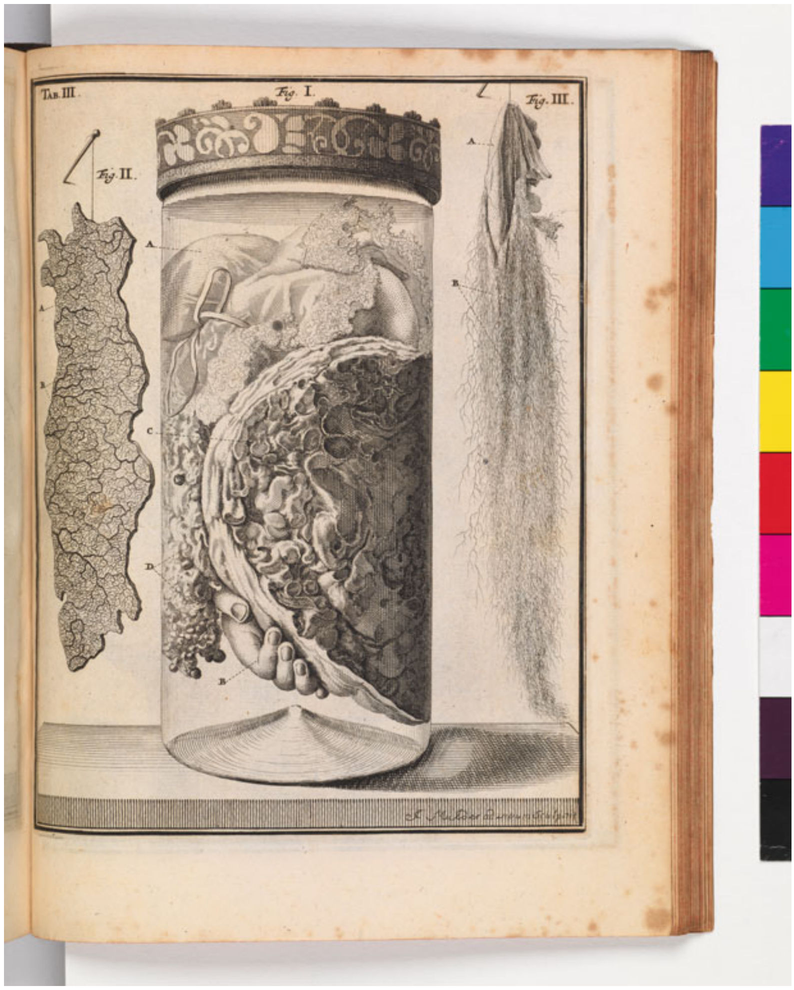

Fig. 6 Anatomical illustration from the *Opera omnia anatomico-medico-chirurgico* by Frederik Ruysch, 1725. Reproduced courtesy of the University of Glasgow Library Archives and Special Collections [Hunterian W.5.7–10]

with an apprenticeship under artist Willem van Aelst and she continued producing art until her death at age 86. During her life, some of her paintings sold for higher prices that Rembrandt's works. However, as a woman, Rachel was excluded from studying male nudes and her name is mostly missing from anatomical art.

Rachel's perspective on art and beauty provides a unique and memorable angle which has impacted on the lasting memory of her father's work on anatomical displays. In medicine, how should we remember Rachel Ruysch?

Do you think it matters that Rachel Ruysch was not credited in her father's work?

Banning women from attending anatomy drawing lessons with male nudes was presented as a measure to ensure propriety. Can you think of any other societal objectives this exclusion might have served?

When considering consent, does Rachel's artistic work and her 'decoration' of human remains cause any additional ethical concerns?

Does looking at the unadorned, purely anatomical Ruysch illustration change your perception of how Rachel Ruysch should be remembered? (Fig. 6)

6 Summary

Anatomy and art have a strong and rather interlinked relationship with visualisation being a shared denominator. 'Objects' from historical collections be it in the form of anatomical illustrations, museum artefacts, anatomy specimens or even medical instruments provide unique visual aids not only in terms of helping us to develop a better understanding of the human body, but also enabling us to acquire a deeper insight into the history of medicine and relevant ethical matters. The suggested lesson plan, alongside the historical anatomical context and the considerations, can be adapted depending on availability of existing resources and the topics that you would like to discuss with your audience. Medical, and in a more broad sense health-related, humanities are a rapidly expanding discipline and the integration of such topics in vocational and science curricula will allow learners to better appreciate challenging topics by actively deliberating and debating them.

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Using Photogrammetry to Create a Realistic 3D Anatomy Learning Aid with Unity Game Engine

Katrina M. Wesencraft and Jennifer A. Clancy

Abstract

Learning and processing complex 3D structures can be challenging for students, particularly if relying on 2D images or if there is limited access to the study material. This applies to many fields including anatomy, where students report difficulty visualising complex structures such as the nervous system. We aimed to address this by creating a realistic model of part of the nervous system—the sympathetic nervous system which is known for the 'fight or flight' response. Photogrammetry was chosen to create a 3D digital model of a dissection of the sympathetic nervous system. The 3D model was then incorporated into an interactive learning aid that allowed users to manipulate the model and provided relevant text information and labels. Evaluation of the learning aid by students (n = 7) was positive with 71.4% strongly agreeing that using this application improved their understanding of the anatomy. The majority of students (85.7%) also agreed or strongly agreed that this application provided them with a view of the sympathetic nervous system that they had not seen before. Photogrammetry is a relatively simple and inexpensive method to create realistic 3D digital models that can promote self-directed learning and a greater understanding of complex structures.

Keywords

Photogrammetry · Anatomical education · Sympathetic nervous system · 3D learning application · Gamification

1 Background

The incorporation of new visualisation technology into science curricula is a popular area of research. Many STEM subjects require the comprehension of complicated 3D structures, and educational researchers have shown that visualisation is a key step in information processing. 3D digital models can greatly improve student comprehension, and the development of interactive learning aids should be a central focus of modern educators (Gilbert 2004).

In many cases, students' ability to view real structures is limited. This can be due to location, or lack of resources; or for structures too large

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(e.g. in naval architecture or aerospace engineering) or too small (e.g. protein structures) to be appreciated by eye. Access to digital models can enable these students to accurately visualise new information. One field that is embracing online learning aids, 3D digital models, and augmented and virtual reality is anatomical education.

As a subject, anatomy is highly dependent on 3D data. Whether studying at the cellular or the organ level, students must learn and process structural information. Cadaveric dissection is the preferred method for teaching anatomy (Ghosh 2017), however, due to time constraints, anatomy curricula mainly consist of lectures. This causes a reliance on 2D images, and can be insufficient to show the extent and connections of complex anatomical structures. The images used are often illustrations which are also subject to artistic impression (Manson et al. 2015). While textbook diagrams and illustrations are good for reference, they can be confusing due to their variability.

The use of 3D resources has been reported to enhance student learning of spatial relationships, particularly in complex areas such as neuroanatomy (Manson et al. 2015). The aim of this study was to produce a 3D digital learning aid to improve student understanding of the nervous system, an area of anatomy that students often find challenging.

1.1 Current Challenges in Learning 3D Anatomy

For students studying medicine or biological sciences, anatomy lessons are often their first experience of learning a subject that is so highly dependent on 3D concepts (Marks 2000). Students have reported that they struggle to find the correct orientation of specimens when they are in the dissection lab, and that they struggle to form a mental image of the 3D structures outside of the lab (Kramer and Soley 2002). It is well-documented that students perceive neuroanatomy as particularly difficult, with some educators referring to the phenomenon as 'neurophobia' (Schon et al. 2002). Improving the resources for learning neuroanatomy may not only improve student attainment, but could also have a positive impact on the student learning experience as a whole (Hall et al. 2018).

Traditionally, the dissection of human cadavers was the only method available for anatomy students to appreciate the spatial relationships within complex body systems. However, many universities are moving away from dissection due to time pressure, rising costs, increasing class sizes, and a shortage of deceased donors (Granger 2004). Dissection classes are frequently substituted for prosections: demonstrations where specimens are dissected by an experienced anatomist. Prosection is frequently incorporated into anatomical curricula and its effect on student learning has been widely studied. It has been found to be equivalent to dissection in facilitating learning (Yeager 1999). The use of prosection can help to reduce the complexity of anatomy lessons, and emphasises key body structures for students so that they are not overwhelmed (Topp 2004).

Prosection is popular with both lecturers and students, and can be time-saving during highly pressured medical courses that leave little time for dissection laboratories. Some universities can provide students with access to prosections that have been plastinated. This preservation technique renders specimens hard and odourless so that they can be handled by students (Hagens et al. 1987). However, this still requires students to learn in a supervised laboratory setting, using textbook diagrams for reference. Furthermore, creating these specimens is costly. Skilled staff are required in order to prepare them, and they are difficult to maintain.

Outside of laboratory sessions, textbooks and anatomy atlases are students' main resource for accessing images of dissected specimens (Sugand et al. 2010). However, they are limited in the number of images and viewpoints they provide. Advances in computer visualisation have led to the development of virtual anatomy. When introduced to anatomical course content, these digital resources have enhanced student learning (Griffin 2003). As advanced imaging technology becomes routinely available, and with new developments in computer graphics and 3D gaming technology, the creation of sophisticated educational tools has become more accessible (Van Eck 2006). Despite this, many digital anatomy resources still rely on the use of 2D images to explain complex 3D structures such as the nervous system.

1.2 Potential of Digital 3D Models in Neuroanatomy

An interactive digital resource containing 3D models of prosected specimens could supplement course content and encourage students to learn in their own time. Unlike anatomy atlases, this learning aid would provide students with the option to interact with the model and explore from multiple angles. Research suggests that interactive resources provide students with a deeper understanding of the anatomical structures in question (Gehrmann et al. 2006).

The spatial relationships of one division of the nervous system, the autonomic nervous system (ANS), that regulates involuntary control over the internal organs, are particularly challenging for students to understand (Griffin 2003). The ANS has branches distributed widely throughout the body and helps to maintain a constant internal environment. It consists of two parts, the sympathetic and parasympathetic divisions; with the sympathetic nervous system best known for mediating the 'fight or flight' response (Jansen et al. 1995). Disorders of the ANS can affect any body system, and there is mounting evidence to implicate sympathetic over-activation in a vast array of chronic conditions (Fisher et al. 2009), including depression, inflammation, obesity and heart failure (Milby et al. 2008; De Herdt et al. 2009; Val-Laillet et al. 2010; Zannad et al. 2015). Despite its importance, the anatomy of the sympathetic nervous system is often poorly understood by students.

It is possible that the sympathetic nervous system is particularly difficult to visualise due to its wide distribution and complex connections with organs. For this reason, students are unlikely to encounter complete dissections of the sympathetic nervous system in either the dissecting room or from prosections. Students also have limited time in which they can access dissected material and appreciate the spatial relationship between delicate neural structures. The ability to view realistic 3D digital prosections outside of pressurised laboratory sessions could aid student learning, however, there are currently no such models of the sympathetic nervous system. We investigated whether the creation of a realistic digital model of the sympathetic nervous system using photogrammetry would aid student learning.

1.3 Photogrammetry

Digital photogrammetry is a technique which enables 3D space to be modelled from 2D images by collecting geometric information from overlapping photographs (Egels and Kasser 2001). The technique was initially developed for use in surveying and mapping as it can be used to accurately measure distances between landmarks. Photogrammetry was typically carried out using aerial photography, but recent advances in digital imaging and automated processing have enabled 3D object reconstruction via close-range photogrammetry (CRP).

Photogrammetry has a long history as a medical imaging technique (Mitchell 1995). The ability to accurately measure the distance between points makes it particularly attractive in biostereometrics—the spatial and spatio-temporal analysis of form and function. However, the realistic models that can be created makes photogrammetry a valid tool for medical education. Photos provide a faithful depiction of real structures and, unlike freehand modelling, photogrammetry produces realistic 3D digital models.

2 Creation of an Interactive 3D Anatomy Learning Aid

The first step in any photogrammetric process (Fig. 1) is image acquisition. A Nikon D810 36.3 Megapixel camera was used to photograph a cadaver with previously dissected sympathetic nervous system. This high specification camera was used in order to capture the complex nerve plexuses and is a higher specification than the average user will require. Photography was undertaken in the dissection laboratory at the University of Glasgow in accordance with the Anatomy Act (1984) and Human Tissue (Scotland) Act (2006). Photographic permission was previously granted by the donor.

The photogrammetry software Agisoft Metashape, formerly known as Agisoft Photoscan, calibrates common points between photographs and is able to triangulate the camera position from which the picture was taken (Fig. 2). Both a professional and a free standard package are available (for a full list of the software used, see Table 1). This information enables the software to create a point cloud which can be edited by the user. The software uses an algorithm to produce geometry, or a polygonal mesh, representing the surface of the photographed object. Minor edits can be carried out to confirm the geometry of the mesh before it is textured by the photographic images to give a realistic appearance (Agisoft LLC 2013).

Photographs should be shot in raw format as, unlike JPEG images, raw files are uncompressed, record all of the data captured and record greater levels of brightness. Uniform shooting conditions are essential when undertaking CRP. As photogrammetry software automatically detects any common points between images, shadows or shiny materials can be problematic. Highlights can be matched incorrectly, creating an anomaly in the point cloud and potentially a hole in the polygon mesh. Care must be taken to avoid changeable light levels; however, minor alterations can be corrected via careful pre-processing with photo editing software (Guidi et al. 2014). A gazebo was erected in order to reduce the natural light reaching the specimen. This avoided any fluctuations in light intensity, and improved the contrast between background and specimen. Fluorescent softbox lights were used to create uniform illumination. Number, position, and height of the lights can be determined by eye, adjusting so as to not cause specular reflections. Should reflection be unavoidable due to the nature of the object being photographed, camera polarising filters can be used to minimise this effect (Wells et al. 2011).

The camera must be stationary when used as the software is unable to identify any common points between a blurred image and one that is in focus. The camera was mounted on an adjustable arm which was clamped onto a portable scaffold (although a tripod would also suffice). A circuit around the specimen was undertaken and a series of test shots were captured. The camera was manually adjusted to optimise settings for the conditions. On this occasion, the camera was set to a low ISO and a shutter speed of 3 s.

Discounting test shots, more than 170 photographs were taken of the cadaver to ensure approximately 60% overlap between photos (this should ensure that all common points are identified). As there are important nerve plexuses along the midline of the body, extra effort was taken to photograph those areas with increased overlap to ensure the fine detail was preserved. Once the camera was focussed correctly, a piece of string was used to measure the distance from the specimen to the camera and cut to length.

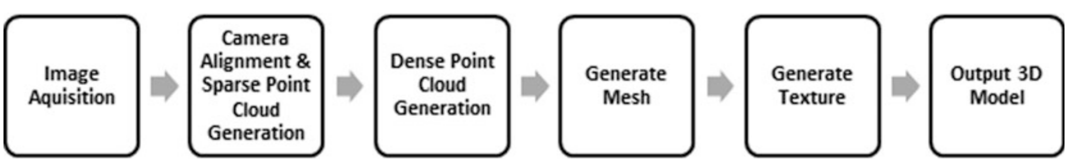

Fig. 1 The photogrammetric workflow used to create 3D models with Agisoft PhotoScan Pro

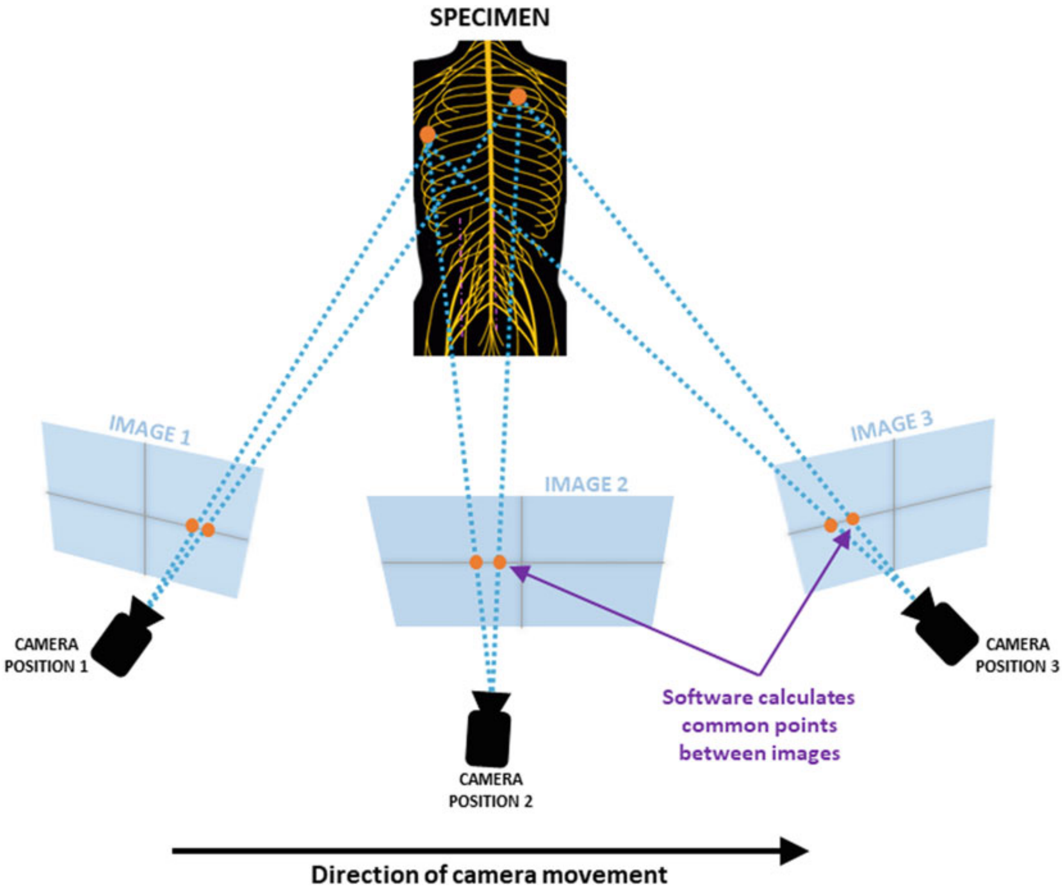

Fig. 2 The core principle of photogrammetry: record multiple overlapping photographs of the target specimen. Software calculates the common feature points between images to generate a model (specimen adapted from Servier Medical Art by Servier—licensed under https://creativecommons.org/licenses/by/3.0/legalcode)

Table 1 Software used to create the 3D model of the prosection and the interactive learning aid

Software	Version
Adobe Bridge CC (https://www.adobe.com/products/bridge.html)	6.0.1
Agisoft PhotoScan Pro (https://www.agisoft.com/features/professional-edition/)	1.2.5
Autodesk 3ds Max (https://www.autodesk.com/education/free-software/3ds-max)	18.0 student
Unity (https://unity.com/)	5.2.1f1

This length of string was used as a reference when moving the camera rig during image capture. The photographs were taken from five heights, and a remote trigger was used to avoid pressing the shutter button and shaking the camera.

Photographs were converted from RAW to TIFF files using Adobe Bridge CC and imported to Agisoft PhotoScan Pro (Table 1). All images were successfully aligned. This generates a point cloud in which unnecessary voxels can be selected and deleted in advance of creating the dense cloud. This ensures that no unwanted objects are modelled and cuts down on processing time. Alternatively, the active region can be resized so that only the region of interest is processed. The models produced from these images were highly detailed—generating a 'medium quality' mesh resulted in upwards of one million polygons.

3D editing software may not be able to handle models of such high complexity and, as Unity game engine (Table 1) was used to create the learning aid, the number of polygons in the mesh models were reduced. Agisoft PhotoScan Pro has a 'decimate mesh' feature, allowing the user to reduce the resolution of the model to a specified size. Unity has a polygon limit per model, so the number of polygons was limited to 60,000 as a precaution. The final stage in the photogrammetry workflow is to texture the models with the photographic data. Agisoft PhotoScan Pro provides a selection of methods for texture generation. The preferred texture mode was selected by eye. For models with uniform brightness throughout imaging, the 'mosaic' texture mode can provide excellent results (Fig. 3). The 'average' mode produces a texture of lower quality than 'mosaic'

Fig. 3 **a** Anterior view of the model of the cadaveric specimen textured with 'mosaic' mode (sympathetic plexuses along the midline emphasised using black card), **b** lateral view of the same model displaying the sympathetic chain and intercostal nerves

mode, but can be useful when images have varying brightness. The 3D photogrammetry model was then imported to Unity to create an interactive learning aid that users could manipulate.

2.1 Application Development and Evaluation

Educators do not require an extensive knowledge of software development to create 3D learning applications to support student learning. Unity (Table 1) and other game engines provide a development framework for game creation, providing access to essential components such as 3D graphics rendering and asset creation. This enables the user to create games without the need for advanced programming. For those with little coding skills, an online script library (compiled by other users) is available in Javascript, Boo, and C# languages.

Game engines can be used to create more immersive educational tools, encouraging the user to engage with 3D information through navigation and camera manipulation (Mackenzie et al. 2003). Unity was chosen as it has previously been used effectively by academics to design interactive biology-based visualisation systems; bypassing the complexity of traditional software development (Lv et al. 2013). In order to produce a prototype learning aid, the downsized photogrammetric model was imported into Unity. Scenes were created; these consisted of a 'Main Menu', introductory scenes and a cadaveric model. A user interface (UI) was designed to allow easy navigation between scenes through the use of buttons. The main aim of this application was to improve students' understanding of the structure and function of the sympathetic nervous system. Textual content was developed aimed at undergraduate life sciences or medical students. The introduction provided general information about the sympathetic nervous system including its function in health and disease.

As the photogrammetric model was the main focus of the application, it was essential that students are able to interact with it. A series of 3D colliders were created around structures of interest (Fig. 4). A panel was attached to the UI on the right side of the screen and labels were created that correspond to each collider. Pop-ups were created so that when the mouse cursor is placed over the collider, a corresponding label appears in the panel (Fig. 5). This is highly customisable, and even the fade time of the text can easily be adjusted.

The models must be lit in the game 'scene'. This can be achieved by drag and drop; using directional lights ensured that key features of the sympathetic nervous system could be seen and were not cast in shadow. Mouse controls were added that allow the user to rotate the models and to zoom in on important features. If required, limits can be set for the maximum and minimum rotation in the x and y axes.

A group of postgraduate students (n = 7) from a range of backgrounds, studying anatomy as part of their MSc programme, were approached to evaluate the prototype. The evaluation process centred on a pre-test/post-test design. The questionnaire consisted of seven statements requiring the students to self-evaluate their knowledge of the sympathetic nervous system. This required the students to select the most appropriate response on a Likert scale.

The majority of the students (71.4%) strongly agreed that using this application improved their understanding of the anatomy of the sympathetic chain. The students also agreed or strongly agreed (85.7%) that this application provided them with a view of the sympathetic nervous system that they had not seen before. While this is small sample group and reliant on self-evaluation, the results indicate that students value this type of learning resource. This supports the ongoing development of realistic and interactive 3D learning aids in not just anatomy but also other areas involving complex structures.

