Current Cardiovascular Imaging Reports (2021) 14: 3
https://doi.org/10.1007/s12410-021-09553-7

INTRAVASCULAR IMAGING (A.G. TRUESDELL, SECTION EDITOR)

Computational Simulation, Bench Testing, and Modeling: Novel Tools to Strategize and Optimize Interventional Procedures

Mirvat Alasnag[1] · **Khaled Al-Shaibi**[1] · **Goran Stankovic**[2]

Accepted: 16 June 2021

Abstract

Purpose of Review Although simulation was adopted many years ago to complement training programs, more recently it has become an integral part of planning individual invasive procedures as well as understanding and developing new devices and techniques. Here, we review the different types of simulation and modeling and their impact on the field of interventional cardiology.

Recent Findings Three-dimensional model printing has been employed to strategize complex structural procedures for various congenital heart defects and valvular heart diseases. Ex vivo bench testing permitted understanding the relationship of new technologies with neighboring structures and enabled the refinement of the devices and procedural steps themselves. In vitro simulation and computational analyzes have enhanced our understanding of flow dynamics in bifurcation diseases, transcatheter therapies, congenital defects, and predicting outcomes for transcatheter valve technologies and techniques.

Summary Incorporating simulation, bench testing, computational analyzes, and three-dimensional modeling will enable the field of interventional cardiology to expand while optimizing techniques and maintaining best practices.

Keywords Simulation · Modeling · Bench Testing · Interventions

Introduction

The field of interventional cardiology has evolved significantly over the last decade permitting a more predictable and detailed understanding of disease physiology and anatomy, approved devices and the endorsed techniques. Cadaveric dissections and wet labs were conventionally used to refine operator skills and test devices. More recently, the advent of computed tomography (CT) imaging and models allowed a more sophisticated means to both improve operator skill, and test techniques and devices. In this review we provide an overview of the latest developments that include three-dimensional (3D) model printing, ex vivo bench testing, in vitro simulations, and ultra-CT imaging for structural, endovascular, and coronary interventions.

Three-Dimensional Modeling

3D printing was first described by Charles Hull in 1986 and further developed thereafter. Today, generating a 3D model begins with image acquisition using a CT, cardiac magnetic resonance (CMR) image or echocardiographic image that is volume rendered and processed in segments. ECG-gated CT has the advantage of providing submillimeter tissue resolution with a very high spatial resolution. It can often image metal implants like pacing wires, mechanical prostheses, and calcification without significant artifact. Volumetric 3D echocardiography is another option that is readily available, low cost, and with no radiation exposure to the patient. However, it is limited by artifacts, shadows, and a limited beam making it most suitable for chambers and valve leaflets only. CMR provides high resolution images without radiation and is particularly useful for congenital heart defects and tumors. The commonest limitation of CMR is pacing wires and mechanical prostheses, and its spatial resolution doesn't allow evaluation of the valves and

---

Topical Collection on *Intravascular Imaging*

✉ Mirvat Alasnag
mirvat@jeddacath.com

[1] Cardiac Center King Fahd Armed Forces Hospital, PO Box 9862, Jeddah 21159, Saudi Arabia

[2] Department of Cardiology, Clinical Center of Serbia, and Medical Faculty, University of Belgrade, Belgrade, Serbia

coronary arteries well. The processed segments are then reconstructed, and a patient specific model is generated. This model is then printed with different material. [1•]

Stereolithography fabricates a solid object from a photopolymeric resin using digitally guided ultraviolet laser or visible light to harden the surface layer of a polymer liquid. Layer by layer fused deposition creates a 3D structure by extruding melted thermoplastic filaments. The physical support material later dissolves away and the model is created. PolyJet technology is created using laser and fused metal/ceramic powder. Jetting thin layers of liquid photopolymers are instantly hardened by ultraviolet light creating models with smooth surfaces and thin walls suitable for patient-specific anatomical models. [2••]

