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3D Models at IMMR: Enhanced Anatomical Insight Speeds Innovation

Ventricular view of a human mitral and tricuspid valve

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3D Models at IMMR: Enhanced Anatomical Insight Speeds Innovation

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The third dimension is key to understanding fully the anatomy and function of complex organs. Historically, however, most medical imaging in cardiology and other fields has been limited to two dimensions. Three-dimensional (3D) CT and echocardiography provide tremendous insight and are important adjuncts in preprocedural planning. Being able to hold a 3D anatomic structure in one's hands provides even further value for evaluating and understanding specific anatomy and to be able to rehearse a surgical or interventional procedure. While 3D modeling has an obvious role to play in human medical procedures, we believe it can also improve preclinical studies as well: Better preparation means less failure, use of fewer animals and more cost-effective research.

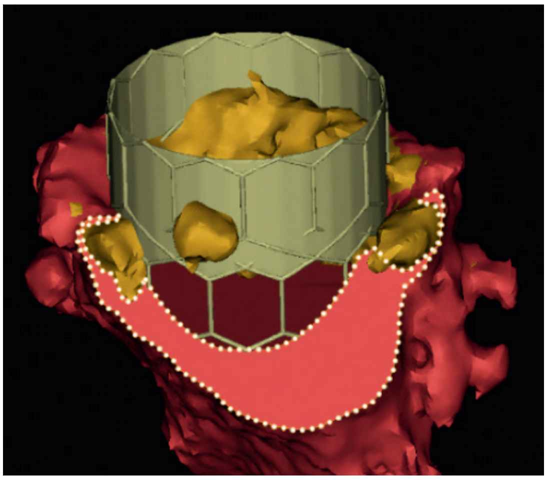
Thomas Modine, MD, PhD is a cardiovascular surgeon and heart valve specialist in the Heart Valve Unit of the University Hospital Center (CHU) in Bordeaux, France. Karen De Leener is a Cardiovascular Market Specialist at Materialise in Leuven, Belgium. We spoke with Dr. Modine and Karen about the role of 3D Planning and 3D printed models in cardiovascular innovation.

Karen, would you please tell us a bit about what 3D technology is?

KDL: Let me start with the concept of a virtual patient. This is a computational model that is an exact replica of a patient's normal or diseased anatomy that is acquired from medical images, such as CT or MRI. This virtual patient can be used to study how the real patient would respond to a certain intervention, a process we call 3D Planning. Using this computational model, you can also 3D print the anatomy of interest into a physical model that you can hold in your hand and look at from all angles. In the development of cardiovascular medical devices, such 3D models can be highly instructive.

Thomas Modine

Karen De Leener



3D Planning with Materialise Mimics Enlight software to prepare for a TMVR procedure by virtually implanting a prosthetic device and assessing the corresponding neo-LVOT.

TM: I think it's very important to highlight the fact that we now have a real opportunity to match CT images with a computational model and also a 3D printed model, to move from 2D to virtual 3D and to actual 3D. I believe this will make a lot of difference in terms not only of assessing and quantifying images, but also as physicians being able to reproduce and visualize the real anatomy that we need to treat. For example, trying to figure out how a medical device like a heart valve or an arterial stent would behave inside the heart, even as we prepare to test our prototypes in the preclinical lab. The technology of Materialise is based on a true reconstruction of the anatomy in 3D, while other software may be based on volume rendering. The latter limits us to 2D Planning, which is less accurate than true 3D Planning. We go to IMMR to conduct research and to be able to use the best tools available. I believe that utilizing Materialise technology at IMMR can be even more powerful in making a complex project successful.

As you think about the R&D process, and particularly about the early stages of perfecting a product's design, how do you see the role of 3D printed models in guiding and possibly accelerating this?

KDL: In the R&D process, the goal is to design a device that can treat a target patient population. While 3D techniques can be used to model any one given patient, an advanced analysis called statistical shape modeling can be used to create an average virtual representation – a synthetic virtual patient – that combines the characteristics of a diverse patient population to provide both an average anatomy as well as its degrees of variation across the population. This can help inform to what proportion of a population a device with certain specifications would apply, and whether multiple sizes of a device would be needed to adequately treat the patient population.

"3D IS MORE REALISTIC THAN 2D. WHEN YOU WANT TO UNDERSTAND AND OPERATE IN THE HEART, THE CLOSER YOU GET TO 3D, THE THINNER THE SEAM BETWEEN TECHNOLOGY AND REAL ANATOMY, AND THE MORE IMMERSIVE THE EXPERIENCE." **Dr. Modine**

As an example, consider the development of a transcatheter tricuspid valve replacement device to treat patients with tricuspid regurgitation (TR). We see two main R&D benefits of using a 3D printed or virtual model: The first is to use statistical shape modeling to quantify the target population to gather relevant design input. From that, you can produce a 3D model of an average heart with TR that can be used to measure and visualize important dimensions such as those of the tricuspid annulus and the inferior or superior Vena Cava that can inform valve sizing, and to evaluate angles that the delivery catheter would have to be able to navigate in order to place the prosthetic valve. A second use of having a 3D model would be to be able to test a prototype device to see whether it functions correctly or not. There are two main options to validate a prototype in a realistic test set-up: in vitro validation with 3D printed benchtop models and in silico validation with simulations on virtual 3D models.