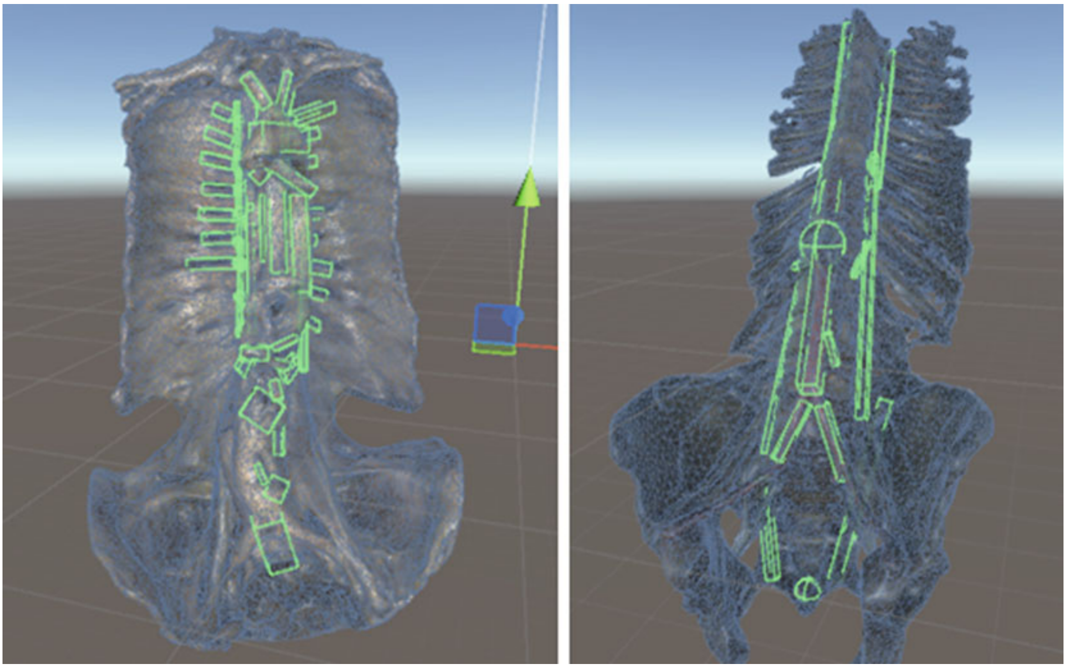

Fig. 4 Developer scene in Unity—'colliders' are game components used to define the shape of an object for physical collisions. These are invisible during gameplay, so rough boxes and spheres dragged over the area of interest are sufficient. Simple scripts were used to trigger corresponding information to 'pop-up' when the user's mouse is over a collider

3 Advantages and Disadvantages of Photogrammetry

Photogrammetric models of pre-dissected prosections provide students with a unique resource for learning the anatomy of the sympathetic nervous system. While a certain amount of expertise is required to dissect the sympathetic nervous system, photogrammetry is relatively quick and easy. It does not require the purchase of expensive equipment or software; depending on what is being modelled, a mobile phone and open source software may suffice.

Models and animations can also be produced freehand by creating a polygonal mesh with a 3D computer graphics program such as 3ds Max (Table 1). However, as with educational illustrations, the models produced will be variable and are dependent on artistic impression. If creating anatomical models, this can be combated by basing schematic models on medical imaging data. However, the resolution of CT or MRI imaging does not compare with that of a digital SLR camera. While it is technically demanding to dissect anatomical structures such as the sympathetic nervous system, CT and MRI scans often do not have sufficient contrast to distinguish between individual nerves and surrounding soft tissue.

Open source software such as 3D Slicer (https://www.slicer.org/) can be used to segment scans into distinct anatomical structures (Kikinis et al. 2014) although this can create fairly crude models that require smoothing and other manipulation. Surface texture and colour also must be determined by the artist. With photogrammetry, models appear 'real' as they are textured with photo data. However, photogrammetry effectively provides a surface model of your specimen with no internal structure. Should the developer wish to provide information about

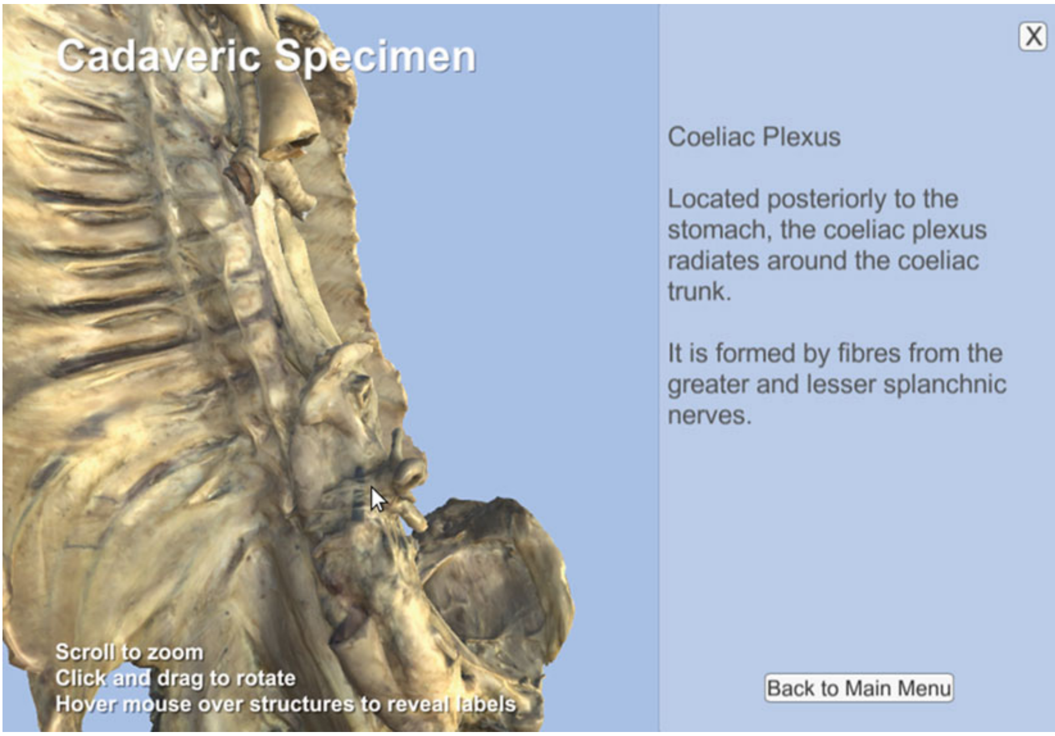

Fig. 5 User interface during gameplay—when the mouse is over the collider corresponding to the coeliac plexus, ‘pop-up’ information is triggered on the right of the screen. The information changes as the model is rotated and different structures are highlighted with the mouse

different body layers or compartments, then this requires multiple rounds of dissection and modelling.

4 Gamification

In recent years there has been great interest in the development of educational games. Students of today have grown up surrounded by technology and it is possible they may process information differently as a result (Prensky 2001). This concept has been widely discussed, and educators have increasingly been incorporating digital resources into their curricula. It is believed that traditional instruction methods are no longer engaging these students, as they prefer a varied lesson structure with short and frequent interactions with information. Game-based learning is one method which has been highly successful in engaging students (Van Eck 2006).

With the development of serious games on the rise, there is ongoing debate over the definition of what constitutes a ‘serious game’ and the literature currently fails to meet a consensus. Generally speaking, a serious game must have a purpose other than being purely for entertainment (Ratan and Ritterfeld 2009). Instructionist games are those that have been developed with the main goal of delivering educational content (Kafai 2006) and several of these systems are available for teaching anatomy. However, the majority of these applications cannot be classed as games in the usual sense as they are lacking key game features such as award systems or the ability to ‘win’ (Ma et al. 2012). As such, the field of serious games encompasses a broad range of technology and the term is often used to describe forms of E-learning that lack conventional game qualities.

Interactive digital learning aids are often described as serious games when they have been developed using a game engine such as Unity. With educators encouraging self-directed learning at universities, serious games are an excellent resource to encourage students to work independently. Adding a game element can also provide an incentive to work outside of the classroom.

5 Further Applications

Photogrammetry software has recently become more widely available and user-friendly. Open-source software packages such as MeshLab (Cignoni et al. 2008) have reduced the cost of CRP—it is now a relatively quick and inexpensive method of producing 3D models. Previously, 3D photogrammetric modelling was limited to institutions that could afford expensive laser scanning equipment (Waas and Zell 2013). The cost-effective nature of CRP has particularly benefited small companies, museums, and conservation charities, allowing individuals to contribute to larger projects. As the use of CRP has become more widespread, applications have been developed across a variety of fields, including animation, conservation, heritage visualisation, and medicine.

For historians and archaeologists, photogrammetry has revolutionised the way that specimens are archived, shared and displayed. The 3D models produced have enabled the study of artefacts which were previously too delicate or too valuable to handle. The ease with which these models can be shared has also been beneficial, allowing experts around the world to study specimens from different geographical locations (Falkingham 2012).

Photogrammetry is increasingly being used to digitise art gallery and museum collections. Museums can present interactive exhibitions online—these are excellent for education and public engagement, and also help to preserve records of the collections. Photogrammetry was also used in this study to model a unique specimen from the Hunterian Collection in the Museum of Anatomy at University of Glasgow (Fig. 6). This specimen was of interest when creating the learning aid as it is a prosected model displaying the sympathetic nervous system. It is believed that the specimen is approximately 250 years old, and that it is preserved by varnishing—a rare technique. This 3D digital model will provide an accurate digital record of this delicate specimen in event of its loss or damage over time (Jocks et al. 2015). Furthermore, students can now study this specimen outside the museum in their own time without risking damage from repeated use.

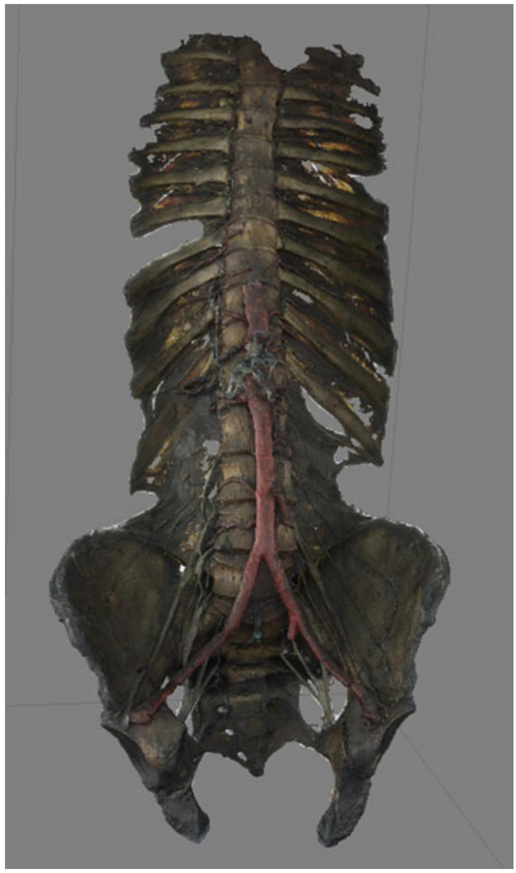

Fig. 6 Textured photogrammetric model of anatomical specimen from the Hunter collection. Model textured using 'average' mode

In addition to digital display, models produced through photogrammetry can be 3D printed and used as classroom resources (Li et al. 2017). This has clear educational value; digital 3D models are still viewed on a 2D screen—actually handling a model can improve appreciation of surface features. It also provides students with the opportunity to handle plastic replicas of fragile items.

Models produced through photogrammetry can be incorporated into games, but can also be used in virtual and augmented reality (AR) applications. This can be used to create an immersive learning experience in a variety of fields. For anatomists, students can walk around specimens, and explore different viewpoints as if they were in a real laboratory setting. There are currently several smartphone apps in development that aim to exploit improvements in AR. Several of these involve the alignment of anatomical models with users, creating an overlay that reveals the true placement of anatomical structures. The realism of photogrammetry models also makes them ideal for surgical training applications.

This study created a learning aid that provides students with a unique and interactive way to study a complex area of anatomy. Research of the relevant literature found that no 3D models of the sympathetic nervous system existed prior to this development. Positive feedback from students indicated that interacting with the photogrammetric models improved their anatomical knowledge and that this tool has potential for further development.

Combining photogrammetry models with Unity game engine enables the creation of interactive visualisation aids in a variety of fields. The technique is ideal for digitally preserving or sharing rare artefacts, scientific specimens, or even locations. Photogrammetry can be undertaken with no experience, inexpensive equipment, and open source software. While prior coding experience is beneficial in using Unity game engine, the excellent online tutorials and coding wiki community (Unify Community Scripts) mean this is not a prerequisite to create effective educational tools.

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Innovative Education and Engagement Tools for Rheumatology and Immunology Public Engagement with Augmented Reality

Timea Kosa, Louise Bennett, Daniel Livingstone, Carl Goodyear and Brian Loranger

Abstract

Rheumatoid arthritis (RA) affects around 1% of the population, which places a heavy burden on society and has severe consequences for the individuals affected. The early diagnosis and implementation of disease-modifying anti-rheumatic drugs significantly increase the chance of achieving long-term sustained remission. Therefore, raising awareness of RA amongst the general public is important in order to decrease the time of diagnosis of the disease. Augmented reality (AR) can be tremendously valuable in a teaching and learning context, as the coexistence of real and virtual objects aids learners in understanding abstract ideas and complicated spatial relationships. It has also been suggested that it raises motivation in users through interactivity and novelty. In this chapter we explore the use AR in public engagement, and detail the design, development and evaluation of a blended learning experience utilising AR. A set of informative printed posters was produced, enhanced by an accompanying interactive AR application. The main user testing was conducted with 27 participants at a science outreach event at the Glasgow Science Centre. Findings report mean positive attitudes regarding all aspects of the study, highlighting the potential of AR for public engagement with topics such as RA.

Keywords

Rheumatoid arthritis · Augmented reality · Public engagement · Rheumatosphere · 3D model

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1 Introduction

The National Co-ordinating Centre for Public Engagement (NCCPE) defines public engagement as:

> The myriad of ways in which the activity and benefits of higher education and research can be shared with the public. Engagement is by definition a two-way process, involving interaction and listening, with the goal of generating mutual benefit. (NCCPE n.d.)

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The idea of a two-way conversation in the engagement process is crucial to the success of the engagement. This change from thinking that we must fill a deficit in public understanding to a meaningful and two-way dialogue is now recognised by scientists, funders and policy makers (Stilgoe et al. 2014). However, keeping the information that we wish to discuss with the public accessible and understandable to a wide range of audiences can be challenging.

Even today, there are regrettably still some in the STEM professions that do not appreciate the importance of public engagement. In response, NCCPE have laid out five guiding principles of public engagement that also help emphasis why engagement with the public matters. Firstly, we are accountable for the public funding that we receive, with the UK government investing over £10 billion annually into research and development over the last 5 years (Office of National Statistics 2018), and we must be transparent in how this money is spent. Secondly, Universities conduct research with the ultimate aim of benefitting both the local and wider communities, and as such we have a responsibility to explain this research and its implications to those communities. At times, the long-term benefits of some forms of research (such as basic science) can be hard to see directly, and so we must be effective in helping the public to understand our motives, the downstream effects of research, and our ultimate end goals. It is easy to lose sight of these values when there is a massive drive for Research Excellence Framework within the university setting, which often leads to engagement being overlooked as a meaningless or pointless activity. However, the NCCPE have encouraged us to make public engagement a core value of the University, and to use the dialogue in engagement to help to get back to what drives us as researchers in the first place. Thirdly, in a climate which is increasingly hostile to a perceived academic elite, building trust between the public and academic institutions is of the utmost importance. We are no longer able to function solely on the terms of the academic institute; instead we must now listen to the opinions of the wider community. The public engagement dialog can help the wider community to develop informed opinions about what we do and ultimately build trust in our work and research. Fourthly, if we are responsive to the comments of the wider public and respond positively to them, the relevance and impact of our research is improved significantly. A well-developed public engagement strategy is the best way to build this relationship and the subsequent dialogue. Finally, we must be relevant in the manner in which we engage, not only with the content of our engagement and how our research can be integrated into the world that we currently live in, but also in the means by which we communicate. Today's world has a wealth of communication modalities beyond the traditional didactic lecture. This ranges from social media platforms, podcasts, and online videos, to newer, more interactive mediums such as augmented and virtual reality tools. We must ensure that we are using the most effective and relevant media to engage with our target audience.

2 New Ways to Engage with the Public

Engagement is not a new concept and there are many examples of good engagement activities and different forms of media that we can use to engage the public. In today's age of fast paced technology advances, it is important to stop and explore new media that are available as engagement tools, such as augments and virtual reality, as these may offer more effective means of engagement for wider audience groups.

New technologies can now allow for easier visualisation and comprehension of complex scientific information. In 1997 Azuma defined augmented reality (AR) as a system that allows real time interaction in a combined and accurately aligned blend of virtual and real environments (Azuma 1997). Due to these unique attributes of AR, we can help to breakdown complex scientific concepts such as immunological relationships in Rheumatological disease states and this merging of real and augmented realities together can also add new dimensions to learning. There are two types of AR:

"location-based" and "image-based". Its name suggests, location-based AR uses a location (such as GPS or Wifi connection) as a marker to overlay relevant augmented information for the users. Alternatively, image-based AR relies on an image to trigger augmented information. This image can be a pre-made marker for a specific application, such as a symbol on a poster (marker-based) or it can rely on makers that already exist in the real world (such as a human face). AR is fast becoming a popular tool in public engagement and this is perhaps partly due to the lack of 'high tech' equipment that is required, as an AR program can be loaded onto a tablet, smartphone or smart glasses.

Another advantage in using AR as an educational tool is its potential to reduce cognitive overload, caused by presenting an individual with too much information at once or having information in multiple places in which the user has to switch focus from the task to read instructions for the next step of their given task (Bower et al. 2013). Using markers or anchors, the designer can choose when extra information is given, ensuring that only information that is relevant to that precise moment or situation can be seen by the user, reducing the risk of cognitive overload. In addition, by giving the user the option to choose to see additional information or information of increasing complexity, the risk of cognitive overload can also be reduced (Bower et al. 2013).

Wu et al. (2013) identified 5 distinct features of AR that can complement learning and teaching. These are: learning about 3D content and being able to manipulate it; collaboration with the AR environment; a sense of presence and immersion in a subject; visualising invisible content; and bridging formal and informal learning. These features are all sought after in science education, especially in the fields of anatomy and medicine. (Evidence showing AR in formal education). In principle, they also lend themselves to public engagement, though the efficacy of AR remains relatively unexplored in such an informal setting. One study of the use of augmented reality to improve learning in a science museum supported the idea that the use of digital augmentations helps the development of scientific knowledge (Yoon et al. 2017), suggesting that continued exploration of the use of AR for public engagement could be worthwhile.

3 Why Do We Need New Tools for Rheumatology Public Engagement?

Public engagement can be challenging, especially where the scientific material is complex. In the field of immunology, for example, most of the subject matter is at the microscopic level and is based on many complex relationships. This can be hard to convey through traditional media and risks leading to cognitive overload. By using the aspects of the real environment overlayed with AR, we can help to break down these complex components and concepts. Take, for example, an immune reaction that causes inflammation within the body. In the real world environment, we can identify inflammation caused by an immune reaction due to its painful, red and swollen appearance. With the use of AR, however, we could see beyond this outward appearance and look under the skin, looking down a "virtual microscope" at the immune cells and molecules that drive inflammation. Similarly, in a disease such as rheumatoid arthritis, the joints affected can be identified as being swollen and stiff, but the microscopic drivers of the disease and the complex interactions that potentiate the inflammation cannot be seen without additional resources. Due to the failing of other forms of media to the convey complex nature of autoimmune disease states such as rheumatoid arthritis, we must now turn to new technologies that have been shown to be promising for this educational purpose.

Engagement with regards to rheumatoid arthritis is often difficult, as the wider public have misinformed opinions that have become an accepted norm. Several studies have shown that the general public believe that RA is benign and only associated with aging and the elderly, when in fact it is a disease that can affect anyone at any age and severely affects quality of life, but can be successfully treated if identified early. Changing these engrained attitudes and opinions is challenging. To this end, the European League Against Rheumatism (EULAR) launched a campaign called 'Don't Delay, Connect Today' (DDCT) that aimed to raise awareness of rheumatological conditions, encouraging people to be aware of the early warning signs and the need for early diagnosis and treatment of these conditions. This campaign is especially important in younger individuals who often believe that arthritis will not affect them, or who feel embarrassed that they have symptoms that are commonly associated with the elderly. Engagement is also important for patients already diagnosed with RA. A study conducted by Walker et al. (2007a, b) showed that if patients were given an information booklet about the disease they not only gained significantly more knowledge about their disease but were also less anxious and depressed than those who did not receive the booklet.

It is well established that there is a great need for effective methods in raising awareness of the importance of early diagnosis in RA, as missing the 12 weeks 'window of opportunity' can result in worse remission rates (van der Linden et al. 2010). Adequate outreach has proven to decrease diagnosis delay over time (Zafar et al. 2012). Implementing innovative ways of informing the public could result in greater engagement with RA, and therefore shorter periods before diagnosis. AR presents itself as an ideal method for achieving greater engagement, as it enables the explanation of complex ideas in adaptable ways and may raise motivation in users through interactivity and novelty (Bacca et al. 2014).

However there remains a wide lack of awareness of RA, and accordingly a need to investigate other methods of engaging and informing the public on RA. As noted above, prior work on Augmented Reality has rated highly for being engaging and effectively supporting knowledge transfer, and accordingly we set out to create a Public Engagement application for RA using AR.

4 Interactive Print

Combining AR with printed material presents itself as an ideal method for public engagement. The familiarity of printed educational material combined with the novelty of AR can promote the intrinsic motivation for exploration of a subject (Liarokapis and Anderson 2010). These materials are referred to as interactive print.

Large quantities of virtual information can be added to these printed pages, which risks negatively impacting on the cognitive load of the reader. Accordingly materials should be designed with this risk in mind, allowing free exploration where learners can decide the amount of content they consume, thus reducing the risk of cognitive overload (Nadolny 2017). Some studies suggest that irrelevant material should be omitted altogether. Presenting learners with additional unnecessary information may over load cognitive processing capacity and thus learners might not achieve the expected learning outcomes.

5 Rheumatosphere

Rheumatosphere is a research group at the University of Glasgow, which organises public engagement events on a regular basis. One frequent venue for events is the Glasgow Science Centre, a science museum, open to the public, where a diverse range of people can be reached. Therefore, the design of the applications and print material had to cater to a wide age range and fit into a science centre environment. It was established that the final products must be easily portable, as Rheumatosphere organises outreach events all over Glasgow and Scotland.

Interactivity, ease of use and quick access were important principles during the conceptual design process. The initial idea was a small booklet with an accompanying AR application, that shares information on the nature of RA, its symptoms and causes, as well as the importance of early diagnosis. The concept of a booklet was later revised to be a series of posters, as the poster format lends itself to a more explorative way of use with the AR application in a public engagement setting for a number of reasons. First, there is no strict narrative throughout the posters, allowing participants can explore the elements that interest them, and at the pace and order of their liking—rather than following the order imposed by leafing through a booklet. Large format, image-heavy posters also stand out more in a busy exhibition environment and presented greater prospects of getting people more interested in the content.

The implementation of AR could also promote intrinsic motivation for the exploration of the subject, as it is still a relatively novel technology that can raise interest in the general public. AR also allows for including large amounts of information without overwhelming the reader, as the amount of interaction is defined by the user (Nadolny 2017).

6 Rheumatosphere AR

A series of five augmented posters were designed and a companion tablet AR app developed. The first poster provided basic information on the project, highlighted common symptoms of RA and encouraged participants to seek medical advice if they experienced some of the early signs. This poster was not augmented. The remaining four posters all included augmented content, and are detailed below.

The second poster (Fig. 1) describes in greater detail the symptoms, causes, and the toll the disease exerts on the individual and society. This poster triggers augmented reality content (Fig. 2) in the companion app.

The AR content for this poster shows a 3D model of a human skeleton and additional information in the form of a set of text pop-up bubbles. By rotating the skeleton, users can see joints that can be susceptible to RA, including some spinal joints, highlighted.

The third poster (Fig. 3) shows a diagram of a healthy joint explaining the structures found in the synovium and a short explanatory text on how synovial joints work. A second diagram depicts a joint affected by RA and describes the changes the disease causes inside the joint capsule. The two diagrams trigger two different AR instances.

An image of a healthy joint triggers the display of a 3D model of the metacarpophalangeal joint. Users can zoom in on this, and click on parts of the joint to find out the name of the structures. The image of the RA affected joint triggers a similar 3D model, this time showing inflammation of the synovium and destruction of the cartilage and bone.