The model is used to educate the individual patient and provide a detailed explanation of the procedure and potential risks. Since they are a patient specific replica, they can be used by the operators to predict individual risks and consider strategies to avert them. Several successful examples have been published as case reports delineating the role of 3D printing are available including that of transcatheter aortic valve replacement (TAVR), tricuspid valve replacement, left ventricular assist devices, and congenital heart defects. [3–5] Figures 1 and 2 are examples of patient specific 3D printed models used to plan tricuspid valve replacement of a patient with a permanent pacemaker and leads across the valve as well as 3D printed model used to identify the appropriate access for TAVR in a patient with coarctation of the aorta. Larger series have allowed more streamlined guidance into the role of printed models for a variety of procedures such as mitral valve interventions, paravalvular leak closure, left atrial appendage occlusion and trans-septal punctures. [6–8] These models allowed hands-on procedural sizing and planning as well as device training for such structural interventions.

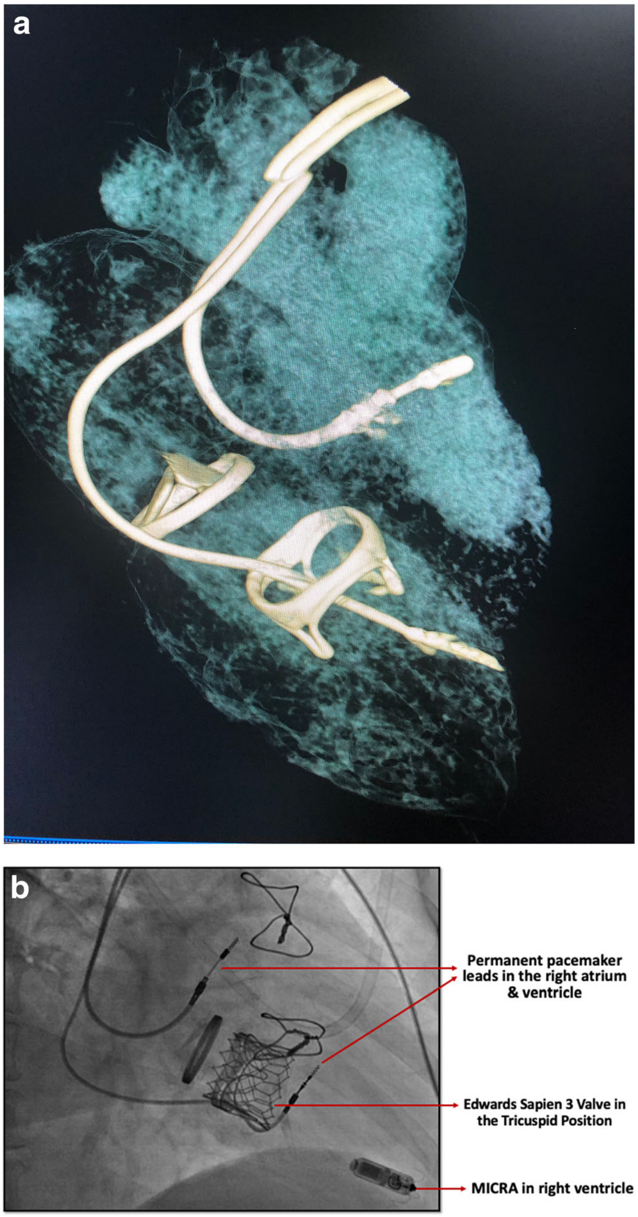

Fig. 1 Panel **A** Cardiac computed tomography derived three-Dimensional model of the permanent pacemaker leads in the right atrium and ventricle used to plan percutaneous transcatheter tricuspid valve replacement (Alasnag M, et al. 3-Dimensional modeling to plan tricuspid valve in valve in a patient with a permanent dual-chamber pacemaker. HeartRhythm Case Rep. 2020 Jun 5;6(9):588-590.). Panel **B** Fluoroscopic image post-procedure demonstrating a deployed Edwards Sapien 3 valve in the Tricuspid Valve position with the leads of the previous maker and MICRA leadless pacemaker (Alasnag M, et al. 3D model guiding transcatheter aortic valve replacement in a patient with aortic coarctation. *JACC Case Rep.* 2020; 2: 352-357.)

