Editorial

Insights into 3D printing in medical applications

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Three-dimensional (3D) printing has been increasingly used in the medical field with reported applications showing great value in assisting clinical decision-making and improving patient care (1-10). Patient-specific 3D printed models derived from medical imaging datasets, mainly from computed tomography (CT) and magnetic resonance imaging (MRI) are shown to play an important role in pre-surgical planning and simulation of complex surgical procedures, medical education and patient-doctor communication (1-14). In this special issue of *Quantitative Imaging in Medicine and Surgery* (*QIMS*), we invite papers reporting the usefulness and clinical value of 3D printing technique in medical applications. This special issue focuses on the expanding and new applications of 3D printing technique used in research and clinical practice which aims to improve patient management and clinical outcomes.

The goal of this special issue is to bring together experts in the field of 3D printing to share recent research progress and developments in medicine and to demonstrate novel applications of 3D printed models based on patient's imaging data. The special issue has attracted 12 articles covering a wide range of 3D printing topics and corresponding medical applications. Of these 12 articles, 8 are original research studies, 3 technical notes and 1 review article. Details of these papers are summarized as follows.

Of 8 original articles, 4 focused on the usefulness of 3D printing in cardiovascular disease with 2 of them studying the optimal computed tomography pulmonary angiography (CTPA) protocols based on their developed 3D printed pulmonary artery model (15,16). Pulmonary embolism was simulated by inserting the animal blood clots in the main pulmonary arteries with CTPA scans performed on the 2nd generation of

dual-source CT scanners (15). Different kVp and pitch values were used comprising 70, 80, 100 and 120 kVp, pitch of 0.9, 2.2 and 3.2. Dose reduction up to 80% was achieved when lowering kVp from 120 to 100 or 80 without significantly affecting image quality in detecting main pulmonary embolism, while use of 70 kVp and high pitch of 3.2 was not recommended due to suboptimal image quality when CT scans were done a 128-slice dual-source CT. However, in the subsequent experiments of simulating peripheral pulmonary embolism using the same approach, authors tested the same CTPA protocols on the latest 192-slice 3rd generation dual-source CT scanner with images reconstructed using advanced modelled iterative reconstruction (ADMIRE) (16). Both qualitative and quantitative assessments of image quality showed that low-dose CTPA is achievable with use of 70 kVp and high pitch of 2.2 or 3.2, with significant dose reduction while still maintaining diagnostic images of detecting small emboli in the pulmonary arteries. These two studies represent the new research direction of using 3D printed realistic models for developing optimal CT protocols (17).

The third study investigated the effect of spatial resolution on the visualization of coronary plaques and assessment of coronary stenosis by high resolution synchrotron radiation CT (18). Coronary CT angiography has low to moderate diagnostic accuracy in determining coronary stenosis caused by heavily calcified plaques due to beam hardening and blooming artifacts. This can be overcome by use of high resolution synchrotron radiation CT because it has the ability of acquiring images with spatial resolution of more than 10 fold higher than that of modern CT scanners (19-21). In this study, authors created patient-specific 3D printed coronary models with

simulation of calcified plaques in the left coronary arteries and scanned the 3D printed models with a resolution of 0.019 mm using a range of beam energies between 30 and 50 keV. Original dataset was reconstructed to generate synchrotron radiation CT images with spatial resolution ranging from 0.095 to 0.208, 0.302 and 0.491 mm. Results showed that overestimation of coronary stenosis was seen in images reconstructed with a slice thickness of 0.491 mm, while accurate assessment of coronary plaques and lumen stenosis was observed in images reconstructed with other thin slice thicknesses (18). This study further highlights the importance of using high resolution images for more accurate assessment of calcified coronary plaques.

The 4th study by Witowski *et al.* compared 3D printing with augmented reality (AR) in planning and treating patients with chronic thromboembolic pulmonary hypertension (22). Authors in this study evaluated the usefulness and clinical value of 3D printed model and AR system in planning and guiding pulmonary interventional procedures in 2 cases with chronic pulmonary hypertension. 3D printed models were presented to the surgical team before the procedure, while AR system was available before the operation and on site with the aim of assisting physicians to deal with the cases. This technical note shows the feasibility of using 3D printed models and AR for pulmonary interventions, with AR system especially useful for navigation and guidance during interventional procedures, while 3D printed pulmonary artery models serve as a preoperative tool for surgical planning.

Of the other 4 original studies, 2 reported the quantitative assessment of model accuracy of liver and biliary anatomical structures and pathologies (23,24). 3D printed models are proved to assist pre-surgical planning and simulation of hepatobiliary disease (25,26), and these two studies offered further evidence of model accuracy in delineating anatomies. Witowski *et al.* created 15 patient-specific 3D printed liver models including normal hepatic structures and tumours (23). These 3D printed models were CT scanned with analyses compared to those from original CT images in terms of liver parenchyma and tumour volume, as well as diameter and length measurements of hepatic structures. Bland-Altman plots did not show significant bias in these 2D measurements of internal anatomy and liver volume, although tumour volume measurements from the CT scanned model images were found to be significantly undersized when compared to the original ones. Another study by Allan *et al.* presented the accuracy of 3D printed model in replicating normal bile

ducts and biliary cyst based on a patient diagnosed with congenital cyst (24). Similar to Witowski's study, authors also did CT scanning of the 3D printed model, performed quantitative measurements of anatomical landmarks, and conducted comparisons between three different stages, namely, original CT images, Standard Tessellation Language (STL) and CT images of the 3D printed model. Results showed significant differences in measurements between the STL/CT images of the 3D model and original CT images, with no significant differences in measurements between STL file and CT images of the 3D model. These two studies add valuable information to the current literature regarding model accuracy and necessity of further studies with inclusion of more cases.