The fourth poster (Fig. 4) is printed with a diagram of the cells active inside the RA joint, as well as some links for people wanting to find more out about the disease. The diagram triggers an AR scene with the cells depicted in 3D and with animated arrows showing the relation between each immune cell. A small information text panel is shown for each cell, explaining their role and how they stimulate each other in the disease.

The fifth poster (Fig. 5) shows the bones and joints of a healthy hand and describes the complications RA can have on bone structure. It was designed to be displayed horizontally, as it requires physical interaction (putting one's hand on the purple hand sign) to trigger the AR component assigned to the poster.

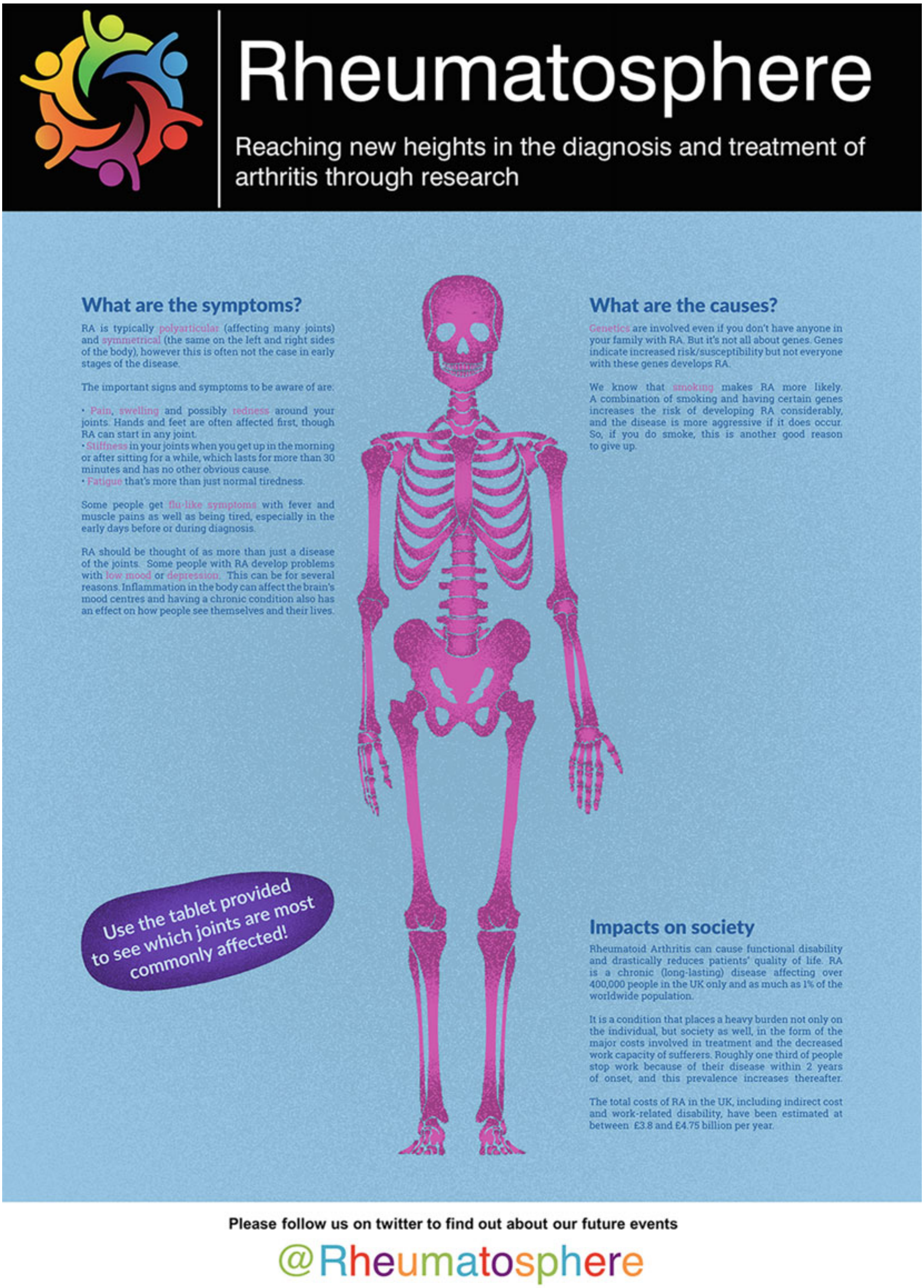

Fig. 1 The second of five posters, and the first to have augmented reality content linked through the companion app

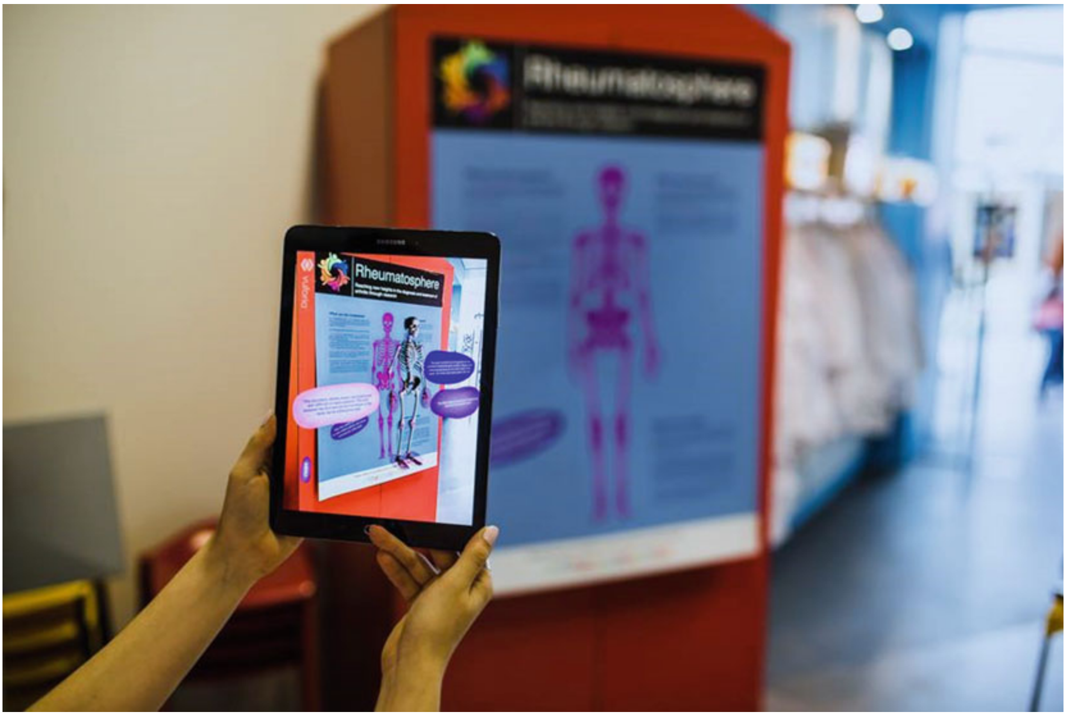

Fig. 2 Using the companion app, a 3D skeleton model and additional information is overlaid over the second poster. *Image* Glasgow Science Centre

7 Pilot Study

The posters were displayed at a public engagement event at The Glasgow Science Centre—'Science Lates: Move'. This took place in early August 2018. During the evening, 27 visitors used the app and completed a survey. The app on was made available on Samsung Galaxy S2 tablets with the application preloaded that were set up ready for visitors to use. This avoided any requirement for visitors to download the app for their own devices.

Visitors were recruited to participate during the event and were able to opt-in after reading the participant information sheet and signing a consent form. Visitors choosing not to participate in the study were still allowed to explore the posters and AR content. All visitors were able to take as much time with the application as they wanted and access as much of its content as they wished. When finished, participants completed a questionnaire about their experience (Fig. 6).

8 Results

A majority (16) of the (n = 27) participants were in the 25–34 years age group. A large number of participants also had at least an undergraduate degree in a life-science—8 of the 16 participants in the 25–34 years age group, 3 of the 5 in the 18–24 years age group and just 1 of the 6 in the 35 plus age group. This may be indicative of the audience which attends the Science Lates events, which will naturally attract visitors with a strong

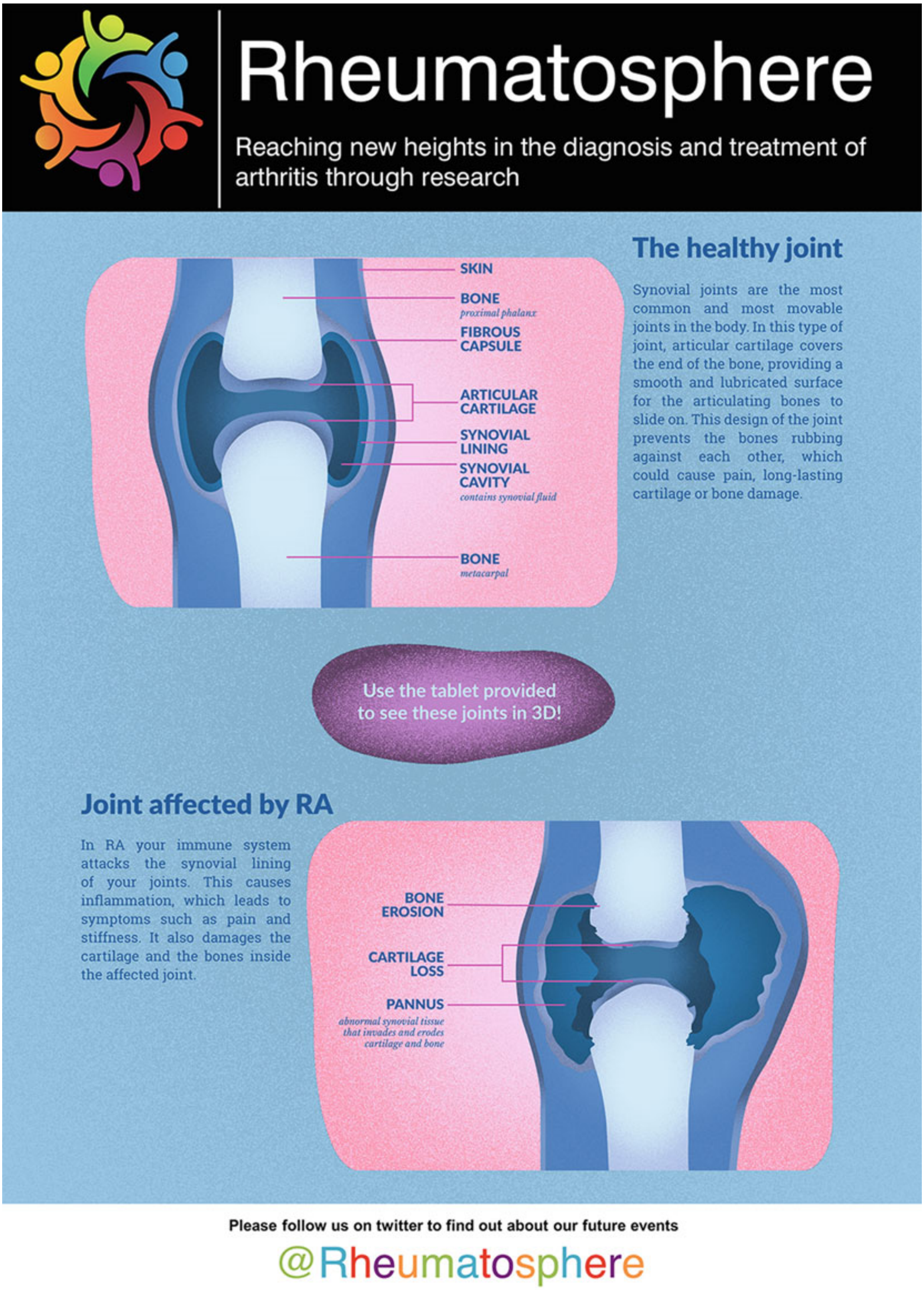

Fig. 3 The third poster features two different diagrams, each of which has augmented content in the companion app

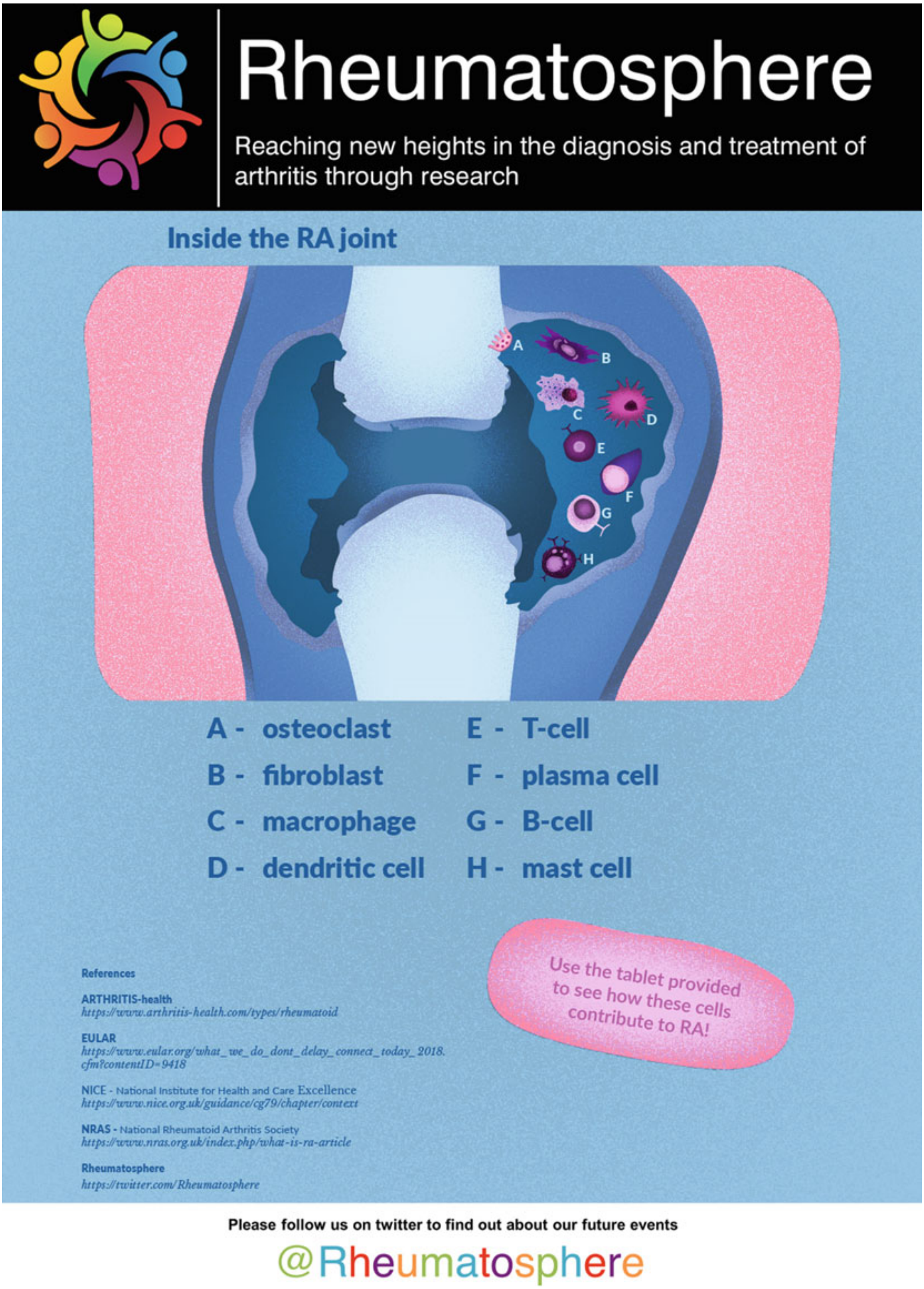

Fig. 4 The fourth poster has a single diagram and matching AR content

Fig. 5 The fifth poster is printed as a smaller scale for display on a table, and is designed to display AR content over a visitor's hand

interest in science. Three of the participants reported that they had a diagnosed musculoskeletal condition. Less than half of the participants (44%) had used AR before, with younger participants more likely to have previous experience.

The application was rated very strongly in all aspects related to usability. For example, the participants found the application easy to use (89% agree/strongly agree), and thought that most people would be able to learn to use the application quickly (96% agree/strongly agree), and there were no negative responses related to ease of navigation and understanding.

Similarly, participants found the application engaging, with users with no prior AR experience giving slightly more positive response here—potentially showing a 'novelty' factor, although the difference was not statistically significant. Again, there were no negative results on the question "I found the AR component fun and interesting", and the vast majority of participants (92%) stated that they would like to use similar applications in the future.

Finally, the AR experience also scored very highly for helping participants learn about RA and the human body (again, 92% agreement), and over half of participants stated that they would let friends and family know about the risks, symptoms and diagnosis of RA—an important result for effective public communication, potentially multiplying the direct impact from reaching attendees at the event itself.

9 Conclusions

The engagement experienced with Rheumatosphere AR was very strong, with a very positive response from visitors. This alone is highly encouraging, and we aim to continue the use of AR in our ongoing public engagement activities.

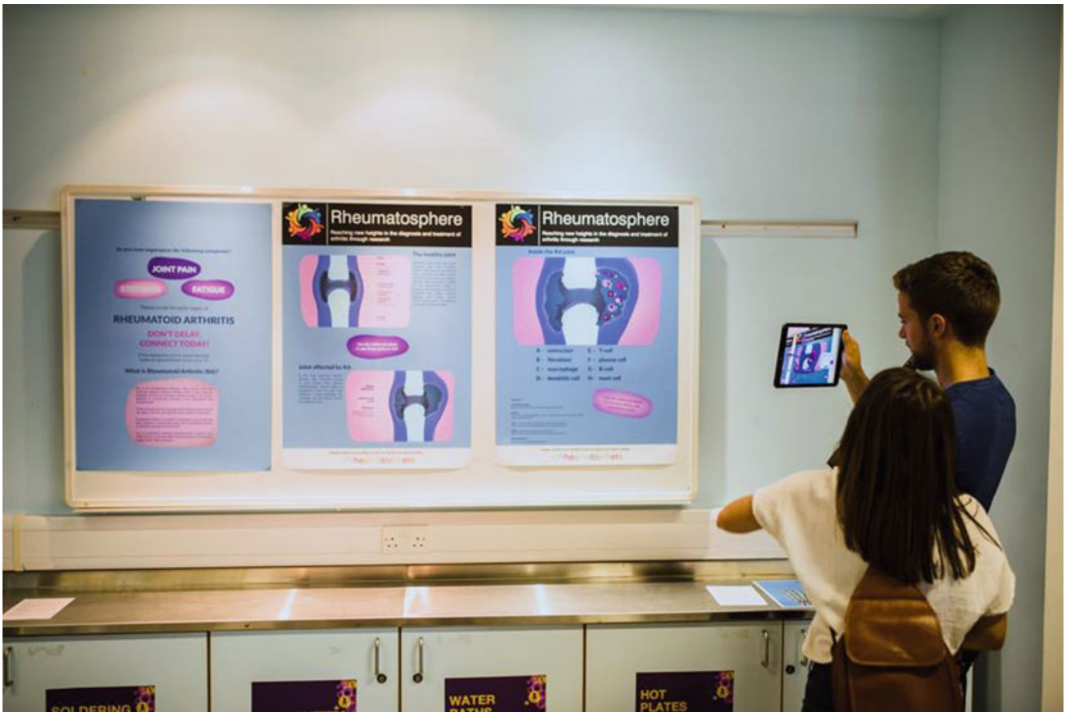

Fig. 6 Visitors at the Glasgow Science Centre using the application to view augmented reality content over the posters. *Image* Glasgow Science Centre

The experience was particularly popular with visitors who had no prior experience of AR, and was well received overall. From our experience, we summarise the advantages of interactive print posters for public engagement as:

- The AR poster plus app format allows for rich and detailed content while reducing the need for the posters themselves to be overloaded with text and information, resulting in more visually attractive posters
- The AR app attracted visitors to engage with the exhibit
- Visitors were very positive about the AR experience, but this did not overshadow the content with visitors stating that they had learned from the experience.

The limitations in comparison to traditional posters are that:

- Additional development costs and time to create app as well as poster
- As users become more familiar with AR there may be a diminishing return as people may be less attracted to the novelty of using AR to explore educational/informational content.

There were some additional limitations that were observed during the study. It was noted that some visitors would skip over text and focus purely on the AR enhanced diagrams, potentially missing much useful information. Potentially audio narration could be used, to be played while users view 3D models and animations. Playing or presenting information after relevant interactions may also be a more effective means of embedding information in the app.

Finally, we recognise that the design of the study presented here is limited. A more comprehensive and larger study might have compared the engagement and impact of traditional versus interactive print versions of the Rheumatosphere posters. However, we found the strong and highly positive engagement very promising and feel that the project highlights the potential that augmented reality can have in public outreach and for raising awareness of medical conditions.

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A Game Changer: 'The Use of Digital Technologies in the Management of Upper Limb Rehabilitation'

Rachael Ballantyne and Paul M. Rea

Abstract

Hemiparesis is a symptom of residual weakness in half of the body, including the upper extremity, which affects the majority of post stroke survivors. Upper limb function is essential for daily life and reduction in movements can lead to tremendous decline in quality of life and independence. Current treatments, such as physiotherapy, aim to improve motor functions, however due to increasing NHS pressure, growing recognition on mental health, and close scrutiny on disease spending there is an urgent need for new approaches to be developed rapidly and sufficient resources devoted to stroke disease. Fortunately, a range of digital technologies has led to revived rehabilitation techniques in captivating and stimulating environments. To gain further insight, a meta-analysis literature search was carried out using the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) method. Articles were categorized and pooled into the following groups; pro/anti/neutral for the use of digital technology. Additionally, most literature is rationalised by quantitative and qualitative findings. Findings displayed, the majority of the inclusive literature is supportive of the use of digital technologies in the rehabilitation of upper extremity following stroke. Overall, the review highlights a wide understanding and promise directed into introducing devices into a clinical setting. Analysis of all four categories; (1) Digital Technology, (2) Virtual Reality, (3) Robotics and (4) Leap Motion displayed varying qualities both—pro and negative across each device. Prevailing developments on use of these technologies highlights an evolutionary and revolutionary step into utilizing digital technologies for rehabilitation purposes due to the vast functional gains and engagement levels experienced by patients. The influx of more commercialised and accessible devices could alter stroke recovery further with initial recommendations for combination therapy utilizing conventional and digital resources.

Keywords

Technology · Rehabilitation · Upper limbs · Leap motion · Virtual reality · Robotics

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1 Introduction

1.1 Stroke

According to the World Health Organization (2018), stroke is one of the leading causes of death worldwide. Post-stroke effects can incur emotional and behavioural challenges reducing an individual's ability to perform activities of daily living (ADL). Rehabilitation is therefore vital to ensure a decent quality of life (QOL). Whilst, physical limitations following stroke are vast ranging from difficulty swallowing to balance disorders there appears to be significant gaps in the literature on the effects on the upper extremity of post-stroke interventions. Following acute stroke, 75% of survivors have upper limb problems (Lawrence et al. 2001). Stroke can affect upper-limb function in numerous ways including: paralysis, apraxia (difficulty planning movements), muscle tone, subluxation, contracture, swelling and pain. The affected limb is known as the paretic upper limb and a wide array of frameworks are recruited to classify its functionality.

For example, the International Classification of Functioning, Disability and Health (ICF) accounts for significant deviations, movement related functions and impaired muscle movements. Patients may also present with multiple impairments including weakness in both the arms, wrist and hand. To examine dysfunction, behavioural task analysis may be recruited. Impairments fall under 3 categories; (1) Learned non-use—results from non-use of the limb due to paralysis following stroke. As time progresses, individuals may adapt a habitual non-use for the limb. This can be increased by chronic pain and sensory impairments. (2) Learned bad-use-compensatory behaviour and spasticity following initial period which if repeated and reinforced can change initial learned movement. For example, flexion of trunk for reaching purposes as opposed for normal elbow extension (Cirstea and Levin 2000) and (3) Forgetting. Likewise, to objectively quantify stroke severity the National Institute Health Stroke Scale (NIH) is recruited measuring limb ataxia, drift and grip strength. Frequent assessment of motor impairment and precise mapping upper extremity impairment is fundamental to planning next-stage interventions by healthcare services such as National Health Service (NHS) in the UK.

