Personalized treatment planning for heart interventions using tissue-mimicking 3D printing

Zhen Qian^{*,1,2} & Mani A Vannan²

¹Department of Cardiovascular Imaging, Piedmont Heart Institute, 95 Collier Road, STE 2075, Atlanta, GA 30309, USA

²Marcus Heart Valve Center, Piedmont Heart Institute, 95 Collier Road, Atlanta, GA 30309, USA

*Author for correspondence: Tel.: +1 404 605 2797; Fax: +1 404 605 0276; zhen.qian@piedmont.org

“The most important contribution of our research was the development and the validation of the novel sensor-enabled tissue-mimicking 3D printed phantom. We have demonstrated the feasibility of manufacturing such a phantom to provide not only an accurate anatomic model but also a benchtop testing platform that gives very important pathophysiologic information regarding the cardiac intervention.”

Percutaneous valve treatment has been frequently targeted for 3D printing-guided preprocedural planning. In a recent study, we have developed a novel treatment planning platform using sensor-enabled tissue-mimicking 3D printing to quantitatively predict the occurrence, severity and location of paravalvular leak after transcatheter aortic valve replacement. This platform consisted of two major components: a novel tissue-mimicking 3D printing technique and an *in vitro* imaging-based strain quantification technique. We have demonstrated the feasibility of manufacturing, such a phantom to provide not only an accurate anatomic model but also a benchtop testing platform that gives important pathophysiologic information regarding the cardiac intervention. As cardiovascular medicine is shifting more toward personalized treatment, 3D printing will play a more important role in patient-specific planning for heart procedures.

First draft submitted: 20 November 2017; Accepted for publication: 29 November 2017; Published online: 30 April 2018

3D printing has become a subject of great interest in the field of cardiovascular medicine. Empowered by the recent development in high-speed and high-resolution 3D imaging (e.g., the multidetector row CT technology for cardiovascular imaging), 3D printing has been used to replicate patient-specific cardiac anatomies for a variety of applications, such as physician training, patient communication and treatment planning [1]. Recent development in the multimaterial jetting technique using colorful materials of variant hardness and pliability is enabling the creation of lifelike anatomic phantoms, which provide both realistic visual representations and natural tactile sensations of the human organs.

Due to the rapid growth of percutaneous treatments for valvular heart disease and the inherent complexity of the catheter-based intervention on a beating heart, percutaneous valve treatment has been frequently targeted for 3D printing-guided preprocedural planning. Transcatheter aortic valve replacement (TAVR) is an established therapeutic option for symptomatic patients with severe aortic stenosis (narrowing of the aortic valve opening) who are at high risk for surgical aortic valve replacement. Despite the fast evolution of the TAVR technology, post-TAVR paravalvular leak (PVL) is still a significant drawback and this complication occurs more often than with surgical valves [2]. Moderate-to-severe PVL after TAVR has been shown to be an independent risk factor for increased short- and long-term mortality. Even a mild PVL post-TAVR has been found to be associated with a poorer outcome [3]. Given the emerging expansion of the TAVR indication to the lower risk population, prevention of post-TAVR PVL becomes even more critical.

A number of PVL risk factors have been identified, such as valve under-sizing and landing-zone calcification. However, the mechanism of the occurrence of PVL is complex and multifactorial. It is still difficult to predict

the occurrence and degree of PVL before the TAVR procedure. In a recent proof-of-concept study [4], our collaborative research team at Piedmont Heart Institute and Georgia Institute of Technology developed a novel TAVR preprocedural planning platform using 3D printing to quantitatively predict the occurrence, severity and location of post-TAVR PVL *in vitro*. Experimental results have demonstrated the superior performance of our approach over the other established predictors in predicting PVL post TAVR. Our 3D printing-based platform consisted of two major components: a novel tissue-mimicking 3D printing technique and an *in vitro* imaging-based strain quantification technique.

Compliant 3D printing materials are the cornerstone of the manufacturing of lifelike 3D printed medical phantoms. However, it is still challenging to find materials that perfectly match the mechanical properties of biologic tissues. For example, a flexible Polyjet material, the 'Tango Plus', has been widely used to approximate the cardiovascular tissues in 3D printing. However, the Tango Plus material lacks the strain-stiffening and anisotropic properties of cardiovascular tissues. In addition, the printing direction and postprocessing method significantly affect the Polyjet-printed model's mechanical behavior. Therefore, to better simulate the mechanical property of biological tissues, specifically the human arteries, our team developed a novel metamaterial 3D printing technique that incorporated two or more kinds of printing materials using specially designed structural patterns. Such structural patterns allowed us to improve the metamaterial's mechanical nonlinearity and anisotropy in the large strain range when subjected to deforming pressure [5]. The predicate behind this technology is to embed directional wavy fibers in the 3D printed model to mimic the elastic fibers (e.g., the elastin) found in the extracellular matrix of human arteries. A number of designs of the wavy fibers, such as the sinusoidal wave, the helical thread and the interlock structure, can be adopted. The shape and size of the wavy structure can also be adjusted to fine tune the mechanical property of the resulting metamaterial. In-house software has been developed to construct the metamaterial structure within the 3D model. The metamaterial-enabled tissue-mimicking phantoms can be readily manufactured using a conventional 3D multimaterial jetting printer with commercial printing materials. The printing time, cost and postprocessing of the metamaterial phantoms were comparable to those of the conventional multimaterial printed models.