In these ways, if you use the synthetic virtual TR patient to make 3D models, then you can assess questions like how to approach the tricuspid valve, whether a device would deploy correctly, and whether it would fit in the blood flow without obstructing it. From this, the design can be iterated and refined, allowing you to move forward with preclinical studies and eventually human trials with more confidence.

Dr. Modine, from a clinical perspective, in terms of preparing or training for procedures, how do you see the potential clinical benefits of using these kinds of models?

TM: I have three indications in mind. For valve-in-valve Transcatheter Aortic Valve Interventions (TAVI), with this approach you can visualize the whole picture, including the surrounding anatomy above, below, and all around where you will place your TAVI device, rather than just rotating a flat 2D image. This allows us to assess the anticipated behavior of the native valve in the presence of the new one and, importantly, how this valve-in-valve would behave in proximity to the coronary arteries. This is a major interest, because while we have learned a great deal about TAVI, we do still have some dark zones, and valve-in-valve is one of them.

A second application could be bicuspid aortic valves with their unique anatomy. We see essentially three types of bicuspid valves and being able to analyze how a TAVI would behave in the setting of a particular bicuspid anatomy is very important in order to expand the indications for TAVI, especially to treat younger patients with bicuspid aortic valves.

A third application would be in the mitral and tricuspid space, mainly if we are planning transcatheter valve replacement, because we need to see how the new device will conform and can be anchored to the surrounding anatomy. One of the problems of TMVR is what we call the neo-LVOT and its degree of narrowing. Today we exclude 30% of screened patients based on having inadequate neo-LVOT area as it is currently calculated, but this could be at least 50% wrong. The reason for this is that the heart is a chamber not a plane, and we typically calculate the neo-LVOT by reconstructing it with a 2D approach. 3D technology will be invaluable here, as well as for tricuspid interventions.

Sometimes investigators arrive at the preclinical lab and find out that they don't have the right size device, or that the prototype doesn't fit the anatomy and the study fails. Do you see the potential for this kind of modeling to prevent those kinds of issues, where unnecessary loss of animals occurs?

TM: Absolutely you put your finger on a critical consideration. I think this type of analysis can help guide or fine tune startups or even large companies that are developing new products. For example, you may want to reduce the profile of a stent, but by how much, how many degrees? Instead of just making an empirical decision you could, based on a 3D, more realistic reconstruction, minimize the risk of failure from making the wrong choice. Before going into animals and investing a lot of money and time to do it, you can use the 3D reconstruction to help avoid trial and error. So, this is a tool that can be helpful, not only for clinical applications, but also for any type of research prior to human clinical investigation.

KDL: To provide another example, Materialise conducted a collaboration with the FDA in which statistical shape models of swine were used to define the most suitable animal model that best mimics human conditions for certain device implants. The aorta and femoral arteries of swine from 50 to 250 pounds were modelled, and it was observed that the diameter changes along the femoral arteries varied much more than along the aorta. This information helped to determine the appropriate sample sizes to evaluate such devices and to determine an appropriate but not excessive number of animals that needed to be studied.

Dr. Modine, as you look more broadly at structural heart disease, are there other clinical applications of 3D printed anatomic models that that you're excited about?

TM: Everything that is related to the heart can be explored by this 3D printed models. For heart valves, thus far we have only been talking about the mitral, tricuspid, and aortic valves because they are the most frequent ones affected in adults. But if you look at congenital heart diseases, we also have disorders of the pulmonary valve and other abnormalities that need surgical repair and reconstruction. There is huge potential here in terms of training and preparing for difficult cases. I also believe this could be applied to other organs as well, for example in neuro- and orthopaedic surgery, among others.

At IMMR we work with nonhuman species. Is there a role for 3D reconstruction or printing of nonhuman anatomy to help improve the success of preclinical studies?

KDL: : For sure, I'm convinced 3D printed animal models are useful as well, and I see two main benefits: The first one is that you can approach your animal studies with greater confidence after you have studied your concept in a 3D reconstruction and a 3D printed animal model. A second one is when you are preparing to transition from animal to human studies, then it can be really helpful to have both an animal printed model and a human 3D printed model so that you can compare and really see the differences you'll encounter and be prepared for those.

Karen and Dr. Modine, thank you both for your time and your insights today

3D Printed Tricuspid Regurgitation model that can be used for Transcatheter Tricuspid Valve Repair (TTVR) device R&D as well as anatomy and pathology education.

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Accelerating your innovative research

Prepared with: Nicolas Borenstein, Robert Kieval, Cécile Jung
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