1.2 NHS

Current pressures faced by the NHS UK has led to an urgency for rapid scrutiny and inquiry into spending and treatment programmes in prevalent diseases including stroke. An increasing recognition that new technologies could be beneficial for patients and staff alike has led to growth and development of numerous digital technologies (DT) aimed categorically at diagnostic and rehabilitation purposes for healthcare. The government's healthcare mandate for 2017–18 discusses the proposed increase in out-patient care aiming to integrate digital services and technology transforming patient care (GOV.UK 2018). A study commissioned by The Health Foundation asked a sample group of 2083 people aged 15 and over "How willing or unwilling would you be to allow NHS organizations access to lifestyle data you have collected yourself via an app or fitness tracker for the purposes of delivering care?". Over half of the study population (57%) where willing to share the data (Castle-Clark 2018). Therefore, public attitudes suggest a willingness to incorporate technology into healthcare offering sizable benefits. DT have the potential to deliver feasible treatments helping a struggling healthcare service. Surveying economic influence of these interventions could further aid government and healthcare professional's adjudication on DT use.

1.3 Economic Impact

Increasing incidence of stroke has led to profuse evaluation of the societal and economic burden of the disease. It is estimated the total annual direct cost of stroke is approximately £9 billion or 5.5% of total expenditure on UK health care (Saka et al. 2008). This finding highlights the pressing appeal for economic evaluation to ensure there is efficient use of resources devoted to stroke disease. Whilst there is immense spending on stroke, surprisingly the annual UK spend on research from governmental and charitable bodies for stroke is a minor 7% following cancer at 64% and Coronary Heart Diseases at 19% (Luengo-Fernandez et al. 2015). Despite, an attempt by governmental bodies to increase funding for stroke, the total overall research is negligible compared with is burden and notably disproportionately low when compared with other abundant diseases.

Contemporary studies are evaluating cost-effectiveness in unconventional therapies including the low-cost gaming systems such as the VR-based Nintendo Wii (Tsekleves et al. 2014). Such valuable comparison tools may aid NHS decisions in choosing costly physiotherapy sessions which incurs an average £325 per patient (Capital Physio 2018). Robotic technologies to replace inadequate physiotherapy has become increasingly abundant over the past decade. A recent study aimed to analyse the cost and clinical effectiveness of robot assisted training specifically on post-stroke patients with upper limb impairments using the results to inform health-care commissioners (Rodgers et al. 2017). Digital resources such as gaming software offer a self-rehabilitation approach that could potentially aid currently under-resourced programmes such as physiotherapy. Studies incorporating economic considerations aid post-stroke rehabilitation decision on appropriate use of conventional therapy (CT) with new techniques.

1.4 Conventional Therapies

Previously mentioned was the current pressures faced by the NHS and this can be evaluated by longstanding CT programs role in stroke. The principal aim of post-stroke recovery is to minimize further impairments and assist in ADL. Physiotherapists aim to progress basic movement synergies and return a pre-stroke state of motor functions through various physical exercises. A recent study indicated that 4 weeks of physiotherapy promoted recovery in all patient post-stroke (Carvalho et al. 2018). However, contradictory evidence by a systematic review highlighted the amount of time spent undertaking physically active during physiotherapy sessions. It was found stroke survivors spent less than 2/3 of the session engaged in physical activity thus insufficient to recover optimal motor potential (Kaur et al. 2012). Additional studies have highlighted the concerns of physiotherapy. For example, research has highlighted the abundance of patients discharged as satisfactory to the physiotherapy services but still unable to reintegrate into areas of work and education therefore with a perceived lower QOL (Kusambiza-Kiingi et al. 2017). Furthermore, patients belonging to rural practices are believed to be at disadvantages on physiotherapy waitlists (Merchant et al. 2016). DT offer potential benefits of home recovery programs bypassing current obstacles of CT such as time spent undertaking physical activity and availability to all patients.

An emerging area in rehabilitation is robot-mediated physiotherapy (RMT). A study focusing on elbow and wrist therapy outlined the benefits of the technology attempting to standardise applications for clinical use (Peter et al. 2017). Also a plethora of studies have investigated the economic cost of physiotherapy. It was found that an increase in strength training and general intensity of studies resulted in better recovery rates and lower costs (Chan 2015). Therefore, long-standing physiotherapy practices could be implemented into DT to drive a most efficient, intensive recovery for all patients. Consequently, whilst an abundance of research and substantial interventions appear to be in place for recovery purposes the promise of emerging digital techniques could be recruited alongside these treatments for a beneficial and improved recovery for stroke survivors. New DT also offer enhancements of motivation and improved mental well-being compared to CT.

1.5 Mental Health

Post stroke patients are often affected by mental health disorders such as depression and anxiety consequently following frustrations with physical incapability and an increasing dependence on spouse and family. Patient motivation and interaction following a stroke is important to reduce detrimental mental well-being. There are tremendous potential benefits with patient interaction in recovery displayed in early findings using DT. Although there is scarce research into the psychological comparison of utilizing technologies for rehabilitation purposes instead of interactive physiotherapy sessions several studies have considered participant's mental well-health in experimental-design. For example, a 2009 study by Chen measured psychological well-being across four different symptoms; energy, tiredness, calmness and tension using a virtual reality based experiment. Results suggest positive trends in all facets improvements in mood therefore may lead to enhanced performance and adherence. Additionally, current evidence suggests accustomed treatments such as anti-depressants and psychotherapy are evidently falling short of patient needs. The use of dynamic reinforcement utilized by DT has addressed psychological shortcomings in mental illness patients undergoing physical rehabilitation (Graham et al. 2016). Supplementary studies have displayed the urgency for change as stroke patients with chronic mental illness may need additional intervention to improve rehabilitation performance. As development continues into use of digital technology dynamic behavioural models, system design and individual tailoring can effectively advance and amend current shortcomings in post-stroke survivors with mental-illness (Naslund et al. 2017). Currently developing DT can be individualised, motivational and dynamic to overhaul current disparities including low patient mood and motivation.

Through gaming techniques, DT can make use of longstanding psychology concepts such as positive reinforcement thus facilitating training, exercise improvement and ultimately recovery (Sinclair and Saposnik 2010). However thus far, a minority of studies have addressed the emotional, cognitive and physical effects simultaneously when using technology as a method of rehabilitation. This is alarming as evidence suggests mental health is often affected long-term for stroke survivors and recovery rates slow in suffers of depression (West et al. 2010).

1.6 Digital Technology

A review of the literature highlights an increasing acceptance of the potential benefits that DT offers against modern healthcare challenges such as mental health issues, NHS constraints and strained CT. With commercialisation of devices such as heart rate trackers there is broadening public awareness to the use of such technologies on healthy individuals. Lesser known is the substantial and sustainable changes that are needed in healthcare across numerous diseases. The incorporation on technology is immensely increasing for major health corporations and for the general public. The recognition of changes required in the 2018 Government Mandate outlined the future influence of technology in healthcare. Technology has the prevailing capacity to change healthcare, but is dependent on government legislation, NHS infrastructure, political context and public expectations. Innovative DT appear to be at the forefront of stroke rehabilitation training spearheading an age of recovery against an increasingly prevalent disease.

1.7 Limitations of Current Literature

Whilst the benefits offered by technology to healthcare are numerous there is limited understanding about the effects of DT specifically on rehabilitation of the upper limb. A limitation of previous review articles, concerning DT and stroke rehabilitation, have not provided a robust overview generalising attitudes of studies. Furthermore, previous studies have not included economic evaluation and effects of intervention on patient mental well-being simultaneously. Our review aims to include patient and therapist opinions in conducting studies to ensure all recovery factors of stroke disease are covered including reported outcome measures of quantitative measure to perceived accessibility and motivation through qualitative findings. This primitive type of review is to provide information on the use of several DT on rehabilitation following stroke with specific interest on mood benefits, economical costs and the comparison to CT. We further aim to understand whether these effects are pro/neutral or negative for their use.

2 Materials and Methods

2.1 Prisma

An extensive systematic review was carried out 4 times to gain insight into the following categories: (1) Digital Technology (DT) (2) Virtual Reality (3) Robotics and (4) Leap Motion.

These terms were chosen after review of surrounding literature as each individual technology was prominently associated with upper extremity rehabilitation programmes and stroke disease. Articles were selected using the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) approach which was developed in 2009. PRISMA analysis can be adopted for a thorough evaluation of interventions whilst simultaneously reporting meta-analysis for review purposes. Analysis was executed following the published PRISMA statement from 2009, which consists of a review checklist and flowchart to aid meaningful analysis while using the approach. Furthermore, the PRISMA approach was adopted due to the transparency of reporting and evaluating randomized trials. Analysis took place from the original search date 29th September 2018 and final date 3rd November 2018.

2.2 Search Strategy

The meta-analysis was carried out using two widely accepted databases; PubMed and Google Scholar. From review of broader literature, the following search terms were used as keywords for analysis: ["Stroke Rehabilitation" AND ((1) "Digital Technologies" OR (2) "Virtual Reality" OR (3) "Robotics" OR (4) "Leap Motion")]. A target number of 30 articles from each respective data-base (PubMed and Google Scholar) using the above search strings was desirable to gain comprehensive knowledge from a multitude of articles. As previously mentioned, recruitment of articles ceased on 3rd November as the desired number of articles was mostly achieved.

2.3 Exclusion Criteria

Studies were only included if accepted by pre-determined criteria. Any duplicate studies were removed prior to further to explicit inquiry from brief analysis of title and author. Primitive analysis was carried out, by searching databases, reading solely titles and abstracts. Studies were only eligible for full analysis if; (1) The study was published in English; (2) The study was dated from 2009-2018 (3); The study was original research (4); The study chiefly focused on the upper extremity (5); The study principally focused on stroke disorders (6) The study exclusively focused on rehabilitation following previous clinical diagnosis of stroke disease. Analysis of eligible studies was then executed to gain a prevailing consensus on the literature.

As previously mentioned, we limited the search to devices assisting in upper limb rehabilitation only, thus, technologies aiding remote healthcare communication (i.e. telemedicine) or boosting capabilities of healthy individuals were excluded. Articles addressing stroke prevention were excluded to support the aim of enhancing knowledge solely on rehabilitation in post-stroke groups. There were no distinguished criteria for recruitment of devices. Devices aiding any functional gain (for example muscle strength, motor acceleration and range of motion) were accepted. Additionally, for purpose of the survey systematic review articles were excluded. Focus on pilot studies and original randomised controlled trials studies were deemed appropriate for full text analysis. Research utilizing DT for gait movements of lower limb chiefly were excluded even if the device could also be used on the upper limb. After exclusion, articles were pooled into sub-categories of attitudes (pro/neutral/negative) and outcome measures used (quantitative/qualitative/both).

2.4 Data Collection Process

Categorising of articles was executed based on our objectives; content of the included paper was analysed across the 4 categories [(1) DT, (2) VR (3) Robotics (4) LM] using the following principles:

1. Was the study pro/neutral/negative for use of DT?
2. Was qualitative/quantitative or both analysis techniques used to measure objectives?
3. What were the main outcomes of the study?

Additionally, for category (1) DT, the type of technology was noted and for category (3) Robotics, the name and country of the robot was noted. This supplementary information was recorded to gain a comprehensive account of the extensive and vague terms of "Robotics" and "Digital Technology". Findings on VR and LM used the above 3 principles only as these terms were believed to be unequivocal.

Classification of measurements followed a predefined framework. Articles were deemed qualitative if their measured outcomes were from participant/therapist feedback via questionnaires or interviews. Studies using qualitative approaches chiefly focused on patient satisfaction from therapy sessions through objective questions where participants could respond openly. Studies monitoring functional recovery through video analysis were also categorized as qualitative as interpretation was detected by researchers and not based on physical parameters.

Quantitative articles assigned a numerical measurement of functional gain to the patient conditions through various stroke, motor and clinically developed tests. As previously mentioned, devices aiding any functional gain were accepted thus assessment tools were not used as an exclusion element. All functional tests were reviewed to understand objective and relation towards the paretic limb.

The main outcome of all studies was noted by main themes in discussion and limitations section of articles. Lastly, articles were categorised on attitude (pro/negative/neutral) by a full analysis of text. Concluding remarks of the text supported classification purposes. Studies deemed neutral had balanced interpretations towards DT or many limitations including adverse effects or uncertainty about future integration of devices. Articles regarded as pro had positive comments on functional gains and social aspects of DT. Majority of pro articles had distinct attitudes for utilising devices for in home settings and were regarded as engaging. Articles presumed negative had lack of functional gains or believed there was no benefit of using devices over CT.

3 Results of Categories

3.1 Synopsis of Included and Excluded Articles

The documentation of the followed criteria is shown in the Fig. 1 which outlines a brief synopsis of the generated included studies prior to in-depth analysis.

A total number of 216 papers (n = 216) were chosen and evaluated. Following the outlined criteria 106 articles were excluded. Initially, filtering removed 20 duplicate articles and a further 19 were excluded as published prior to 2009. Secondary analysis was carried out by reading the article abstract. As displayed in Fig. 1, majority of excluded articles were review articles

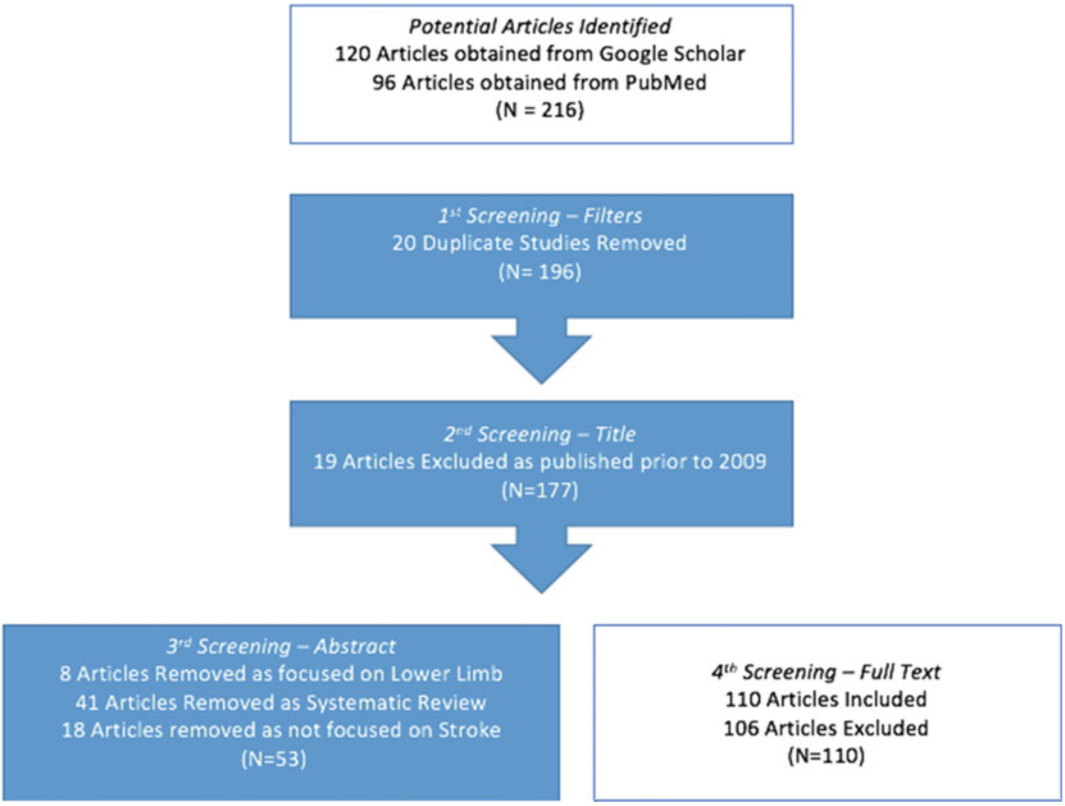


Fig. 1 Flowchart displaying inclusion and exclusion of journal articles

(n = 41) and thus removed. Articles focused on lower limb (n = 8) and not focused on stroke (n = 18) were also excluded.

A total sum of 110 articles remained for further review and were used in our meta-analysis. The 110 included articles were gathered across the 4 categories; (1) Digital Technology (2) Virtual Reality (3) Robotics and (4) Leap Motion. Meta-analysis was carried out 4 times to gain an in-depth appreciation of literature surrounding technology use in stroke recovery of the upper extremity. Initially, a review was carried out on the broad term—"Digital Technology and Stroke Rehabilitation".

3.2 Data on Digital Technology

The umbrella term of DT was used for primary meta-analysis of literature as all types of devices and electronic equipment were incorporated in the search. As previously outlined, search engines Google Scholar and PubMed were used for identification of associated literature. The ill-defined search using terms "Digital Technology and Stroke Rehabilitation" was undertaken to gain broad overview of the available devices before sub-categorising. Type of technology was additionally noted for this category.

Of a potential 454,000 Google scholar and 188 PubMed journals, 30 articles were chosen from the initial "best match" displayed pages respectively. Of these 60 articles, n = 31 articles did not meet the criteria and were thus excluded. Excluded articles were chiefly due to the study not predominantly focusing on stroke (n = 11) and dating prior to 2009 (n = 7). This was expected due to the generalised term "Digital technology' which inhabits communication technologies and other devices not specific to stroke rehabilitation of the upper limb. Thus such articles were deemed unsuitable and excluded. Additionally, review articles (n = 6), duplicates (n = 5) and articles focused on gait and lower limb (n = 2) were removed.

Of the remaining 29 articles, (n = 25) were pro; (n = 2) neutral and (n = 2) negative for the use of DT in stroke rehabilitation. These findings were backed by qualitative (n = 5), quantitative (n = 19) and use of both measures (n = 5) to statistically interpret results. Table 1 introduces the 29 included articles with the type of technology recruited for the study and the main outcome.

Upon in-depth analysis of the full text main correlational themes of functional gain (n = 11) and social engagement (n = 7) were noted as the major emerging themes of the 29 included DT studies for this primary category.

Additionally, Table 1 highlighted the prevalence of studies investigating one particular technology. Of the 29 studies, the majority of articles recruited virtual reality (n = 8) or robotic assisted therapy (n = 5). Thus, across the broad umbrella term of DT there was highest prevalence of VR, robotic and leap motion devices recruited.

3.3 Data on Virtual Reality

A secondary meta-analysis was carried out on the recent phenomenon most affiliated with the gaming community is an immersive technology known as Virtual Reality (VR). Presently using headsets, VR generates realistic visual and sensory feedback making use of haptic vibrations through game controllers. This tactile information stimulates user's physical presence in various virtually developed worlds ranging from underwater worlds to on sporting fields. VR was chosen as a primary category in this review due to the growing recognition as the device in clinical settings and prevalence in the previous meta-analysis for category (1) Digital Technology.

Adopting the PRISMA approach, the use of VR in stroke rehabilitation of the upper limb was examined using the search term "Stroke Rehabilitation and Virtual Reality". A possible 38,700 Google Scholar articles and 523 PubMed articles were identified and the first 30 chosen from the two databases respectively. Following the outlined criteria, of the 60 articles, 26 articles were included and 34 excluded. Of the excluded material, systematic review articles were highly prevalent (n = 17), followed by duplicated (n = 8) and outdated studies (n = 6). Lower limb focused literature only represented 3 of the 34 excluded articles. Of the 26 included articles majority were pro (n = 19) for the use of VR with 2 negative and 5 neutral approach. Majority of the articles primarily utilized quantitative measures (n = 20) with 4 articles using qualitative approaches and 2 adopting both measures for purposes of the research. Table 2 summarises the database article was obtained from, the articles attitudes to the device and what assessment method was recruited. This allowed further investigation into the reliability and correlational themes across the studies.

Notably, two of the included 36 studies used the System Usability Scale (SUS) to interpret usability of VR software in therapy training. This qualitative questionnaire assesses acceptability and ease of use were found. Most studies utilized Likert scale questionnaires examining the enjoyment of the VR world's and tasks

Table 2 displays the main outcomes highlighting that there were persistent themes across the included articles. Firstly, the use of VR for functional recovery of the paretic limb was generally positive across the studies when compared to the control groups. Fourteen of the 36 included articles reported an increase in functional gains.

Eight studies of the 36 included studies also discussed the likelihood of introducing VR to a clinical setting. From these 8, there was diversified outlooks with 6 pro; 1 neutral and 1 negative for its introduction of VR into clinical settings.