Ex Vivo Bench Testing

Ex Vivo bench testing is routinely used by industry as they develop their products to test function and durability permitting appropriate modifications to the technology. Often several generations of devices are produced and subsequently tested in vivo in randomized controlled trials. A prime example is stent technology with open and closed cell designs, absorbable polymers (subluminal or otherwise), and drug coating.

Ex vivo simulation involves test stenting of porcine or cadaveric human donor hearts using the Visible Heart perfusion circuit (Medtronic Visible Heart, University of Minnesota, http://www.vhlab.umn.edu/). This has permitted the evaluation of evaluation of implantable devices such as transcatheter heart valves, permanent pacemakers and implantable defibrillators, and stents. An important development in this area was the application of bench testing to optimize percutaneous coronary interventions in bifurcation disease. When this type of simulation is combined with ultra-CT or invasive optical coherence tomography (OCT), more detailed definition of stent configuration, apposition, expansion, scaffolding, overlapped layers at each step can be documented and refined. [9•, 10••, 11••] The latest

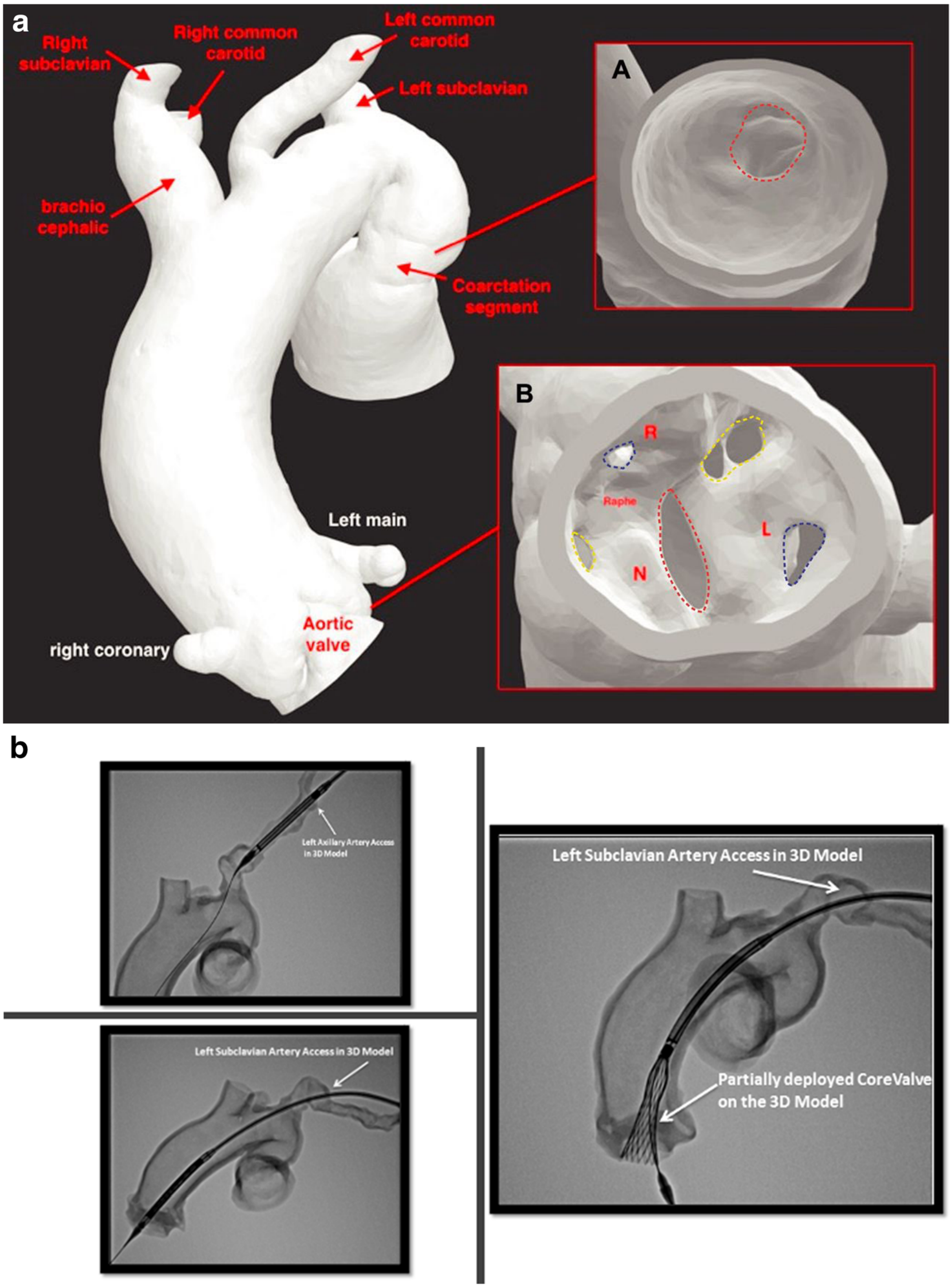

Fig. 2 Panel **A** Three-Dimensional model of a stenosed bicuspid aortic valve and coarctation of the aorta used to plan percutaneous transcatheter aortic valve replacement. Panel **B** Fluoroscopic images of the ex vivo simulation using the three-dimensional model to identify the most suitable access point for the procedure

European Bifurcation Club Consensus Document referenced simulation as a key technology to study patient specific anatomies, train interventional cardiologists, and further improve on bifurcation techniques. [12••]

As for TAVR, bench testing on the Visible Heart Model (Medtronic Visible Heart, University of Minnesota) proved useful in the assessment of coronary arteries after implantation of self-expanding valves. [13] Endoscopic evaluation of the coronary ostia demonstrated the various issues related to co-axial and selective engagement of the coronary arteries using different catheters. Jailed ostia treated by the chimney and snorkel techniques were studied further using ultra-CT technology that reconstructed the relationship between the deployed stent and valve cage. These images demonstrated that these techniques are able to maintain coronary patency in spite of adverse commissural post alignment.

The future direction of ex vivo bench testing is fascinating. There are preliminary reports of a biorobotic hybrid heart composed of organic endocardial tissue from a preserved explanted heart with intact intracardiac structures and intermixed with active synthetic myocardium that can conceivably drive the motion of the heart.