The advantage of using the tissue-mimicking metamaterial technique was that it greatly improved the fidelity of the procedural simulation on the 3D printed phantoms. In our research, the same type and size of TAVR valves as in clinical use were deployed in the tissue-mimicking phantoms. During the simulation process, the deployment depth and angle could be easily adjusted and different deployment techniques could be tested. The deformation and interactions of the self-expanding prosthesis and the passively dilating aortic root could be closely monitored. Furthermore, we have developed a CT-based strain quantification technique to quantify the post-TAVR aortic root strain distribution. There are actually a variety of sensors that we could add to the 3D printed phantom for quantitative assessment of the relevant pathophysiological parameters. For example, flexible sensors could be directly written or attached onto the surface of the 3D printed phantom. They can be used to assess the pressure, temperature, flow velocity and tissue strain. In addition, imaging landmarks can work with ultrasound/CT/MRI to track tissue deformation and assess tissue strain. These measurements can be potentially applied to various clinical scenarios in cardiovascular medicine. In our study, using radiopaque beads and CT imaging, we have found a novel indicator, the annular bulge index, which outperformed the other morphologic variables in predicting PVL. The annular bulge index was a measure of the focal annular strain unevenness post TAVR. It was thought that such a mechanical variable could be more closely related to the mechanism of the occurrence of PVL, and therefore, worked better than the other imaging-based morphological variables.

Like most complications associated with percutaneous cardiovascular interventions, the occurrence of post-TAVR PVL results from the complex and dynamic interaction between the native aortic root, the implanted transcatheter valve and the blood flow. To elucidate the role of the blood flow in the genesis of post-TAVR PVL, we have developed an *in vitro* flow test platform, in which a validated mock circulation loop was used to generate realistic physiological and pathological flow waveforms with desired flow pressure. As shown in [Figure 1](#), MRI cine and phase-contrast flow images and high-resolution echocardiography were acquired to study the post-TAVR flow pattern in the vicinity of the prosthetic valve and the motion of the prosthesis leaflets, respectively. For instance, [Figure 1B](#) showed a representative case of reduced leaflet mobility in the *in vitro* flow test, which was believed to be associated with post-TAVR subclinical thrombosis.

The most important contribution of our research was the development and the validation of the novel sensor-enabled tissue-mimicking 3D printed phantom. We have demonstrated the feasibility of manufacturing such a phantom to provide not only an accurate anatomic model but also a benchtop testing platform that gives very

Figure 1. *In vitro* flow imaging of the 3D printed phantom pre and post valve deployment. (A) MRI cine and phase-contrast flow images and (B) high-resolution echocardiography were acquired to study the post-TAVR flow pattern in the vicinity of the prosthetic valve and the motion of the prosthesis leaflets, respectively.

important pathophysiologic information regarding the cardiac intervention. Among certain high-risk patients, our technique may refine the current approaches of valve selection and valve deployment, and potentially reduce the rate of post-TAVR PVL. These concepts can be extended to planning transcatheter mitral valve replacement (TMVR) and tricuspid valve repair and replacement therapies.

In the near future, as cardiovascular medicine is shifting more toward personalized treatment, it is believed that 3D printing will play a more important role in patient-specific planning for heart procedures. It will help the physicians better select the percutaneous device, assess the procedural risk, optimize the deployment technique and practice for rare and difficult cases *in vitro*. However, before 3D printing can be routinely performed in the daily clinical practice, several technical limitations associated with medical 3D printing need to be addressed. The lack of high-fidelity printing materials that mimic the material properties of various soft biological tissues remains a bottleneck for the broader application of medical 3D printing. Recently, 4D printing techniques have been reported to manufacture 3D objects that actively deform [6]. However, it is still very difficult to simulate a fast beating heart that exerts high-level active forces. In addition, the length of time it takes for image segmentation and 3D modeling, the high printing cost and the time-consuming 3D printing and model postprocessing all hinder the widespread use of cardiovascular 3D printing. As substantial advancement in the software and hardware of 3D printing is expected in the years to come, these technical obstacles will be eventually cleared and cardiovascular 3D printing will potentially become an essential everyday clinical tool to improve patient care in interventional cardiology.

Acknowledgements

The authors would like to thank K Wang, C Zhang, B Wang, V Polsani and M Padala for their help in generating the flow experiment images.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

References

- 1 Vukicevic M, Mosadegh B, Min JK, Little SH. Cardiac 3D printing and its future directions. *JACC Cardiovasc. Imag.* 10(2), 171–184 (2017).
- 2 Leon MB, Smith CR, Mack MJ *et al.* Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. *N. Engl. J. Med.* 374(17), 1609–1620 (2016).
- 3 Kodali SK, Williams MR, Smith CR *et al.* Two-year outcomes after transcatheter or surgical aortic-valve replacement. *N. Engl. J. Med.* 366(18), 1686–1695 (2012).
- 4 Qian Z, Wang K, Liu S *et al.* Quantitative prediction of paravalvular leak in transcatheter aortic valve replacement based on tissue-mimicking 3D printing. *JACC Cardiovasc. Imag.* 10(7), 719–731 (2017).
- 5 Wang K, Wu C, Qian Z, Zhang C, Wang B, Vannan MA. Dual-material 3D printed metamaterials with tunable mechanical properties for patient-specific tissue-mimicking phantoms. *Additive Manufacturing* 12, 31–37 (2016).
- 6 Raviv D, Zhao W, McKnelly C *et al.* Active printed materials for complex self-evolving deformations. *Sci. Rep.* 4, 7422 (2014).