Table 1 Displays the included articles for DT search including assessment used and main outcome

Author(S), year	Google Scholar/PubMed	Pro/neutral/negative	Quantitative/qualitative/both	Assessment method(S) used	Comment(S) on main outcome	Type of technology
Liao et al. (2011)	Google Scholar	Pro	Quantitative	– Fugl-Meyer Assessment (FMA) – Motor Activity Log	– Increased functional outcomes	Robot Assisted Therapy
Patel et al. (2010)	Google Scholar	Pro	Quantitative	– Functional Ability Scale	– Increased functional outcomes	Wearable Technology
van den Hoogen et al. (2009)	Google Scholar	Pro	Qualitative	– Interviews	– Motivating – Socially engaging	Motion Capture
Lindqvist and Borell (2011)	Google Scholar	Pro	Qualitative	– Questionnaire	– Forces development of routines – Socially engaging	Computer-based assistive technology
Zhao et al. (2013)	Google Scholar	Pro	Quantitative	– Box and Block Test	– Motivating	Digital version of Box and Block Test
Behrendt and Schuster-Amft (2018)	PubMed	Pro	Both	– System Usability Scale (SUS) – Action Research Arm Test	– Increased functional outcomes – Assist in ADL	Digital version of Action Research Arm Test
Psychouli et al. (2018)	PubMed	Pro	Quantitative	– FMA	– Motivational – Home use	Leap Motion
Bird et al. (2016)	PubMed	Pro	Quantitative	– Modified Motor Assessment Scale – Box and Block Test	– Socially Engaging – Cost Effective	Virtual Reality Videos
Cusmano et al. (2014)	PubMed	Pro	Quantitative	– Clinical tests – FMA	– Increased functional outcomes	Robotic technology
Cordo et al. (2013)	PubMed	Pro	Quantitative	– FMA – Box and Block Test – Stroke Impact Scale	– Increased functional outcomes	Robot-Assisted feedback
Kizony et al. (2016)	PubMed	Neutral	Both	– Time – Accuracy – Questionnaire	– Increased functional outcomes	Tablet App-based hand activities
Maris at al. (2017)	PubMed	Negative	Quantitative	– Wolf Motor Function Test – Range of Motion	– Absence of functional outcomes	Robot Mediated Training (RMT)
Salbach et al. (2011)	Google Scholar	Pro	Qualitative	– Interviews	– Socially engaging	RMT
Nam et al. (2013)	Google Scholar	Pro	Quantitative	– Stroke Scale	– Cost effective	Virtual Reality

(continued)

Table 1 (continued)

Author(S), year	Google Scholar/PubMed	Pro/neutral/negative	Quantitative/qualitative/both	Assessment method(S) used	Comment(S) on main outcome	Type of technology
					– Self-management	
Alankus et al. (2010)	Google Scholar	Pro	Quantitative	– Range of Motions	– Allows coordinated motions – Home Use – Socially engaging	Virtual Reality Games
Chen et al. (2014)	Google Scholar	Pro	Both	– FMA – Box and Block Test – QUESTIONNAIRE	– Enjoyable – Increased functional outcomes	Virtual Reality Games
Chou et al. (2018)	Google	Pro	Quantitative	– Time	– Enjoyable – Increased functional outcomes	Functional Electrical Stimulator
Yin et al. (2014)	Google	Negative	Both	– FMA – Motor Activity Log – Participant feedback	– Increased functional outcomes – Not superior to control group	Virtual Reality
Durfee et al. (2009)	Google	Pro	Quantitative	– Functional Independence	– Home use – Feasible	Biofeedback Motion System
Hsiao et al. (2013)	Google	Pro	Quantitative	– Box and Block	– Increased functional outcomes	Digital Box and Block
Matamoros et al. (2009)	Google Scholar	Pro	Quantitative	– Grip Strength	– Cost effective – Accessible	Virtual Reality Games
Nasr et al. (2009)	Google Scholar	Pro	Qualitative	– Interviews	– Self-management	Wrist sensors
Chen et al. (2017)	PubMed	Pro	Quantitative	– Time	– Increased functional recovery	Infrared Camera
Au et al. (2017)	PubMed	Pro	Qualitative	– Boston Process Approach	– Future potential	Wrist sensors
Kassab et al. (2017)	PubMed	Pro	Quantitative	– Edinburgh Inventory	– Feasible – Home use – Socially engaging	functional near-infrared spectroscopy and EEG
Mace et al. (2017)	PubMed	Pro	Both	– FMA – Edinburgh Inventory – Questionnaire	– Socially engaging	Virtual Reality Therapy
Al-Dughmi et al. (2017)	PubMed	Pro	Quantitative	– Trail-making Test	– Increased functional outcomes	Off-Line Motor Learning
Quinn et al. (2018)	PubMed	Pro	Quantitative	– Index Tests – Goldman Assessment	– Feasible	Android-Based Digital Assessment
Cious et al. (2015)	PubMed	Neutral	Quantitative	– Motor Assessment Scale	– Little benefit for patient’s certain mobility levels	Virtual Reality

Table 2 Displays the included articles for VR search including assessment used and main outcome

Author(S), year	Google Scholar/PubMed	Pro/negative/neutral	Quantitative/qualitative/both	Assessment method(S) used	Comment(S) on main outcome
Laver et al. (2011)	Google Scholar	Negative	Quantitative	– FMA	– Adverse effects – Insufficient evidence about motor functions
Shin et al. (2014)	PubMed	Pro	Quantitative	– FMA – Modified Barthel Index	– Enjoyable – Implication into clinical setting Feasible – No adverse effects
Yin et al. (2014)	PubMed	Negative	Quantitative	– FMA	– Adverse effects – Implication into clinical setting not feasible
Valdés et al. (2018)	PubMed	Pro	Qualitative	– Interviews	– Accessible – Usable
Turolla et al. (2013)	Google Scholar	Pro	Quantitative	– FMA – Functional Independence Measure	– Best paired with conventional therapy – Implication into clinical setting
Da Silva Cameirão et al. (2011)	Google Scholar	Pro	Quantitative	– FMA – Chedoke Arm and Hand Activity Inventory.	– Usable – Increased motor function
Piron et al. (2009)	Google Scholar	Pro	Quantitative	– FMA – ABILHAND and the Ashworth scales	– Increased motor function – Satisfied
Cameirao et al. (2010)	Google Scholar	Pro	Both	– FMA – Box and Block Test	– Usable – Increased speed in VR group
Sin and Lee (2013)	Google Scholar	Neutral	Quantitative	– Psychometric	– Increased motor function – Motivation – Disruption and Calibration in trials
Song and Park (2015)	PubMed	Pro	Quantitative	– Beck Depression Inventory – Rehabilitation Complexity Scale	– Increased motor function – Improved mental well-being
Brunner et al. (2014)	PubMed	Pro	Quantitative	– Action Research Arm Test	– Motivating – Feasible – Implication into clinical setting
Cipresso et al. (2014)	PubMed	Pro	Quantitative	– Unilateral Spatial Neglect	– Motivating – Cognitive deficits
Kwon et al. (2012)	PubMed	Pro	Quantitative	– FMA	– Increased motor function

(continued)

Table 2 (continued)

Author(S), year	Google Scholar/PubMed	Pro/negative/neutral	Quantitative/qualitative/both	Assessment method(S) used	Comment(S) on main outcome
				– Manual Function Test	
Connelly et al. (2010)	Google Scholar	Neutral	Quantitative	– FMA – Box and Blocks test	– Feasible – Increased motor function in only some subjects
Lewis et al. (2011)	Google Scholar	Pro	Quantitative	– FMA – Box and Block Test	– Feasible – Implication to clinical setting – Motivating
Subramanian et al. (2012)	Google Scholar	Pro	Quantitative	– FMA	– Enjoyable – Implication into clinical setting
Meldrum et al. (2011)	Google Scholar	Neutral	Qualitative	– System Usability Scale (SUS)	– Motivational – Adverse effects
Lloréns et al. (2014)	Google Scholar	Pro	Quantitative	– Brunel Balance Assessment	– Usable – Increased motor function
Frisoli et al. (2009)	PubMed	Pro	Quantitative	– Reaching task	– Increased motor function – Usable
Kiper et al. (2014)	PubMed	Neutral	Quantitative	– FMA – Functional Independence Measure scale – kinematics parameters	– Feasible – Increased motor function – Not superior to conventional therapy
Sucar et al. (2014)	PubMed	Neutral	Quantitative	– Partially Observable Markov Decision Process	– Neutral approach to implication into clinical setting – Socially engaging
Paquin et al. (2016)	PubMed	Pro	Qualitative	– Interviews	– Recommend to others – Interactive
Lee et al. (2016)	PubMed	Pro	Both	– FMA – SUS	– Socially engaging – Increased motor function – Implication into clinical setting
Tsoupikova et al. (2013)	PubMed	Pro	Quantitative	– FMA	– Increased motor function
Kang et al. (2012)	PubMed	Pro	Quantitative	– Motor Evoked Potentials	– Socially engaging – Increased motor function
In et al. (2016)	PubMed	Pro	Quantitative	– Berg Balance Scale – Function Reaching Test	– Increased motor function

3.4 Data on Robotics

Table 1 highlighted the incorporation of DT including robotic mediated therapies (RMT). Robotic technology incorporates disciplines of engineering and science constructing a computer designed machine with control, feedback and information processing abilities.

Following VR, RMT was a preeminent intervention in Table 1. A search was conducted on the application of robotics in stroke rehabilitation using the search term "Stroke Rehabilitation and Robotics". Of a possible 35,500 Google Scholar and 1167 PubMed articles the first 30 were chosen from each search engine respectively. Of the 60 articles selected, 28 were excluded; 32 included. The main reason for exclusion was the prevalence of review (n = 15) articles and outdated articles (n = 5). Duplicates (n = 4), articles focused on lower limb (n = 3) and literature not focused on stroke rehabilitation (n = 1) were also removed. From the 32 included articles 23 were pro; 4 negative; 5 neutral for the use of robotics using mostly quantitative measures (n = 27). Secondly, studies employed qualitative methods (n = 4) or both quantitative and qualitative (n = 1). Table 3 shows the range of emerging devices and research across countries.

Certain key themes were recognized and discussed across robotic devices. The comparison between robotics and CT was discussed in 9 of the 32 included studies with 6 studies believing robotics should be used alongside CT; 2 studies finding there was no benefit of robotics compared to CT and only 1 study outlining that robotic devices were better than CT. Another theme discussed in 6 of the 32 included articles was the economic sustainability of devices. Five studies concluded robotics was a cost-effective method with 1 study disputing this with no economical difference found compared to CT.

Also, Table 3 displays the extensive array of robotics developed across continents. Development of devices spanned across 14 different countries with main presence of advancements emerging from USA (n = 8) and Italy (n = 6).

3.5 Data on Leap Motion

Another contemporary intervention developed in 2008, is Leap Motion (LM) which combines virtual system technology and physical experiences from the upper limb as input but requires no controller (Richardson et al. 2013).

A systematic review of LM in stroke rehabilitation was carried out using the PRIMA approach. Although undesirable in comparison to our target number of 30, of a potential 6 PubMed articles, all were included. As previously defined, of a potential 56,000 Google Scholar articles the first 30 were chosen. Thirteen articles did not meet the outlined criteria and thus 23 articles of an overall 36 articles remained. The main reason for exclusion in this topic was articles not focusing on other diseases and not exclusively stroke (n = 6). Review articles (n = 3), duplicates (n = 3) and outdated literature (n = 1) were also removed. Of included 36 articles, 14 were pro; 9 neutral and no included studies were negative for use of LM in stroke rehabilitation therapy. These findings were backed by quantitative (n = 7), qualitative (n = 10) and both (n = 6) statistical methods. Table 4 presents findings of the included articles on LM.

The overall results for LM displayed only neutral or pro findings with no reported negative aspects on the technology in rehabilitation training. This may be due to the apparent increase in recovery abilities in the upper limb particularly the hand as displaying in Table 4. One apparent theme was the accessibility of LM. Ten of the 23 included articles discussed the potential of using LM in a home setting. Of these 10, 9 believed the device was suitable for home-use; 1 study disputed this.

Table 3 Displays the included articles for Robotics Search including assessment used and main outcome

Author(S), year	Google Scholar/PubMed	Pro/negative/neutral	Qualitative/quantitative/both	Assessment method(S) used	Comment(S) on main outcome	Country	Type/name OF ROBOT
Ho et al. (2011)	Google Scholar	Pro	Quantitative	– FMA – Action Research Arm Test	– Improvement in limb functions	China	– Exoskeleton Hand
Chang and Kim (2013)	Google Scholar	Neutral	Quantitative	– FMA	– To be used alongside CT	Korea	– End-effector – Exoskeleton
Kan et al. (2011)	Google Scholar	Neutral	Qualitative	– Questionnaire	– Satisfied – To be used alongside CT	Canada	– Partially Observable Markov Decision Process Agent (POMP)
Masiero et al. (2014)	Google Scholar	Negative	Quantitative	– Modified Ashworth Scale – FMA – Box and Block Test	– Improvement in limb functions – Did not appear better than CT	Italy	– NeReBOt
McCABE et al. (2015)	PubMed	Pro	Quantitative	– FMA – Arm Motor Ability Test	– Improvement in limb functions – To be used alongside CT	USA	– Robotics plus Motor Learning
Stefano et al. (2014)	PubMed	Neutral	Quantitative	– FMA – Modified Ashworth Scale	– Cost Effective	Italy	– NeReBot
Mazzoleni et al. (2014)	PubMed	Pro	Quantitative	– FMA – Motor Status Scale	– Cost Effective – Satisfied	Italy	– Inmotion2 Robot
Martinez et al. (2013)	PubMed	Pro	Quantitative	– Range of Motion	– Improvement in limb functions – Safe	USA	– Wrist Gimbal
Hsieh et al. (2014)	PubMed	Negative	Quantitative	– FMA – Wolf Motor Function Test	– Did not appear better than CT	Taiwan	– Robot Assisted Therapy
Pinter et al. (2013)	PubMed	Negative	Quantitative	– Motricity Index	– No reorganisation in brain – Absence of functional gain	Austria	– Robotic-assisted finger-hand training program
Song et al. (2013)	PubMed	Pro	Quantitative	– FMA	– Improvement in limb	China	– Surface Electromyography
Novak et al. (2014)	PubMed	Neutral	Qualitative	– Intrinsic Motivation Inventory questionnaire	– Positive use of multiplayer games	Switzerland	– ARMin
Takebayashi et al. (2018)	PubMed	Neutral	Quantitative	– FMA	– To be used alongside CT	Japan	– ReoGo-J

(continued)

Table 3 (continued)

Author(S), year	Google Scholar/PubMed	Pro/negative/neutral	Qualitative/quantitative/both	Assessment method(S) used	Comment(S) on main outcome	Country	Type/name OF ROBOT
Blank et al. (2014)	Google Scholar	Pro	Quantitative	– Performance Error	– Engaging	USA	– MAHI EXO-II
Chiri et al. (2012)	Google Scholar	Pro	Quantitative	– Range of Motion	– Safe	Italy	– HANDEXOS
Lu et al. (2010)	Google Scholar	Pro	Qualitative	– Questionnaire	– Cost Effective	Canada	– N/A
Lo et al. (2010)	Google Scholar	Negative	Quantitative	– FMA – Wolf Motor Function Test	– To be used alongside CT – Not difference in Cost – Absence of gains	USA	– MIT-Manus Robotic System
Ang et al. (2009)	Google Scholar	Pro	Quantitative	– FMA	– Improvement in limb functions	Singapore	– Motor Imagery – face
Boninger et al. (2014)	PubMed	Pro	Quantitative	– FMA	– Improvement in limb functions – Socially Engaging	USA	– End effector Robots – Exoskeletal Robots
Schweighofer et al. (2012)	PubMed	Pro	Quantitative	– Wolf Motor Function Test – Motor Activity Log	– Cost Effective	USA	– Task-Orientated Robot
Freeman et al. (2009)	Google Scholar	Pro	Quantitative	– Range of Motion	– Improvement in limb functions	UK	– Functional Electrical Stimulation
Stephenson and Stephens (2018)	Google Scholar	Pro	Qualitative	– Interviews	– Socially Engaging – Individualised Care	UK	– InMotion2
Dehem et al. (2018)	Google Scholar	Pro	Quantitative	– FMA – Box and Block Test	– As effective as CT	Belgium	– Robot Assisted Therapy
Gasperini et al. (2018)	Google Scholar	Pro	Quantitative	– Motricity Index – Action Research Arm Test	– More effective than CT	Italy	– Functional Electrical Stimulation
Sale et al. (2014)	Google Scholar	Pro	Quantitative	– FMA – Modified Ashworth Scale – Motricity Index	– Implication to clinical practice	Italy	– InMotion2
Meadmore et al. (2013)	PubMed	Pro	Quantitative	– Performance Error	– Improvement in limb functions	UK	– Functional Electrical Stimulation
Kenzie et al. (2014)	PubMed	Pro	Both	– Interview – Thumb Localizing Test	– Improvement in limb functions	Canada	– KINARM
Papaleo et al. (2015)	PubMed	Pro	Quantitative	– FMA – Motor Power	– Improvement in limb functions	Spain	– InMotion2

(continued)

Table 3 (continued)

Author(S), year	Google Scholar/PubMed	Pro/negative/neutral	Qualitative/quantitative/both	Assessment method(S) used	Comment(S) on main outcome	Country	Type/name OF ROBOT
Simo et al. (2014)	PubMed	Pro	Quantitative	– FMA	– Sensitive to small hand changes	USA	– Planar Robot
Wolf et al. (2015)	PubMed	Pro	Quantitative	– Wolf Motor Function Test – FMA	– Home use – Cost- effective	USA	– Hand Mentor Pro
Kazemi et al. (2012)	PubMed	Pro	Quantitative	– Grip Strength	– Improved grip strength – Improved co-ordination	Canada	– Two Degrees of Freedom Robotic
Krebs et al. (2014)	PubMed	Pro	Quantitative	– FMA – Motor Power	– Increased motor performance	UK	– RMK2

Table 4 Displays the included articles for Leap Motion Search including assessment used and main outcome

Author(S), year	Google Scholar/ PubMed	Pro/Negative/ Neutral	Qualitative/ Quantitative/ Both	Assessment Method(S) Used	Comment(S) on Main Outcome
Iosa et al. (2012)	PubMed	Pro	Both	– Pittsburgh Rehabilitation Participation Scale – Abilhand Scale	– Home use – Recovery in hand abilities – High participation – No adverse effects
Zhang et al. (2017)	PubMed	Pro	Quantitative	– Wolf motor function test – fMRI	– No adverse effects
Yu and Chang 2018	PubMed	Pro	Quantitative	– Grip force	– No adverse effects – Recovery in hand abilities
Vanbellingen et al. (2017)	PubMed	Pro	Both	– SUS – Pittsburgh Rehabilitation Participation Scale – Nine Hole Peg Test – FMA	– No adverse effects – Home Use – Recovery in hand abilities
Placidi et al. (2018)	PubMed	Neutral	Qualitative	– Video	– Recovery in hand abilities
Khademi et al. (2014)	Google Scholar	Pro	Quantitative	– FMA – Box Blocks Test	– Recovery in hand abilities
Tung et al. (2015)	Google Scholar	Neutral	Quantitative	– Reaction time – Positional Accuracy	– Recovery in hand abilities
Smeragliuolo et al. (2016)	Google Scholar	Neutral	Quantitative	– Clinical wrist movements – FMA	– Not feasible for home use
Lupu et al. (2016)	Google Scholar	Neutral	Quantitative	– FMA	– Recovery in hand abilities – Engaging
McCartney et al. (2015)	Google Scholar	Pro	Quantitative	– Learning algorithms	– Home use – Recovery in hand abilities
Bracegirdle and Anthony (2014)	Google Scholar	Neutral	Qualitative	– Questionnaire	– Engaging – Adverse effect of arm fatigue

(continued)

Table 4 (continued)

Author(S), year	Google Scholar/ PubMed	Pro/Negative/ Neutral	Qualitative/ Quantitative/ Both	Assessment Method(S) Used	Comment(S) on Main Outcome
Oña et al. (2018)	Google Scholar	Pro	Quantitative	– FMA – Box Blocks Test	– Home use – Recovery in hand abilities
Holmes et al. (2016)	Google Scholar	Neutral	Quantitative	– Target Acquiring Exercise	– Usable – Home use – Adverse effect arm fatigue
Karashanov et al. (2016)	Google Scholar	Neutral	Quantitative	– Gaming Level	– Socially Engaging – No adverse effects – Home use
Baldominos et al. (2015)	Google Scholar	Pro	Quantitative	– Clinical tests – FMA	– Socially Engaging – No adverse effects
Scardovelli and Frère (2015)	Google Scholar	Pro	Both	– Time – Questionnaire	– Socially Engaging
Afyouni et al. (2017)	Google Scholar	Pro	Both	– Range of Motion of Wrist Joint – Questionnaire	– Socially engaging – Home use
Qamar et al. (2014)	Google Scholar	Pro	Quantitative	– Kinematic Analysis	– Recovery in hand abilities – Home use
Andaluz et al. (2016)	Google Scholar	Pro	Both	– Feedback – FMA	– Recovery in hand abilities
Gieser et al. (2015)	Google Scholar	Neutral	Qualitative	– Questionnaire	– Usable – Socially Engaging
Xiong et al. (2016)	Google Scholar	Pro	Quantitative	– FMA	– Home use – Recovery in hand abilities
Matos et al. (2014)	Google Scholar	Pro	Quantitative	– Time – Angle between arm and forearm	– Recovery in hand abilities
Robertson et al. (2013)	Google Scholar	Neutral	Quantitative	– Time	– Socially Engaging

4 Results of All Included Articles

4.1 Quantitative Analysis

As displayed in Fig. 2 of the 110 included articles quantitative analysis was predominantly undertaken (n = 76) followed by qualitative (n = 20) and 14 studies recruiting both methods. As previous, there was no remarkable difference in assessment methods used between VR, Robotics, Leap Motion or DT with majority of studies using clinical tests.

4.2 Qualitative Analysis

Qualitative analysis was undertaken in 20 of the 110 included articles. Majority of qualitative articles recruiting questionnaires for inquiry purposes, subjects and therapists were able to provide feedback on the use of technologies. The majority positively evaluated the questions of usability and expressed their satisfaction. One study utilized qualitative video analysis to examine trajectories in hand and finger orientation (Placidi et al. 2018). Other studies interviewed participants finding correlational themes aiding feedback on views towards CT and system implementation (Stephenson and Stephens 2018). The beck depression inventory was recruited by one study (Song and Park 2015) examining patient mood when undergoing DT therapy. Self-report inventories can be suggestive of depression in patients and important in clinical studies to evaluate patient well-being.

Figures 2 and 3 display the preference for quantitative measures, followed by qualitative and lastly recruitment of both measurement tools.

Displayed in Fig. 3 is the use of the outcome measurements (quantitative/qualitative or both) compared with the article attitude (pro/neutral/negative) towards technology use.

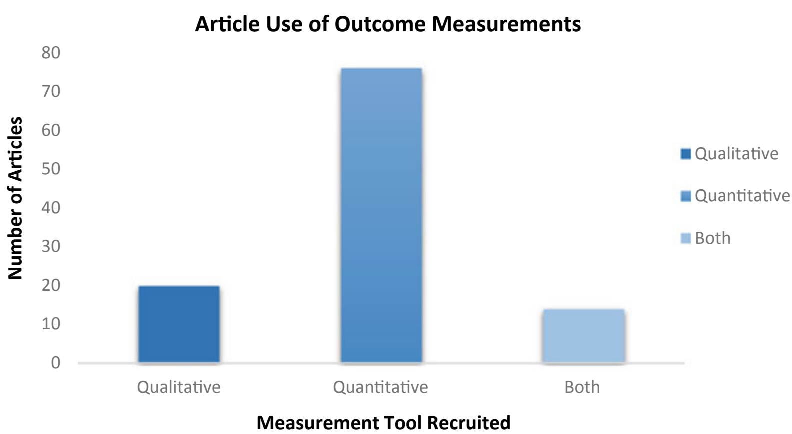
Majority of articles recruited quantitative measures regardless of article attitude. There was a substantial difference between pro articles recruiting quantitative (n = 60) compared to qualitative measures (n = 11). Despite this, the hierarchical selection of measurements remained equivalent across all attitudes.

4.3 Use of Assessment Tools

Notably, of the 110 included articles, 47 studies recruited the Fugl-Meyer Assessment (FMA). This stroke-specific index assesses motor performs and joint function across an impairment scale. This illustrates the examination of motor function and standardisation of practice offered by such scales into VR rehabilitation research. The use of a continuous use of dependable scale across randomised controlled trials may aid the acceleration of VR into a clinical setting.

Assessment methods recruited was mostly consistent across the 4 meta-analysis category reviews. However, one study from the VR pool

Fig. 2 Bar chart displaying article use of qualitative/quantitative/ both assessment methods



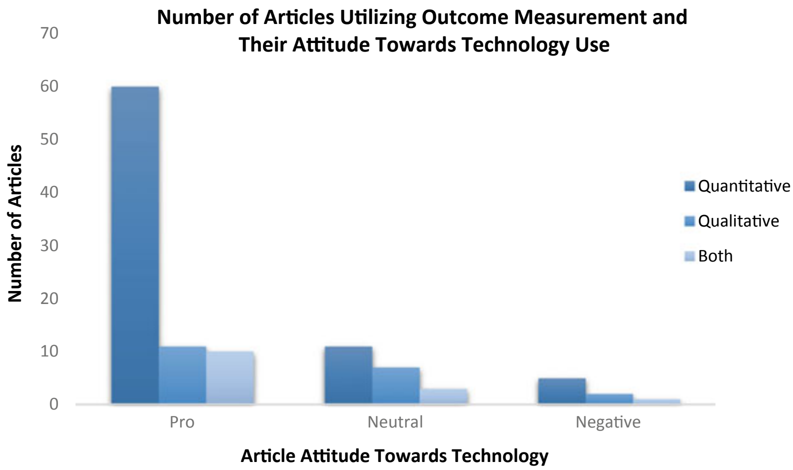


Fig. 3 Histogram displaying the number of articles recruiting outcome measure compared to the article attitude

recruited a Unilateral spatial neglect test which is a stroke specific measurement tool observing one-sided neglect through a reaching tasks. This assessment tool is feasibly more comprehensive for VR use than alternative DT due to the virtual environment and ability to move both limbs without restriction.

Further to this, clinical tests such as the box and block test, modified ashworth scale and wolf motor function test were recruited numerous times. Each of these functional measurement tests quantitatively assess the motor ability of the upper extremity. The use of reliable and transparent assessment index's enhanced the study findings efficacy.

4.4 Pro/Neutral/Negative Attitudes

Succeeding a thorough review of the literature surrounding the four categories of (1) DT, (2) Virtual Reality, (3) Robotics and (4) Leap Motion the prevailing consensus is generally a positive attitude towards introducing DT as a new stroke rehabilitation technique. Of the included 110 articles, 81 were pro; 8 negative and 21 neutral. This is reflected in Fig. 4.