High-fidelity testing of intracardiac devices such as wall grafts, pacemaker leads, and stents require dynamic cardiac models that mimic the complex motion of the heart while maintaining the intricate anatomical structures inside the heart. Other therapeutic experiments on the horizon are hearts that are injected with stem cells to create a reconstructed animal heart and ghost hearts which could be used as scaffolds to grow transplant hearts for patients. [14]

In Vitro Simulation

Unlike ex vivo models, in vitro simulation involves a patient-specific silicone-based phantoms. The phantoms utilized for bench tests were initially rigid and composed of polymethyl methacrylate. More recently, they have been replaced by flexible silicone material that is designed into a 3D structure that can be tailored to the structure evaluated. For example, for bifurcation stenting strategies, vascular branching structure to simulate branching coronary arteries with proximal and distal reference dimensions that are tapering can be designed. Subsequently, images of these structures using the ultra-CT or OCT are obtained. Ultra-CT provides images with a resolution of 10 to 20 μm. The post-processing modules include geometric rotation, cut planes, fly-through animations that simulate OCT imaging and open dissection. OCT images usually have an axial resolution of 5 μm and lateral resolution of 20 μm.

Like industry developers, operators have availed the opportunity to explore new techniques or refine old techniques using in vitro simulation. To continue with the example of bifurcation stenting, patient-specific silicone-based bifurcation anatomies are constructed. All the steps of the various bifurcation strategies (provisional or a priori two-stent strategies) are examined on the model to identify the most suitable technique or stent design. A visual depiction of strut deformation, realignment, and crushing allowed operators to have a control for important steps such as proximal or distal cell crossing, simultaneous versus sequential kissing inflations and proximal optimization (POT), and the impact on the carina with the various strategies. For example, a clear understanding of the wire recrossing in a Double Kiss Double Crush technique (proximal) versus TAP technique (distal) permits better ostial coverage of the side branch and avoids a geographic miss. When evaluated in concert with flow dynamics generated by ultra-CT, flow changes can be registered and studied for different angles, stent designs, and bifurcation strategies. [11••] An example of bench testing to refine the TAP technique and study the neo-carina is provided in Fig. 3 (Courtesy of Yiannis Chatzizisis). These models have allowed more precise positioning of noncompliant balloons during POT that is tailored to the different 2-stent bifurcation strategy which avoids disruption of the neo-carina.