In the remaining two original studies researchers reported their experiences of developing a realistic 3D printed hand phantom for surgery training purpose, and a multi-purpose breast phantom suitable for multi-modality imaging examinations (27,28). Maier and colleagues provided a very detailed approach of creating 3D printed hand model with haptic properties (27). Their design was based on using the metamaterial filled with blowy support material. 3D segmented bone and skin surfaces were obtained from a sample patient's CT and MRI images. Authors only chose the middle finger as a representative part of the hand phantom for 3D print samples which contained different ratios of support material and rubber (TangoPlus/TangoBlack Plus to simulate skin and soft tissue) and rigid (VeroClear/VeroBlack Plus to simulate bone) materials. Test prints showed that a combination of higher support material and lower rubber material resulted in 3D printed fingers being softer and more elastic which imitates soft tissue properties of human hand. This is confirmed by interviewing 11 surgeons who reported their haptic experience on the use of these 3D printed finger models. He *et al.* developed a novel 3D printed breast model which could be used for multi-modality imaging (28). Magnetic resonance images from a sample patient's breast MRI scan were post-processed and segmented to generate the breast mold with use of polyvinyl chloride (PVC)-based tissue mimicking materials for 3D printing. Embedded inserts simulating different types of breast lesions and depth resolution were designed to simulate breast tumours with different sizes. The 3D printed model with these inserts was scanned on mammography, ultrasound and MRI (using different sequences) to determine the sensitivity of lesion detection. Mammography was found to have higher sensitivity of detecting microcalcifications when compared

to ultrasound and MRI (100% *vs.* 45.6%). For visualization of cylindrical tumours, both mammography and MRI were superior to ultrasound, while visualization of hemispherical tumours was similar among these 3 imaging modalities. Results of 3D printed hand phantom can be applied to other body parts for surgical training applications, while 3D printed breast phantom can be used for quality control and optimization of breast lesion detection.

The 3 technical notes showed clinical applications of 3D printed models in different areas (29-31). Zhang *et al.* produced a patient-specific 3D printed chest phantom with tissue-equivalent materials with similar attenuation of chest wall, fat, muscle tissue and bony structures (29). CT images of the phantom were compared to patient's images with attenuation differences being 20 Hounsfield unit (HU) for fat, muscle and tumour, and 55 HU for bone. The 3D printed phantom images were also used to calculate radiation dose delivered to the organs and tumour in the chest through radiotherapy planning. The developed 3D printed chest phantom is useful for radiation dose verification. Denizet *et al.* reported their developed new technique for 3D multi-tissue printing (30). Non-contrast abdominal and pelvic CT images of 4 patients with different degrees of atherosclerotic calcification in the aorta and iliac arteries were selected to generate 3D surface hollow models. The vascular wall was printed with elastomeric and soft resin material while calcified atheroma was printed with rigid acrylonitrile butadiene styrene (ABS) resin. The models were presented to a kidney transplant surgeon for qualitative assessment of its usefulness. The surgeon was highly satisfied with models' clinical value in terms of accurate location of the calcified plaques and simulation of surgical procedures prior to renal transplantation.

The 3rd technical note is about model accuracy and clinical value of 3D printed heart models using low- and high-cost materials (31). Authors selected 2 cases of congenital heart disease (CHD) with one being simple CHD, atrial septal defect (ASD) and another one complex type, having double outlet right ventricle (DORV) and sub-aortic ventricular septal defect (VSD). Cardiac CT images were segmented to create hollow 3D surface models with both cases printed using a low-cost material, Thermoplastic polyurethane (TPU) 95A. The complex CHD case was printed using Tango Plus material, which is considered the most costly material. The cost for 3D printing of the heart models was AUD 50 and 300 for the low- and high-cost materials, respectively. Quantitative assessment of model accuracy based on contrast-enhanced CT images of 3D

printed heart models using both materials showed strong correlation with original cardiac CT images. Qualitative evaluation by 3 cardiac specialists did not show any difference in medical applications between these models.

The last article is a review paper about virtual heart museum project involving multi-institutions (32). Kiraly and colleagues reported this great project with collection of about 400 cardiac specimens with a variety of congenital heart diseases including some rare cases or unique anomalies. They conducted a pilot study on 6 specimens and scanned them with micro CT/MRI with acquisition of high resolution images. 3D virtual models were generated by image post-processing and segmentation with both external and internal structures displayed and compared to the cardiac specimens. Although 3D models were found to accurately demonstrate anatomical details and pathologies, visualization of intracavital details is still challenging, thus requiring further work to improve visualization of the internal cardiac anatomy. This ongoing project will aim to establish a comprehensive database and interactive website which can be used for different purposes, such as medical education, postgraduate training and creation of 3D printed heart models for pre-surgical planning and simulation.

In summary, these 12 papers contributed by researchers with a wealth of knowledge in different clinical and research fields provide readers with useful sources of information on the latest progress in 3D printing in medical applications. This special issue will create opportunities for clinicians and researchers to share research experience in 3D printing and explore collaboration on some research areas. It also serves as a valuable source of references to develop novel research ideas and conduct further studies in 3D printing.

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Footnote

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