4.5 Correlational Themes

As projected in Fig. 4 the mass proportion of studies deemed pro for use of DT reflected 81 of 110 articles reviewed across all 4 categories. This represented as a percentage translated into 74% pro; 19% neutral and 7% negative. Correlational propositions across these studies, appeared encouraging for use of DT in stroke rehabilitation. Of the 110 studies articles whose discussion focused on functional abilities, majority of studies (n = 53) had outcomes of improved functional ability of paretic limb. Contrarily, 4 articles disputed the absence of functional gain in their study with a further 3 studies finding gains but not superior to control CT group.

From the meta-analysis several studies discussed the economic impact, 7 studies deemed pro believed in the suitability of devices with only 1 study discussing the minimal economic impact of DT. Across the 4 categories, perceived social gain and engagement was another significant consideration with 19 articles positively discussing social interactions of DT use. No articles noted negative social aspects across the category reviews. The main discussion at issue was the benefit of utilising DT over CT. Studies

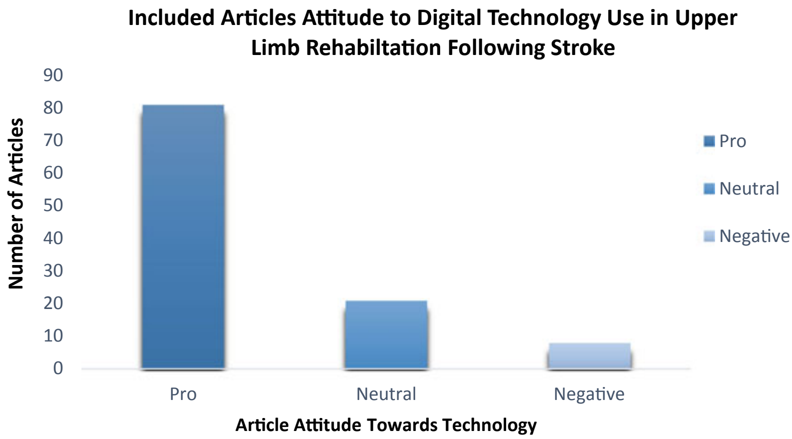


Fig. 4 Bar graph showing attitude of included articles whether pro/negative/neutral

accounting for this in their findings were mainly neutral (n = 8) with many recommending a combined intervention approach. Five studies found DT to have greater outcomes than their CT control group with dissimilar findings in negatively deemed studies (n = 4) believing DT was of lesser benefit than CT.

Generally, the favouring approach of DT is encouraging for future research and integration into clinical settings with an expectation in high levels of social interaction, functional gain and economic sustainability from DT. Whilst the results of the review are encouraging the articles deemed negative (n = 8) about the implementation of DT for stroke recovery purposes raised concerns about the adverse effects, the disadvantages of DT compared to CT and if functional outcomes were sustainable.

5 Discussion

The main objective of this study was to investigate the use of DT in the management of the upper limb following stroke. The recruitment of a broad search strategy has aided an overarching review of heterogeneous articles facilitating in-depth knowledge of intervention factors such as functional gains, economic impact and accessibility of devices. Based on explicit search criteria using the PRISMA method 110 articles (retrieved from PubMed and Google Scholar) discussed themes majorly positive for use of DT in stroke rehabilitation.

Analysis based on these 110 randomised articles have been reported alongside the use of quantitative or qualitative assessment tools and main findings of each study based on the themes from discussion and concluding sections from each article.

Whilst the extensive range of outcome measurements utilised by the articles makes a direct comparison impractical this further encourages recognition of the scope of devices and assessment tools available. This meta-analysis of 4 categories; (1) DT, (2) VR, (3) Robotics and (4) LM identified several potential benefits of utilizing DT through identifying correlational themes. Across studies and categories increase in functional gains and motivation levels were encouraging for technology use in the future of post-stroke rehabilitation. Several topics were undoubtedly encouraging for integrating technology into a clinical setting.

5.1 Improved Functional Outcomes

Of the 110 articles examined, functional recovery of the upper limb appeared to increase across most studies with the type of recovery varying depending on task and DT used. Training utilizing robotics resulted in improved movement coordination and strength in the paretic upper limb (Maris et al. 2017) and improved hand dexterity by isolating finger movements (Cordo et al. 2013; Kizony et al. 2016). VR training led to a further variation of functional gains depending upon the motion facilitated programme used. One study exploited bilateral muscle movements of the limb when submerged in a paddle board VR environment (Lee et al. 2016). The exercise led to increased trunk stability and eventual integration of the paretic limb. Therefore, over-use of the unaffected limb decreased. Another study highlighted the improvement on hand-eye coordination when utilizing VR Wii-games consoles (Paquin et al. 2016). Thus, cognitive-motor rehabilitation appears to benefit from VR therapy. Significant difference in speed of motor movements and hand function of paretic limb compared to the control group was also found when utilizing VR technology (Da Silva Cameirão et al. 2011; Kang et al. 2012; Lloréns et al. 2014).

LM studies also had markedly increased functional reporting due to the ability of the device to monitor all digits and hand joints. Zhang et al. (2017) study monitored neural organization through fMRI following LM trials and found elevated motor functioning from brain plasticity. Another LM study focused on training the upper limb by correcting compensatory trajectories by issuing a warning when the wrong joint was used (Afyouni et al. 2017). Additionally, fine motor movements displayed on tasks such as piano playing increased across training programs (Fu et al. 2011). LM displays a remarkable potential technology for rehabilitation of the hand following stroke. However, observed was that despite LM being able to monitor intricate digit and palmar movements one study had difficulties in executing pronation/supination movements across all subjects. Thus instability of recordings affected patient recovery compared to CT (Smeragliuolo et al. 2016). Additionally, one study highlighted concerns into perceptual differences between virtual and physical tasks. For example, grip aperture may be viewed differently across virtual and physical worlds (Yu and Chang 2018). And so, whilst DT appear to spearhead training of precise hand and upper limb movements further inquiry to specific movements such as pronation/supination and perceived grip aperture in devices recruiting virtual sequences is required before induction into a clinical setting.

However, functional gain across the 4 categories was undoubtedly present. A positive increase in such movements allowed participants to engage in ADL using approved clinical tests such as range of motion and grip strength measurements (Matamoros et al. 2009; Maris et al. 2017; Alankus et al. 2010). Use of varied clinical tests across studies can evaluate efficiently how much the arm has recovered explicitly to the DT used. Results such as following goal-directed tasks e.g. catching a cup in a virtual environment by wrist flexion (Kang et al. 2012) demonstrate activation in the motor cortex leading to a general increase in functional ability of the limb. These exercises integrate activation of proprioceptors in the brain and help carry out ADL such as in a pre-stroke state. DT appears to markedly influence a range of motor factors of the upper limb including speed and precision and therefore its use as a rehabilitation tool should not be overlooked.

5.2 Enjoyment and Social Aspects

Meta-analysis of all 4 categories demonstrated the beneficial social and enjoyment factors of rehabilitation training using technology. Across several articles, positively expressed enjoyment and motivation of patients was apparent. When asked, patients responded to the statement “I enjoyed the task” with the top percentile strongly agreeing with the statement (Cameirao et al. 2010). It is believed achieving a game score alongside visual feedback helped aid patient motivation (Subramanian et al. 2012). Consistent with previously discussed mental health findings enhanced task interest led to increased adherence and faster recovery times (Paquin et al. 2016). Additionally, when compared to CT, higher levels of motivation and enjoyment were found (Meldrum et al. 2011). It was also found, social support is crucial to participant motivation and reintegration into social environments following stroke (van den Hoogen et al. 2009). Additionally, multiplayer games are of greater benefit as can provide extra motivation, competition and collaboration. Upon consultation with physiotherapists a strong preference for multiplayer games was evident (Mace et al. 2017). Multiplayer games also have the potential to increase social bonds between players further assimilating patients into their home environments (Alankus et al. 2010). The believed benefit of combining social factors is increased security, self-management and responsibility for participants (Lindqvist and Borell 2011). Recruitment of human factors such as social influences encouraged participant motivation thus facilitating improved motor performance. Thus, stimulating environments created by technologies such as VR offer beneficial post-stroke recovery aspects aiding mental well-being and motivation levels. This in turn encourages facilitation of therapy programmes through goal-driven gaming behaviour and high adherence levels from stroke patients. Further motivation could be driven by availability of recovery tools to patients.

5.3 Accessibility and Introduction to a Home Setting

Discussed across categories was the potential of utilizing devices in a home-setting. The accessibility of devices is driven from the portability and progressive integration of commercially affordable devices. For example, InMotion2 (IM2) robotics system has the potential to be exploited for home-use as is commercially affordable (Mazzoleni et al. 2014). IM2 allows shoulder abduction/adduction and elbow flexion/extension movements alongside visual feedback thus an indispensable and affordable tool to be incorporated into patient home environments. Practicability and safety was discussed when considering such devices for home-use. A device known as HANDEXOS originating from Italy demonstrates positive safety effects of robots due to the light-weight and non-invasive training (Chiri et al. 2012). Therefore, usability of participants with paretic limbs is practical.

Upon analysis, a potential asset of the LM category was the accessibility to diversified patient groups. Several studies investigated LM and the older population and found LM can be utilized by patients confined to a wheelchair, or unable to handle controllers (Iosa et al. 2012). One questionnaire asked participants if they felt they were too old for using this type of training. Of a subject group of 64, only 3 responded "yes" (Vanbellingen et al. 2017). LM appears to be an encouraging training tool amongst the older generation. However, potential considerations demonstrated arm fatigue as a potential constraint of using LM which may be problematic in older participants with limited strength (Holmes et al. 2016; Bracegirdle and Anthony 2014). Another propitious component of LM, was the potential to be utilized in a home setting. Following the trials across several studies numerous participants specifically asked to prolong their training at home (Vanbellingen et al. 2017; Khademi et al. 2014). Impending studies are aiming to develop open-source software accessible to patients at home without any sensory devices (Qamar et al. 2014). Therefore, DT represent cutting edge interventions that have promising capabilities to safely and affordably train motor movements post-stroke in a home environment. Whilst gross muscle movement devices (persistent with gait training) have been growing epidemically debut of devices such as LM may encourage an influx of research into training smaller motor movements which are unquestionably important in ADL.

5.4 Economic Impact

Economic suitability of utilizing DT training was prevalent across several studies. Thorough examinations outlining the calculated costs (including the degree of therapist supervision required and machine maintenance) found on average per patient there were savings of just above £1000 over 36-week training periods

(Lo et al. 2010; McCabe et al. 2015). The Italian developed Neuro-rehabilitation robot (NeReBot) displayed a minuscule set up time of 5 min and the ability of physiotherapists to monitor 4 robots (Stefano et al. 2014). One study urged future interventions to examine cost-effectiveness as a basis to benefit home use robots (Wolf et al. 2015; Stefano et al. 2014). Studies in the VR category also discussed cost-effectiveness of Wiimote wireless games. Exercise-based video games offer low cost alternatives and an increase in dose of therapy (Matamoros et al. 2010; Bird et al. 2016). Thus with the monumental impact of stroke we can expect more commercially available devices which will generate savings from the NHS and allow trained physiotherapists to monitor multiple patients and technology at once.

5.5 Comparison with Conventional Therapy

Another principal theme across categories and studies was the association with CT. When compared to CT, effectiveness of devices, associated intensity level of treatment programmes aiding accelerating motor function in shorter time periods (Sale et al. 2014). When questioned therapists could envision robotic devices into clinical settings as an alternative to CT (Kan et al. 2011). However, devices such as end-effector robots (e.g. IM2) and the NeReBot appear to have no statistical difference over CT (Masiero et al. 2014; Ho et al. 2011). Hence, robotic devices may not be able to replace CT completely but complement its use in post-stroke recovery.

Combination therapy utilizes DT and CT as an effective option for clinical settings. Patients gain positive effects of CT (such as accurate monitoring and feedback) and robotic training (such as device engagement and motivation) (Takebayashi et al. 2018). One study found that whilst VR offered no statistical advantage, VR training could be used in the first month post-stroke to alleviate typical muscle ache and immobility then late recruit CT in patients with physical improvement (Yin et al. 2014). A study recruiting LM devices proposed that due to the inability of LM to monitor supination/pronation movements the device could not be recommended for wrists movement thus combination therapy may be more suitable depending on the patient condition (Smeragliuolo et al. 2016). The inability of the device to differentiate between volar and palmar surfaces of opposing limbs led to invalidity of recordings. Thus precise joint angles could not be monitored for this range of motion. Hence, feasible technologies such as robotic therapy could be implemented into clinical settings with best practice as combination therapy alongside CT. Incorporation of such interventions could alleviate NHS pressures of currently limited resources to treat paretic limbs of post-stroke survivors without losing efficacy. The evidence base for DT in stroke recovery which is rapidly growing and supportive of a movement towards combination therapy of devices and conventional physiotherapy collectively.

5.6 Introduction to Clinical Setting

Whilst the previously discussed literature is suggestive of positive factors displayed by DT overall, the introduction into a clinical setting is still questionable. Whilst an attempt was made by several studies to adopt clinical considerations such as effective communication, system usability and training programmes for therapists and participants alike (Valdés et al. 2018) several studies whose attitude remained negative against the use of DT for stroke rehabilitation purposes believed there was insufficient evidence to reach conclusions compared to conventional therapy. Additionally, such studies were sceptical on whether recovery effects were sustained over long periods (Laver et al. 2011; Yin et al. 2014). Therefore, the feasibility of DT use for long term purposes has been questioned. Whilst such concerns remain ambiguous predominant findings are supportive of introducing DT into a clinical setting.

5.7 Adverse Effects

Articles whose attitude was regarded as negative discussed adverse effects and found whilst fatigue is more evident in robot-assisted therapies serious effects such as hospitalization, swelling, psychiatric disorders and also death are greater in CT (Lo et al. 2010). DT incorporating visual stimuli, such as VR, studies displayed potential adverse effects of nausea (Meldrum et al. 2011) and headaches (Yin et al. 2014). The latterly coined term "cyber sickness" describes further symptoms arising from technology use such as dizziness, eye-strain, disorientation and fatigue (Kolansinki 1995). Current disputes over DT and cyber-sickness question the physiology of the symptoms and if this effects on performance levels. One theory believes cyber-sickness is due to a disturbance in the equilibrium of the visual, vestibular and proprioceptive systems (Kolasinki 1995). Contradictory to our overall positive findings on technology use, susceptibility to cyber sickness has been found to be more apparent in participants of ill-health (Whittinghill et al. 2015). Therefore, studies hypothesise that stroke patients formerly experiencing nausea and fatigue symptoms may be more vulnerable to the undesirable consequences of digital therapies. Moreover, increase of cyber sickness symptoms is caused by the incorrect use of device equipment. Issues with closeness to screens and heaviness of equipment may induce nausea and headaches as sensitivity to motion sickness is also variable in virtually created environments, likewise with reality (Groen and Bos 2008). In addition to developing technological guidelines for use in a clinical setting precautionary recommendations should be given to reduce adverse effects ensuring maximum benefits are gained from technology use. Usability of such programmes demands further systematic investigation in longitudinal clinical studies with stroke patients. The currently developing field of technological interventions should focus on the underlying cause of cyber-sickness and if this affects performance levels.

5.8 Methodological Issues

Some inherent weaknesses customary to a systematic review approach should be acknowledged. Although the comprehensive search strategy (of the PRISMA) method was recruited the target number of 30 articles, from each data-base per category, may have prohibited the inclusion of other relevant articles. Furthermore, a target number of 30 articles per category and data-base for LM was unachievable due to the lack of articles on PubMed. The initial search which took place 29th September 2018 generated a result of only 6 articles. This a lesser number of articles was recruited for LM category (36 instead of 60). The review and inclusion process of articles was accomplished by one individual. Ideally, two or more researchers would be optimal in this approach to prevent observer bias. Also, use of two search engines reduced potential publication bias, however allowing for more time other academic databases would likely have been utilised such as Education Resources Information Centre (ERIC) and OVID. Additionally, studies published after the final article selection date of 3rd November 2018 were not included. From the original search date 29th September 2018 for the category "Digital Technology and Stroke Rehabilitation" a search on Google Scholar yielded 446,000 results. On 3rd November 2018, this increased by 8,000 to 454,000. Therefore, eminently relevant articles may not have been recruited. Lastly, due to the extensive advancements of technology our study only reviewed a minor number of devices available. Future literature could potentially contribute to stroke recovery by examining other devices such as wearable technology or motion capture which are both progressively more remarkable in the field. However, demonstrated was the ability to comprehensively exploit databases for literature review purposes covering a vast amount of content in a short time period of 3 months. Rigorous reporting of articles using the PRISMA method produced a valuable overview of the use of DT as a post-stroke intervention supporting our preliminary aims.

6 Conclusions and Recommendations

To conclude, the results of this systematic review confirm that the range of DT discussed provide original and efficient management in upper limb rehabilitation following stroke. DT interventions are engaging, motivational and an effective method for increasing numerous functional gains in patients with paretic upper limbs following stroke. The main findings and outcomes appear to be in favour of the movement towards integrating technology into a clinical setting with proposed initial preference for combination therapy alongside CT. Despite concerns over adverse effects and sustainability the included articles overall consensus in this review was pro due to positive aspects such as collaborative gameplay facilitating motivation and increased motor learning offered by devices. This review uniquely evaluates DT use in stroke rehabilitation including considerations of the economic impact, effects on mental well-being and accessibility of devices.

This review could facilitate crucial decision making of healthcare commissioners by drawing conclusions on the current attitudes of incorporating technology into rehabilitation settings. Recommendations of simultaneously applying device use alongside conventional therapy seems the choice proposal for the future of stroke recovery of the paretic upper limb. Developing applications should seek to investigate sustainability and best practice guidelines, considering mental well-being and susceptibility to cybersickness, for optimal DT use prior to moving towards clinical integration.

The rapidly evolving field of technology in healthcare is revolutionary and extremely beneficial for rehabilitation of patient's post-stroke. A movement towards integrating DT into stroke rehabilitation programs seems inevitable.

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The Use of Social Media in Anatomical and Health Professional Education: A Systematic Review

William Pollock and Paul M. Rea

Abstract

Social media is used by many students at universities, with sites such as Facebook, Twitter and YouTube being the most popular. Initially these social networking sites were mainly used for recreational purposes, but they have been increasingly used in an educational setting. Educators in the anatomical sciences and health professions have utilised many forms of technology to supplement and enhance a student's learning. However, the true effectiveness of using social media in anatomical and health professions education has not been fully explored. It has been hypothesised that social media in anatomical sciences and health professional education could enhance learner engagement, raise morale, relieve anxieties and improve communication. However, the evidence is limited. Therefore, the purpose of this study is to undertake a comprehensive literature review to examine the effectiveness, or otherwise, of these tools when implemented. We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) method for reviewing the literature. By using specific keywords and using Google Scholar, PubMed, ERIC and OVID, we performed an extensive literature search to examine the use of social media in anatomical sciences and health professional education. A total of 155 studies were identified in this systematic review, with 99 studies investigating a variety of social networking sites being included. Overall, the evidence is supportive, with 79.8% of the studies supporting the use social media in education. Furthermore, when the use of social media in the anatomical sciences and health professional was investigated, the majority of studies advocated for its implementation. Despite this, there are some factors that limit the significance of these results, and the amount of evidence was indeed limited. Additional research must be carried out if social media is to influence modern pedagogical practices, with more focus on how the intervention affects academic achievement.

Keywords

Anatomy · Education · Social media · Health professions education · Technology

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1 Introduction

Social media is used by a substantial number of students and faculty members at university, with sites such as Facebook, Twitter, Instagram and Youtube being among the most popular (Moran et al. 2011; El Bialy and Jalali 2015). In 2015, Lenhart et al. reported 92% of teens used a social networking site, with 24% said to be online 'almost constantly'. In 2018, Anderson and Jiang reported 45% of teens were now online 'almost constantly'. This demonstrates how social media use is not only ubiquitous, but it is becoming a significant part of a young person's daily life. Initially, these social networking sites were merely utilised for recreational purposes and connecting with friends and family. However, as these sites have updated and evolved, so have their capabilities.

Social networking sites allow people to connect and share information in a variety of ways. Instagram and Youtube predominantly focus on sharing visual content such as videos and pictures, with your friends or a global audience. Facebook facilitates friends or groups to share personal information, photos, events, status updates and has an instant messaging platform. Twitter is a site which allows users to posts 240 character tweets, which can include text, photos and videos. Through all of these sites, you can receive feedback from your posts or give feedback to others, which can include likes, dislikes, messages and many more features. This results in an interface that encourages flexible interaction with other users on these sites and allows the distribution of information in a variety of formats. As a result of these features, social media has been shown to have a wide range of practical applications, not just recreation (Sutton et al. 2008; Hays et al. 2013).

Technology has advanced exponentially within recent years and educational institutions have repeatedly sought to capitalise on this. Anatomical sciences and health professional educators are at the forefront of finding ways to utilise technology for education (Vozenilek et al. 2004; Scalese et al. 2008; Anderson et al. 2013; McMenamin et al. 2014). The use of mobile devices has been investigated in anatomical sciences education, either as a wireless learning resource or as an audience response system in lectures (Trelease 2008; Alexander et al. 2009). The development of new educational applications on mobile devices to enhance the current curriculum has its advantages. However, the financial burden and the hassle for students to install these applications raises some issues. We know most students use social networking sites frequently, should we not utilise these pre-existing platforms instead?

Social media and its role within educational institutions has recently been a recent subject of discussion within the academic community. In terms of attitudes towards social media in education, students are certainly open to the idea, with some already using social media informally for this purpose (Madge et al. 2009; Roblyer et al. 2010). However, socialising with friends seems to remain the dominant reason for using social media for most students (Madge et al. 2009). Faculty members have been shown to be reluctant to use social media in the classroom (Ajjan and Hartshorne 2008; Manca and Ranieri 2016). This could be due to the difference in age within the faculty, with younger members being more likely to use social media than older members of the faculty (Moran et al. 2011). However, the conflicting evidence surrounding the use of social media in education could also be responsible. When Twitter and Facebook have been used to supplement educational curricula, it has displayed promising results, with student engagement and academic achievement being improved (Junco et al. 2013; Evans 2014; Anwar et al. 2017). On the other hand, the use of social media in the classroom has been regarded as a distracting influence which can impede learning (Fox and Varadarajan 2011; Wise et al. 2011). This demonstrates that the evidence for the use of social media for education in general is certainly mixed.

Medical educators are constantly looking for new ways to offer educational content through innovative means. Through this ambition, social media has displayed qualities that indicate it could be a useful supplementary learning tool for medical undergraduates and postgraduates. The educational potential of Twitter has been investigated, with students finding the information posted to the site to be useful and identifying the interface as easy to use (Bahner et al. 2012). Bahner et al. (2012) then point out the benefits of using 'Push Technology' within education, which is technology that allows people subscribed to an account to receive notifications whenever content is posted. This can help facilitate the distribution of interesting educational content which students prefer such as quizzes, which could lead to increased retention of information (El Bialy and Jalali 2015; Webb et al. 2015).

YouTube is very popular among medical students, with educational videos on the site attaining a significant audience worldwide (Ramos-Rincón et al. 2017; Tackett et al. 2018). Medical students have been shown to use YouTube to study practical procedures and examinations, which postgraduates confirm to be a useful educational adjunct (Ramos-Rincón et al. 2017). Furthermore, educational YouTube videos are frequently used within the surgical speciality of medicine, with 90% of students and faculty members reporting the use of such videos for surgical preparation (Rapp et al. 2016). As demonstrated, the medical community either currently use, or has expressed an interest in using social media for education.

The potential benefits of social media in an educational setting has not just interested the medical community, but the whole community of health professionals. Within the field of Dentistry, when various types of social media have been used as an educational adjunct, it was shown to promote discussion between peers and improve access to learning materials (Mukhopadhyay et al. 2014; Rung et al. 2014; Alshiekhly et al. 2015). Nursing students also expressed positive attitudes for the use of Twitter and Facebook, finding they raised awareness of nursing issues, enhanced self-efficacy in their learning and were generally enjoyable to use. (Tower et al. 2014; Stephens and Gunther 2015; Price et al. 2018).

Other health profession curricula have achieved a positive response from the studied population after they utilised social media as supplementary educational material. This includes undergraduate health professionals such as; Pharmacists, Ultrasonographers, Occupational Therapists and Radiologists (Clauson et al. 2013; McAlister 2014; Hamilton et al. 2016; Hempel et al. 2016; Zanon et al. 2018). This demonstrates how educators and students in a variety of health professions are interested in enhancing the curricula through the use of social media.

As mentioned previously, educators within the anatomical sciences have endeavoured to find out if recent advancements in technology can have applications within education. The goal being to find innovative ways to engage students, which would hopefully result in improved academic performance. Therefore, as other health professions have examined the use of social media to aid education, so has the anatomical sciences.

The use of an anatomical Twitter account or hashtag to facilitate the distribution of information and enable interaction with other peers and faculty members has been studied. These were used frequently and valued highly by the students, as they were felt to relieve anxieties, raise morale and aid engagement with anatomy (Hennessy et al. 2016). Additionally, the Twitter feeds were felt to be a good educational resource and students wished to continue following these feeds after the study had concluded (Lee and Gould 2014). However, despite the high frequency of use and positive reactions to the intervention, this did not correlate to significantly better examination scores (Lee and Gould 2014; Hennessy et al. 2016).

Facebook can be utilised by educators within the anatomical sciences to create Facebook groups and pages to try and engage with students. Anatomy students were generally positive towards these Facebook groups and pages, with posts that involve self-assessment being the most popular (El Bialy et al. 2014). Furthermore, the people who engaged with the Facebook anatomy pages the most were shown to experience more academic success (Jaffar and Eladl 2016).

The types of social media investigated is not exclusively Twitter and Facebook, but has been expanded out to social networking sites such as YouTube and Google+. Google+ was studied by analysing the search volume data to identify the nature and timing of search patterns in relation to the anatomical syllabi (Phelan et al. 2016). This information could assist educators within anatomical sciences, highlighting what topics students struggle with and when to supply additional educational material. Another study investigated the use of a YouTube for anatomical education, where 92% of the studied population agreed it helped them learn anatomy (Jaffar 2012). This highlights the variety of social networking sites that can be used within the education of anatomical sciences.

Social media can be utilised in a variety of ways in an educational setting. However, the true effectiveness of using social media in anatomical and health professions education, has not been fully explored. The aim of this study is to undertake an extensive literature review on the use of social media in anatomical education and health professionals, to examine its effectiveness, or otherwise, within education. Through this systematic review, the potential benefits and limitations of this technology will be explored. We hypothesise that the literature will support the use of social media in an educational setting.

2 Methods

A systematic review of the literature was performed using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, between September 2018 to November 2018 (Moher et al. 2009). The search engines that were utilised were PubMed, Google Scholar, OVID and ERIC. The use of OVID was later discontinued as it rendered no studies that met the inclusion criteria for this systematic review. The use of ERIC was also discontinued, as it rendered just one study that could be included in this systematic review. The keywords that were used centered around the use of social media in anatomical sciences education and health profession education. Furthermore, this study also examined the use of social media in higher education. The term social media was defined as websites and applications that allow users to create and distribute content or engage in social networking (Boyd and Ellison 2007). This encompassed sites such as: Twitter, Facebook, Youtube, Whatsapp, Snapchat, LinkedIn, Instagram, Google+. Other social networking applications were included if they satisfied the inclusion criteria. This included studies where social networking applications had been created for the individual study, or a forum was produced which allowed information to be shared.

2.1 Search Terms

The initial search used the search terms within **Rows 1–7** in Table 1, and **Rows 1–6** in Table 2. This failed to generate a sufficient amount of literature to review. In an effort to gather more studies, the search was expanded and more keywords were used. The complete list of keywords used in Google Scholar and PubMed has been shown in Tables 1 and 2. For the database ERIC, the only keyword that rendered any studies that adhered to the inclusion criteria of this systematic review was ‘Medical education AND social media’. The number of studies investigating the use of social media in the anatomical sciences was still minimal. Therefore, a secondary search was performed by selecting studies from the citations of previously collected research. Studies were included if they adhered to the inclusion criteria.

2.2 Inclusion Criteria

To ensure studies were eligible to be included in our systematic review, the following criteria was implemented:

Table 1 Keywords searched using Google Scholar

Google Scholar keywords			
Anatomical education AND Social media	Anatomical education AND Twitter	Anatomical education AND YouTube	Anatomical education AND Facebook
Anatomical sciences education AND Social Media	Anatomical sciences education AND Twitter	Anatomical sciences education AND YouTube	Anatomical sciences education AND Facebook
Anatomical studies AND Social Media	Anatomical studies AND Twitter	Anatomical studies AND YouTube	Anatomical studies AND Facebook
Medical education AND Social Media	Medical education AND Twitter	Medical education AND YouTube	Medical education AND Facebook
Dental education AND Social Media	Medical student AND Social Media	Pharmacy education AND Social Media	Physiotherapy education AND Social Media
Radiologist education AND Social Media	Occupational therapy AND Social Media	Ultrasonography education AND Social Media	Nursing students AND Social Media
Higher education institutions AND Social Media	Tertiary education AND Social media	Education AND Social Media	Higher education AND Social Media
Anatomy Education AND Social Media	Anatomy Education AND Twitter	Anatomy Education AND YouTube	Anatomy Education AND Facebook
Anatomy AND Social Media	Anatomy AND Twitter	Anatomy AND YouTube	Anatomy AND Facebook
Anatomical sciences pedagogy AND Social Media	Anatomical sciences pedagogy AND Twitter	Anatomical sciences pedagogy AND YouTube	Anatomical sciences pedagogy AND Facebook
Clinical anatomy AND Social Media	Clinical anatomy AND Twitter	Clinical anatomy AND YouTube	Clinical anatomy AND Facebook
Anatomical sciences education AND Snapchat OR Instagram OR social networks	Anatomical sciences education AND Facebook AND Medicine	Medical education AND social media AND human anatomy	Medical school AND Twitter AND Youtube AND human anatomy
Dental students AND Social Media	Dental students AND Twitter	Dental students AND YouTube	Dental students AND Facebook
Medical student AND Twitter	Medical student AND YouTube	Medical student AND Facebook	
Dental education AND Twitter	Dental education AND YouTube	Dental education AND Facebook	
Nursing education AND Twitter	Nursing education AND YouTube	Nursing education AND Facebook	
Nursing students AND Twitter	Nursing students AND YouTube	Nursing students AND Facebook	
Pharmacy students AND Twitter	Pharmacy students AND YouTube	Pharmacy students AND Facebook	
Pharmacy education AND Twitter	Pharmacy education AND YouTube	Pharmacy education AND Facebook	
Physiotherapy education AND Twitter	Physiotherapy education AND YouTube	Physiotherapy education AND Facebook	

(continued)

Table 1 (continued)

Google Scholar keywords			
Radiologist education AND Twitter	Radiologist education AND YouTube	Radiologist education AND Facebook	
Ultrasonography education AND Twitter	Ultrasonography education AND YouTube	Ultrasonography education AND Facebook	
Occupational therapy AND Twitter	Occupational therapy AND YouTube	Occupational therapy AND Facebook	
Tertiary education AND Twitter	Tertiary education AND YouTube	Tertiary education AND Facebook	
Education AND Twitter	Education AND YouTube	Education AND Facebook	
Higher education AND Twitter	Higher education AND YouTube	Higher education AND Facebook	
Higher education institutions AND Twitter	Higher education institutions AND YouTube	Higher education institutions AND Facebook	Pedagogy AND social media
Academic engagement AND Social Media	Academic engagement AND Twitter	Academic engagement AND YouTube	Academic engagement AND Facebook

Table 2 Keywords searched using PubMed

PubMed keywords			
Anatomical education AND Social media	Anatomical education AND Twitter	Anatomical education AND YouTube	Anatomical education AND Facebook
Anatomical sciences education AND Social Media	Anatomical sciences education AND Twitter	Anatomical sciences education AND YouTube	Anatomical sciences education AND Facebook
Anatomical studies AND Social Media	Anatomical studies AND Twitter	Anatomical studies AND YouTube	Anatomical studies AND Facebook
Medical education AND Social Media	Medical education AND Twitter	Medical education AND YouTube	Medical education AND Facebook
Dental education AND Social Media	Medical student AND Social Media	Nursing Education AND Social Media	Nursing students AND Social Media
Education AND Social Media	Tertiary education AND Social media	Higher education institutions AND Social Media	Higher education AND Social Media
Anatomy Education AND Social Media	Anatomy Education AND Twitter	Anatomy Education AND YouTube	Anatomy Education AND Facebook
Anatomy AND Social Media	Anatomy AND Twitter	Anatomy AND YouTube	Anatomy AND Facebook
Anatomical sciences pedagogy AND Social Media	Anatomical sciences pedagogy AND Twitter	Anatomical sciences pedagogy AND YouTube	Anatomical sciences pedagogy AND Facebook
Clinical anatomy AND Social Media	Clinical anatomy AND Twitter	Clinical anatomy AND YouTube	Clinical anatomy AND Facebook

(continued)

Table 2 (continued)

PubMed keywords			
Anatomical sciences education AND Snapchat OR Instagram OR social networks	Anatomical sciences education AND Facebook AND Medicine	Medical education AND social media AND human anatomy	Medical school AND Twitter AND Youtube AND Human Anatomy
Dental students AND Social Media	Dental students AND Twitter	Dental students AND YouTube	Dental students AND Facebook
Medical student AND Twitter	Medical student AND YouTube	Medical student AND Facebook	
Dental education AND Twitter	Dental education AND YouTube	Dental education AND Facebook	
Nursing education AND Twitter	Nursing education AND YouTube	Nursing education AND Facebook	
Nursing students AND Twitter	Nursing students AND YouTube	Nursing students AND Facebook	
Tertiary education AND Twitter	Tertiary education AND YouTube	Tertiary education AND Facebook	
Education AND Twitter	Education AND YouTube	Education AND Facebook	
Higher education AND Twitter	Higher education AND YouTube	Higher education AND Facebook	
Higher education institutions AND Twitter	Higher education institutions AND YouTube	Higher education institutions AND Facebook	Pedagogy AND social media
Academic engagement AND Social Media	Academic engagement AND Twitter	Academic engagement AND YouTube	Academic engagement AND Facebook

1. The study would ideally be published within the last 5 years, with some exceptions for studies published within the last 10 years.
2. The paper should include a form of social media, as defined as a website or application that allows users to create and distribute content or engage in social networking.
3. The focus of the paper should be about the applicability of social media to education based upon qualitative or quantitative data.
4. The article should discuss the use of social media in the fields of anatomical sciences and health profession education, as well as education in general.
5. The studies had to be original research.

2.3 Data Extraction

2.3.1 Educational Field

From the articles identified, these were assigned to a particular field of education such as anatomical sciences, health-related subjects or education in general. The studied population involved students at both university and college when an article was investigating education in general. The studied population could involve undergraduates or postgraduates when an article was investigating the anatomical sciences or medicine. The health-related subjects included were: Medicine, Dentistry, Physiotherapy, Pharmacy, Nursing, Radiology, Occupational therapy and Ultrasonography.

Table 3 The instructions on how studies were allocated to be pro, neutral or against the use of social media in the educational field they were investigating

Category	Quantitative	Qualitative
Pro	Quantifiable data expressed numerically that can be analysed using mathematical and statistical methods, which supports the use of social media in the educational field	Descriptive data collected through participant observation and interviews analysed using non-statistical methods, which supports the use of social media in the educational field
Neutral	Quantifiable data expressed numerically that can be analysed using mathematical and statistical methods, which is neutral to the use of social media in the educational field	Descriptive data collected through participant observation and interviews analysed using non-statistical methods, which is neutral to the use of social media in the educational field
Against	Quantifiable data expressed numerically that can be analysed using mathematical and statistical methods, which opposes the use of social media in the educational field	Descriptive data collected through participant observation and interviews analysed using non-statistical methods, which opposes the use of social media in the educational field

2.3.2 Quantitative or Qualitative Data

The research data were identified as quantitative or qualitative. Studies were defined as quantitative if the data could be expressed numerically and was analysed using mathematical and statistical methods. Studies were defined as qualitative if the data was collected through participant observation and interviews and was analysed using non-statistical methods. This has been included in the instructional table in Table 3.

2.3.3 Type of Social Media

The type of social media that was investigated in the study would also be ascertained. The individual types of social media included were: Facebook, Twitter, Snapchat, Instagram, Youtube and Google+. If more than one type of social media was investigated or the study looked at social media in general, then it would be reported as 'Various types of social media'. Other social networking applications would also be included if they were relevant to the systematic review.

2.3.4 Supportive, Neutral or Opposed

The studies were allocated into groups depending on if they were supportive, neutral or opposed to the use of social media in the education field they were investigating. This was determined by analysing the quantitative and qualitative data that was presented by the study. Using the predetermined instructional table, the studies were classified to be pro, neutral or against the use of social media in education. This has been included in Table 3.

3 Results

Through the systematic review of the literature, a total of 155 studies were identified. From these studies, 99 studies were included in the study as they met the inclusion criteria. Of the 56 studies not included in the study; 11 did not relate to the applicability of social media to its educational field, 20 were not original research, 9 were not related to social media, 12 were opinion pieces done by authors and 4 studies would not allow full access to their article. Of the total 99 studies included in this systematic review, 86 studies (86.9%) displayed quantitative data and 13 studies (13.1%) presented qualitative data. This has been shown in Fig. 1.

Within the studies included in this systematic review, there was a variety of types of social media investigated. In terms of individual types of social media investigated, there were 29 studies that investigated the use of Twitter in education, 25 for Facebook and 16 for YouTube. There was only 1

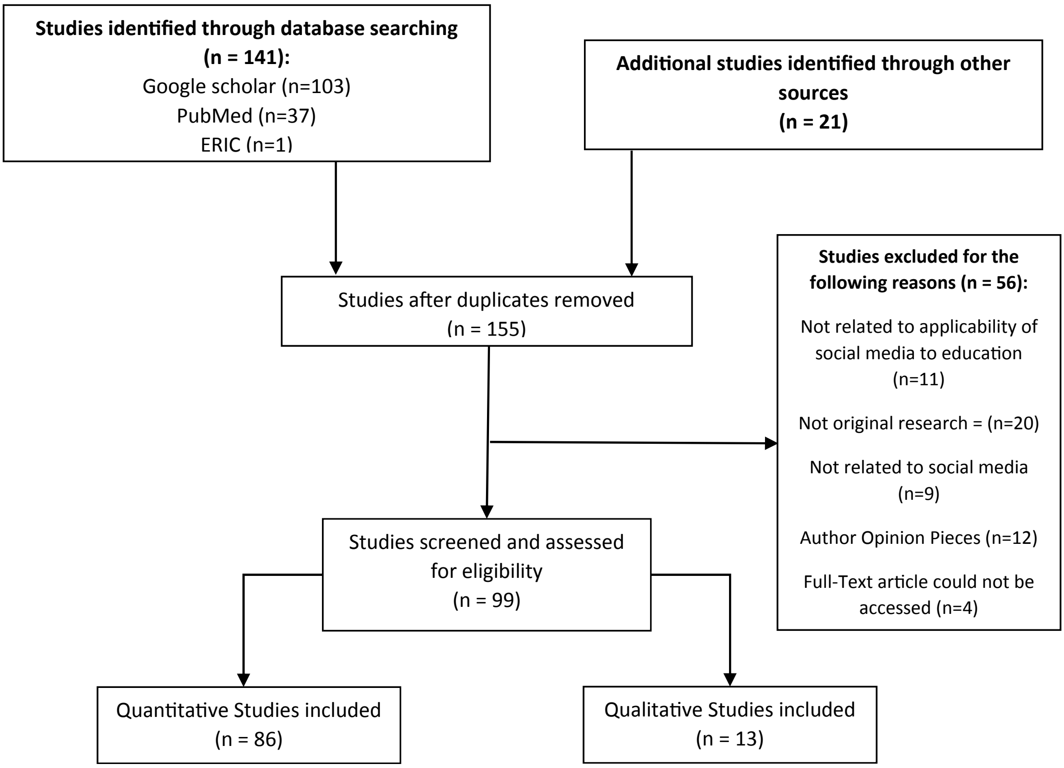

Fig. 1 PRISMA workflow diagram displaying how studies were selected

study that explored the use of Google+ in education and none of the studies investigated Snapchat or Instagram individually. A considerable portion of the studies (26 in total) investigated a multitude of social networking sites. These studies would compare both the applicability or effectiveness of different types of social networks when used for educational purposes. There were 2 other studies which included social networking applications that were specifically made for the study. The types of social networking sites investigated has been displayed in Fig. 2.

From the included 99 studies, 79 studies supported the use of social media in their educational field, 7 were neutral, and 13 were opposed. Within the research that was considered to support the use of social media in education, 69 studies were quantitative and 10 were qualitative. For the studies that were neutral to the use of social media for educational purposes, 5 were quantitative and 2 were qualitative. In the 13 studies that were in opposition to social media being used in education, 12 were quantitative and 1 was qualitative. This is summarised in Fig. 3.

3.1 Higher Education and Social Media

As part of the systematic review, 29 studies were collected that investigated the use of social media in education in general were collated. From the initial 29 studies, 6 were excluded as they did not satisfy the inclusion criteria. Of the remaining 23 studies, 15 supported the use of social media in education, 4 were deemed neutral, and 4 were opposed to the notion. Of the 15 studies that were in the 'Pro' category, 14 were quantitative and one was qualitative. Following this, the 4 studies in the 'Neutral' group consisted of 3 quantitative studies and 1 qualitative study. Lastly, for the 4 studies in the 'Anti' group, 4 of them were

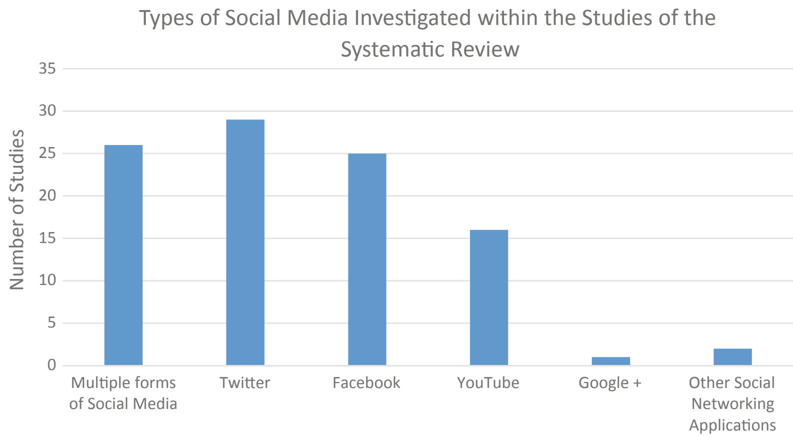

Fig. 2 A graph illustrating the number of studies that investigated different types of social media

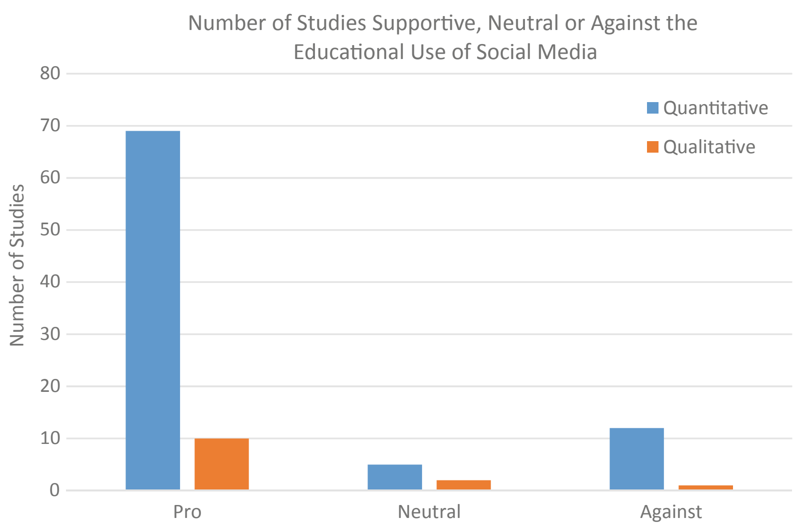

Fig. 3 A graph illustrating the number of studies that are supporting, being neutral, or opposing the use of social media in education. The studies have then been split into groups depending if they presented quantitative or qualitative data

quantitative and none were qualitative. This has been summarised in Fig. 4.

3.2 Health Professional Education and Social Media

There was a significant number of studies investigating the use of social media in the education of health professionals. Initially 89 studies were retrieved, with 32 later being excluded as they did not meet the inclusion criteria. The remaining 57 studies made up 57.6% of the total studies included in this systematic review. There was a variety of health professionals included in the selected studies, such as; 33 in medicine (with 3 in the surgical speciality), 9 in nursing, 4 in dentistry, 4 in pharmacy, 2 in radiology, 1 in occupational therapy, 1 in ultrasonography and 3 that covered a multitude of health professions From these 57 studies, 47 concluded that social media should be used in a health professionals education, 3 were neutral and 7 were against this conclusion. Within the 47 studies included in the

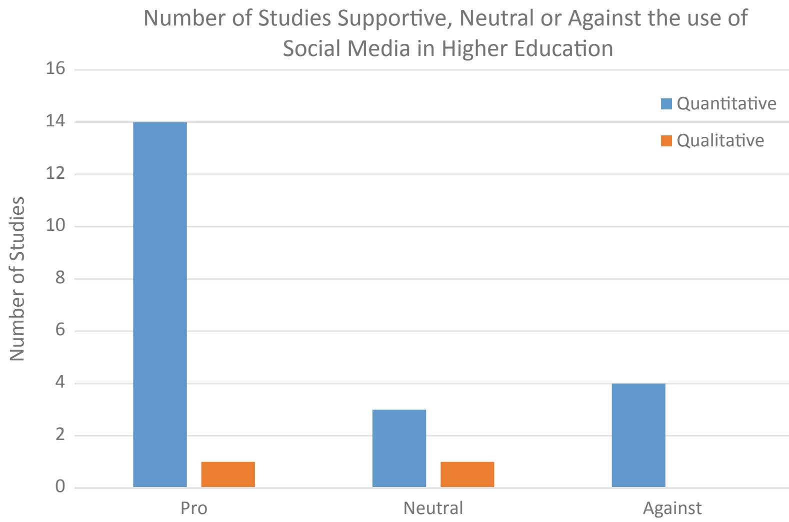

Fig. 4 A graph illustrating the number of studies which supported, were neutral towards, or opposed the use of social media in higher education

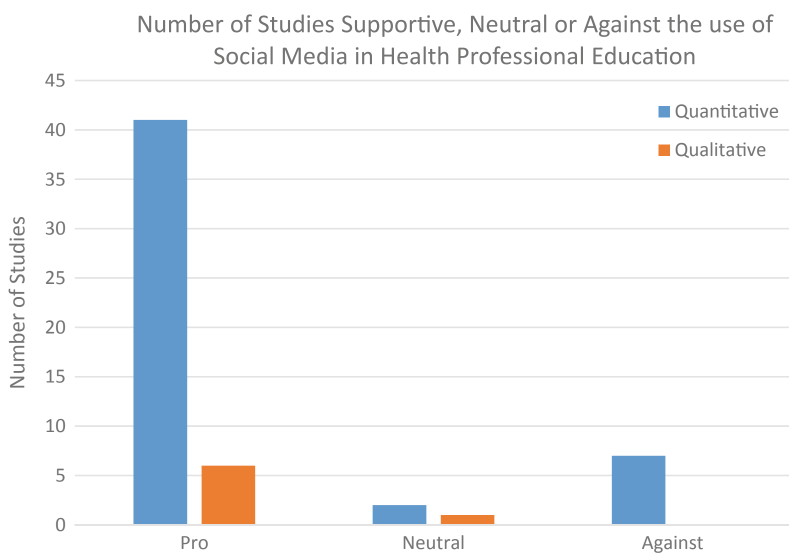

Fig. 5 A graph illustrating the number of studies which supported, were neutral towards, or opposed the use of social media in health professional education

'Pro' group, 41 were quantitative and 6 were qualitative. In the 'Neutral' group which included 3 studies, 2 were quantitative and 1 was qualitative. For the 7 studies that were against the use of social media in health professional education, 7 were quantitative and none of them were qualitative. This has been summarised in Fig. 5.

3.3 Anatomical Sciences Education and Social Media

The number of studies that investigated the use of social media in anatomical sciences education was minimal. Despite using additional keywords and examining further literature, only 32 studies

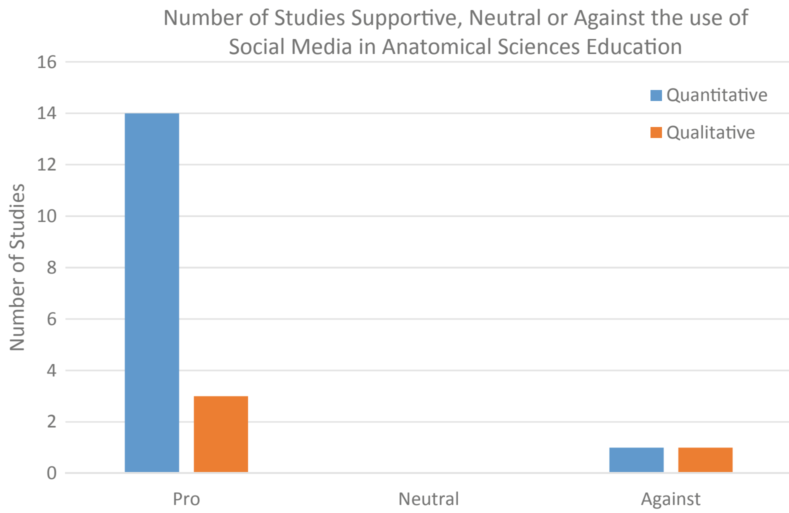

Fig. 6 A graph illustrating the number of studies which supported, were neutral towards, or opposed the use of social media in higher education

were identified. Of these 32 studies, 13 were excluded as they did not meet the inclusion criteria, leaving only 19 studies remaining. This represented just 19.2% of the studies included in the systematic review. From the 19 studies included, the majority of the studies supported the use of social media in anatomical sciences education, with 17 studies falling into the 'Pro' category. Within the 'Pro' category, 14 of the studies were quantitative and 3 studies were qualitative. Following this, only 2 studies were opposed to social media being utilised in anatomical sciences education. Of the 2 studies that were categorized into the 'Against' group, 1 was qualitative and 1 was quantitative. There were no studies that were deemed neutral. This has been summarised in Fig. 6.

4 Discussion

The aim of this study was to undertake an extensive systematic literature review of the use of social media in anatomical sciences and health professional education, to examine its effectiveness, or otherwise, when implemented. Through undertaking the largest systematic review that has incorporated both the anatomical sciences and health professions, this objective was accomplished. The majority of the current evidence surrounding the use of social media in anatomical sciences and health professional education is broadly supportive, with 79.8% of the studies advocating for its implementation. Despite this notable support, there are some factors that may limit the significance of these results.

Within this systematic review, there was 155 studies identified by the PRISMA method, with 99 studies then being included after the inclusion criteria was applied. The PRISMA method was used to promote the complete and transparent reporting of this systematic review. Furthermore, PRISMA has been utilised by multiple other systematic reviews within this field, adding greater reliability to this methodology. Within this systematic review, 57 out of the 99 studies investigated the use of social media in health professional education, which made up a significant amount of the studies included in this systematic review. This could reflect the extensive amount of evidence that exists within the health professions, when compared to the relatively minimal amount of evidence present within the anatomical sciences. However, it should be noted that multiple courses within the health professions were included in this systematic review. Therefore, the larger amount of evidence within the health professionals could be a result of this.

As mentioned previously, the majority of the current evidence supports the use of social media in an educational setting. Within the total 99 studies included in this systematic review, 79.8% of the studies supported the use of social media in education. Furthermore, the educational use of social media was supported within all of the individually investigated fields, although in varying degrees. Anatomical sciences education was shown to have the highest level of support for using social media to supplement their curricula, closely followed by health professional education. The use of social media in higher educational courses was shown to be the least supportive, which will be discussed later.

Of the total 99 included studies in this systematic review, 86 displayed quantitative data and 13 displayed qualitative data. As the majority of the studies were quantitative, this relied less on subjective opinion which could be more likely to be bias. However, the inclusion of some qualitative studies was necessary, as subjective data from interviews can also help explain the trends seen in the quantitative studies. Within the Pro and Against categories, quantitative studies made up 87.3% of the studies in the pro category, and 92.3% in the against category. This demonstrates that the proportion of quantitative studies to qualitative studies remained fairly constant. This makes it less likely that the balance between quantitative studies and qualitative studies had any impact on the level of support or opposition shown overall.

There was a variety of different social networking sites included in this systematic review. A considerable portion of the studies investigated multiple social networking sites, to broadly look at the use of social media in their educational field. Among the most popular individual social networking sites to be investigated were Twitter and Facebook, which represented 54.5% of the studies included in this systematic review. This was expected, as these social networking sites are currently used by the majority of students, with some even currently using it for informal education (El Bialy and Jalali 2015; Madge et al. 2009). The next most popular was Youtube, which accumulated a notable amount of studies pertaining to its educational use. The use of Snapchat and Instagram in education was investigated, but the evidence was extremely limited, and there were no studies that could be included in this review. This was surprising as Instagram and Snapchat are among the most popular social networking sites used by teenagers at the moment (Anderson and Jiang 2018).

4.1 Social Media in Higher Education

The use of social media in a variety of different higher educational courses was investigated. This included courses such as marketing, pharmaceutical, physiology, management and many more. The majority of the studies used educational institutions such as universities, with a smaller number of studies being carried out at colleges. Within this category, 23 studies were included that investigated the use of social media in higher educational studies. Generally, the evidence was found to be mildly supportive towards the implementation of social media in education, with 65.2% of the studies advocating its implementation. As mentioned previously, the level of support for the educational utility of social media within this category is less when compared to health professional and anatomical sciences education. Nevertheless, these studies were useful in highlighting potential issues and opportunities when implementing social media as a supplementary educational tool.

The integration of Twitter within a lecture had mixed results. On the one hand, students recognised the pedagogical and technological potential of the use of Twitter in lectures (Andrade et al. 2012). The technology allowed communication between faculty and students to take place, where questions could be asked by the students and answered by the tutor during the lecture and vice versa. This facilitated a constant dialogue within the lecture and increased interaction from the students present. However, there has been concerns at whether the use of Twitter during a lecture could be counter-intuitive, with some students stating it was distracting and prevented them from taking notes (Fox and Varadarajan 2011). Although the students may enjoy the novelty of using Twitter to interact with other peers and faculty members, its distracting influence may be too hard to overlook.

The use of Twitter as a mandatory part of a higher educational course has been investigated, with evidence indicating it can help increase student engagement and academic attainment (Junco et al. 2010; Junco et al. 2013). Junco et al. (2013) carried out two studies, 'Study 1' in which the student was mandated to use Twitter as part of their course, and 'Study 2' in which the use of Twitter was voluntary. When the use of Twitter was voluntary, there was no difference of student engagement and academic success when compared to the control group. When the use of Twitter was made mandatory, there was an increase in both student engagement and academic success. However, this study provided financial incentives to the participants, which could have influenced student engagement, and therefore academic success. Nevertheless, other systematic reviews have shown that use of Twitter within higher education can lead to increased academic attainment, with its utility as 'Push Technology' being highlighted (Tang and Hew 2017).

Finally, students using Twitter voluntarily within a higher educational course were also examined. Although perceptions towards the use of Twitter were still positive, other measured outcomes such as engagement and academic performance were greatly diminished (Lowe and Laffey 2011; Junco et al. 2013; Evans 2014). Evans (2014) demonstrated that although it helps students engage with university-associated activities such as sharing course content, it did not improve interpersonal relationships between faculty and peers, and did not impact class attendance.

The use of Facebook in higher educational courses was investigated. The attitudes towards the educational use of Facebook from faculty and students are mixed in higher educational institutions. Interestingly, students are much more likely to be open to using social media compared to faculty members (Roblyer et al. 2010). As seen in this review, this may be due to more students initially having a Facebook account, which would make them more comfortable using the platform. Additionally, a key variable affecting whether educators use social media for education is their scientific discipline. In particular, it seems teachers within the Humanities, Arts and Social Sciences are the most likely to use social media for education (Manca and Ranieri 2016). Students did seem to use Facebook for informal education, with students collaborating and sharing resources being the most influencing determinant to adopting Facebook in higher education (Sharma et al. 2016). Despite this, most of the students still predominantly used Facebook for recreation, and responded negatively to its use for formal education (Madge et al. 2009; Wise et al. 2011).

The use of a Facebook group within a higher educational course was examined, with largely positive results. Facebook groups were used to deliver educational content in a variety of ways such as MCQs, articles, links, resources and lecture notes (Cain and Policastri 2011; Anwar et al. 2017). Students generally responded positively towards these groups, with 80% feeling that the group posts enhanced their knowledge and understanding (Anwar et al. 2017). Furthermore, it was shown that students that used the Facebook group experienced better academic performance (Cain and Policastri 2011; Anwar et al. 2017). However, in the study carried out by Cain and Policastri (2011), questions which were part of the course examination was directly related to educational content posted on the Facebook group. The chance that this would affect the improvement in academic performance seen in this study is considerable.

The use of YouTube was minimally examined, with only one study pertaining to its use in higher education. Academic learning is one of the reasons that students use YouTube, with 70.5% of the studied population agreeing that they could learn a lot by watching videos, rather than reading a book (Moghavvemi et al. 2018).

However, there was limited evidence about how YouTube had been implemented in higher educational courses, and whether or not it was effective. While the evidence may be limited in higher education, the use of YouTube in education becomes much more pervasive in health professional and anatomical sciences education.

4.2 Social Media in Health Professional Education

There was substantially more studies investigating the use of social media in health professional education than any other category. Within this section, there was a variety of health professionals included, with the majority of the studies investigating the use of social media in Medicine or Nursing. Overall, the evidence was significantly supportive, with 47 out of the total 57 studies included in this category advocating its use. Despite the lower level of support seen with social media in higher educational courses, it seems that the use of social media within the health professions was considerably more effective. The reason could simply be a result of applying an educational intervention to different courses. The educational content included in the curricula of health professional courses may be more effectively conveyed using social networking sites. Nevertheless, it seems students responded more positively to the applications of social media within the health professional curricula, and educators managed to implement it with greater success.

An international survey demonstrated that 81.89% of students from a variety of health professions were already using social media in their education (O'Sullivan et al. 2017). This is supported by numerous studies within the individual courses themselves. Within medicine, a significant portion of the studied population stated they already used social media for educational purposes (Maloney et al. 2014; Avcı et al. 2015; El Bialy and Jalali 2015). These results have been replicated in studies with students in courses such as Nursing, Dentistry and Pharmacy (Rung et al. 2014; Duke et al. 2017; Hamilton et al. 2016). This demonstrates the existing usage of social networking sites for academic purposes, and this should lay the groundwork for the implementation of social media for education within these courses. However, educators within the health professions are still much less likely to use social media in the classroom (El Bialy and Jalali 2015; Duke et al. 2017). Common reasons for this reluctance could be due to the issues which are brought about by social networking sites. This can include the concern that social media can be distracting and result in wasting time, as well as the potential issues with online professionalism (Arnett et al. 2013; El Bialy and Jalali 2015; Onge and Hoehn 2015).

The use of Twitter within the health professions was investigated with varying levels of success, depending on the method of implementation. A twitter account which simply posted 3 medical facts a day proved to have little effect with students (Reames et al. 2016). Although students believed the Twitter account positively influenced their learning, it did not influence their engagement with the course or academic performance. This is unsurprising, as educational interventions need to be innovative to promote engagement and improve a students learning experience. In another study, faculty members used the platform to post educational tasks and stimulate discussion throughout the curriculum (Diug et al. 2016). This helped improve academic performance, demonstrating how increased interaction with students can result in more promising results. Although academic performance was not measured, the educators within dentistry used the Twitter platform to offer a one-hour Q&A the night before assessments, which the students appreciated (Gonzalez and Gadbury-Amyot 2016). Although the use of Twitter has shown to be a versatile and useful educational tool, it must be stressed that it has not been shown to be more effective than lectures (Webb et al. 2015). Therefore, it still remains to be considered as a supplementary tool in an educators toolkit.

Facebook was identified to be one of the most popular social networking sites used by health professionals for educational purposes (Maloney et al. 2014). The use of a Facebook group has been investigated, with content being posted from both faculty members and students. Within undergraduate medical students undergoing their preclinical years, Facebook groups made by the students themselves has been used to engage in peer-mentoring (Pinilla et al. 2015; Nicolai et al. 2017). This allowed students to pool their learning resources, discuss course content, and offer support and advice within the groups, which seemed to assist their learning. Additionally, Facebook groups designed by the educators seemed to be well received by students, with relatively high levels of engagement with the groups (Sood 2015; Alshiekhly et al. 2015). Educators posted clinical information and questions throughout the semester, while the Facebook group helped to enable interaction between faculty and peers. Lastly, the use of Facebook to create a medical teach forum was investigated, with students feeling more comfortable asking questions on the forum rather than ward rounds (Ravindran et al. 2014). This demonstrates how Facebook groups have been created by students and faculty members to promote an approachable and collaborative environment. However, although Alshiekhly et al. (2015) demonstrated students improved their skills after the use of a Facebook group, most studies do not prove that these groups improve academic performance. Other systematic reviews have drawn similar conclusions about the use of social media in Facebook (Pander et al. 2014)

Youtube presents a unique learning experience, with educational videos presenting information in a visually appealing and interesting way. Currently, YouTube channels posting videos generate significant attention worldwide. The "Osmosis" channel, a medical education focused channel, accumulated 5 million views from a variety of countries (Tackett et al. 2018). The massive attention this channel has received worldwide could be explained by its ability to explain information in distinctive and aesthetically pleasing ways. As YouTube focuses on visual learning, it is not surprising that YouTube has been increasingly used to aid the learning of practical procedures. In a survey of medical students, residents and faculty within a department of surgery, 90% of the studied populations used videos for surgical preparation (Rapp et al. 2016). Within Medicine, YouTube has been used by students to aid their understanding of practical procedures such as male urethral catheterisation and physical examinations (Nason et al. 2015). There is also content on YouTube that can educate students on how to interpret the results from medical equipment which display visual data, such as ECG's (Akgun et al. 2014). This demonstrates how the format of YouTube can be used as an audio-visual educational supplementary tool where sites such as Facebook and Twitter would be less effective. Generally, students felt that these educational YouTube videos enhanced the instructions given by educators, and was a useful educational adjunct (Buzzetto-More 2014; Nason et al. 2015). However, the quality of the YouTube videos currently on the website can be variable, which could result in students receiving inaccurate or misleading information (Akgun et al. 2014; Nason et al. 2015). This demonstrates the importance of how educators need to implement their own accurate educational content for students to enjoy, which has been attempted with relative success (McAlister 2014; Johnston et al. 2018).

As supported by previous literature, the use of social media in health professional education enhanced a student's learning experience, but the effects on academic attainment were variable (Cheston et al. 2013). However, through analysing the different forms of social media used and methods by which they were implemented, it gives room for thought for future educators within the health professions.

4.3 Social Media in Anatomical Sciences Education

The educational use of social media within the anatomical sciences was the most supportive, with 89.5% of the studies advocating its use. Although the evidence pertaining to the anatomical sciences was overwhelmingly supportive, it was also the smallest category of this systematic review, with only 19 studies being included. The limited evidence within this category does undermine the significance of the results, however there is valuable information to be gained from these studies which can help guide future educators.

In the anatomical sciences, the use of Twitter accounts and hashtags to help promote education was investigated. Through the use of a Twitter account, educators would tweet a Multiple choice question relating to course content after each lecture (Lee and Gould 2014). The use of a quiz before and after this social media based educational intervention was used to quantify the educational value, and students perceptions were surveyed. Although there was a slight improvement, there was no significant difference in academic attainment for students using this resource. Another study using a Twitter hashtag to support a students learning of neuroanatomy was carried out (Hennessy et al. 2016). This repeated the findings that there was no correlation between student examination score and their viewing frequency of the hashtag. This is in contrast to the students perceptions, as students engage with the learning resources within these studies, and find the Twitter based educational resources to be valuable to their education (Lee and Gould 2014; Hennessy et al. 2016). When it came to analysing the tweets that students favoured the most, tweets including shared learning, morale boosts or questions were among the most popular (Hennessy and Border 2015). Overall, this highlights how the educational use of social media can be popular with students in the anatomical sciences, but its effects on academic performance is seemingly less effective.

The use of Facebook pages in anatomical sciences education has been implemented in a variety of ways, however the majority of the studies used surveys to analyse success of the Facebook page. One study looked at the use of a Facebook Page to support classroom-based learning, with the use of questions, pictures, revision files videos and comments to deliver educational content (El Bialy et al. 2014). This was shown to be effective in promoting interaction between faculty and peers and establishing an inviting atmosphere. As with Twitter, studies investigating the use of Facebook pages in anatomical sciences have shown that the category of content that students enjoy the most, are self-assessments posts (El Bialy et al. 2014; Jaffar 2013). Jaffar and Eladl (2016) demonstrated that the students which engaged more with the Facebook page performed better than students who engaged minimally. However, the authors explain that the significance of this correlation is uncertain. This study could display how the use of a Facebook has helped to improve a students academic performance. On the other hand, the Facebook page may have made no difference, and the students already destined to be ‘High Performers’ may have just been more likely to use the extra learning resource.

Currently, 78% of students surveyed in one study were shown to be already using YouTube videos to source information (Barry et al. 2015). However, as shown in the health professions, the videos currently on YouTube have been shown to be of mixed quality, with students being warned to be selective (Raikos and Waidyasekara 2013). To prevent anatomical sciences students from being misled, the necessity of educators to either guide students to accurate videos or create their own content is crucial. When faculty members have done this, the majority of the student population engaged with the YouTube channel (Jaffar 2012; Strkalj et al. 2018). Furthermore, the students found the videos to be useful in preparing for practical tests and preparing for laboratory sessions (Strkalj et al. 2018). This demonstrates the effectiveness of using YouTube to help students with areas of the course which require visual instruction and explanations.

Lastly, although only one study investigated the use of Google+ in this systematic review, the use of Google Trends was fascinating. Through the use of Google trends, data was collected on searches carried out by anatomy students which were relevant to head and neck anatomical syllabi. This allowed the faculty to measure what students were searching the most, and when they were searching it within the academic year. The faculty could then identify the topics that students found difficult, and when the students were seeking educational content. Ultimately, this could be used to accurately inform the faculty on what educational resources would benefit the students and when to supply these educational resources. Although it did not measure whether or not the students benefited from this use of Google+, the utility of this information is clearly evident.

4.4 Considerations for Educators

Social media is becoming used by an increasing number of students every year for education, with these sites being currently used to produce a collaborative learning environment. This should encourage educators to embrace the use of social media in their pedagogical practices, and utilise social media in a variety of ways to distribute educational content. This systematic review has demonstrated that social media can display educational value, depending on how the technology was implemented. Faculty members should take notice of the following reasons why certain studies experienced greater success, to inform their future educational use of social media.

The construction of a collaborative and interactive learning environment was shown to be beneficial within this systematic review. This was carried out using Facebook groups and pages, Twitter accounts and hashtags, and YouTube channels. The use of social media in education predominantly utilises the learning theory of Constructivism and Connectivism. Connectivism is a theory that explains how social media has allowed people to learn and share information across the internet (Learning Theories 2015a, b). Constructivism is a learning theory that believes knowledge is subjectively constructed based upon personal experiences and hypotheses (Flynn et al. 2015; Learning Theories 2015a, b). Learners test these hypotheses through social interaction, and inevitably learn from more knowledgeable peers (Flynn et al. 2015). Social media is an example of a platform that can create these educational communities in which knowledge can be gained. With these learning theories in mind, interaction and discussion between students and faculty should be encouraged to harness the educational benefit of this technology.

Studies where the educators or students posted minimal amount of content on the platform experienced ambivalent results (Reames et al. 2016). Studies where the educators or students distributed information frequently and using a variety of formats were more successful. The use of self-assessment tasks within Facebook and Twitter proved to be the most popular and effective within the student population (El Bialy et al. 2014; Jaffar 2013). Furthermore, educators should utilise the ‘Push Technology’ demonstrated by Facebook and Twitter, as it helps notify students when you post content. This requires faculty members and students to appreciate the capabilities of these social networking sites, to unleash their true potential. Some of the studies made social media based learning resources a mandatory part of the course and experienced positive results, however the student population usually disagree with this use of social networking sites (Madge et al. 2009).

Although social media presents educators with many potential opportunities, there are significant obstacles to its use. The implementation of social media could lead to unprofessional behaviour online and breaches of confidentiality, which should not be overlooked. This is particularly relevant within the anatomical sciences and health professions, where patient information and sensitive content are frequently included in the course. However, diligent safeguards are currently utilised by educational institutions in their current pedagogical practices for these courses, so the same could be applied to social media. Before the implementation of social media in the curricula, guidelines for professional behaviour should be promoted and sensitive content should be appropriately modified.

4.5 Limitations of the Study

There were several limitations of this study that should be considered. Firstly, the measured outcomes of the studies do limit the significance of the results. Student engagement and students attitudes about the technology were the main measured outcomes. Few studies measured difference in academic performance. The studies that did measure academic performance displayed mixed results. This may ultimately prove that social media is deemed valuable and enjoyable by the student population, but it fails to demonstrate that it is effective for deeper learning. Furthermore, the use of survey results could result in the study being influenced by survey bias, and may be shown to be more supportive than the interventions actually are. Furthermore, publication bias towards articles that are supportive of the use of social media in education should also be considered.

The decision to categorise the studies as Pro, Neutral or Against was determined with guidelines, but could still be affected by a degree of subjectivity. Additionally, determining whether the study was of high quality was also subjectively assessed by the authors. Using tools such as the Likert scale to assess support or Medical Education Research Quality Instrument (MERSQI) to assess study quality, could have been used to remove this subjectivity.

The number of studies investigating the use of social media within health professional education was substantial, however the amount of literature on the use of social media in anatomical sciences education was minimal. This was representative of the current amount of literature present in the field, so more research is needed within the anatomical sciences. However, for this systematic review, the minimal amount of literature within the anatomical sciences makes the results far less significant.

5 Conclusion

This extensive systematic review has determined that the majority of the current evidence supports the use of social media in an educational setting for both anatomical sciences and health professionals. The current literature has shown this technology has been found to have many potential applications within education, which will only increase as these social networking sites are updated. This systematic review has laid the foundation for further research, while also guiding future educators on how to supplement their curricula with social media for optimal effectiveness. However, although the research is rapidly growing, it's still in its early stages. More studies should be carried out to analyse the effectiveness of social media as an educational tool, with more focus on measuring how it affects academic achievement. This will be a crucial step for social media to influence pedagogical practices within the anatomical sciences and health professions.

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