As mentioned previously, these can be valuable to provide stations for operators to develop their skill set and for societies to endorse specific techniques. However, other potential clinical implications can be extracted from such testing. For instance, for individual patient anatomies the duration and potency of antiplatelet therapy with bifurcation stenting can be reconsidered. This is also fertile ground for future research for bifurcation stenting as an example.

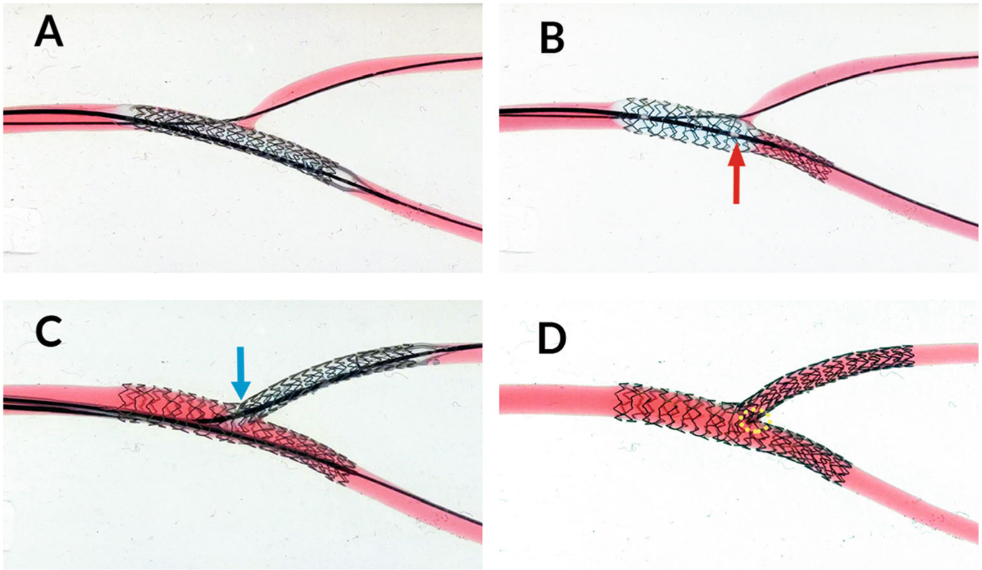

Fig. 3 In Vitro Bench testing of the TAP Bifurcation technique delineating the neo-carina (Courtesy of Yiannis Chatzizisis)

Computational Simulation

Computational simulation is what is commonly referred to as virtual computer generated program. A computer-based algorithm detects patterns, provides scores, or calculates flow dynamics. [15] This has proven to be cost and time effective, feasible, and widely available. This tool has been instrumental in guiding interventions such as closure of congenital defects, especially those with mixed shunting or multiple levels of shunting, paravalvular leaks, TAVR, and stenting using two stent strategies. Computational simulation has proven particularly useful for TAVR. As the indication for TAVR has been extended to intermediate and low risk individuals, it has become imperative to predict and avert risk. Shultz et al reported the feasibility of predicting calcium displacement using both balloon and self-expanding THV with this technology. Modeling was performed in 39 patients treated with a Medtronic CoreValve System and Edwards SAPIEN XT. Quantitative axial frame morphology at inflow and nadir, coaptation, and commissures was compared with multislice CT obtained post TAVR. The displacement of the aortic leaflet calcifications, quantified by the distance between the coronary ostium and the closest calcium nodule was measured. There was a strong correlation between the measured CT and predicted frame dimensions. [16] In another report, Rocatello et al described a patient-specific computer simulation experiment of 112 cases that revealed that maximum contact pressure and contact pressure index are both associated with new conduction abnormalities after CoreValve/Evolut R implantation. [17]

Similarly, Antoniadis et al explored the utility of assessing flow dynamics for bifurcation stenting. [10••] Since the premise that bifurcations are particularly vulnerable junctions for plaque buildup and shear stress, it is conceivable that further research can be undertaken when flow dynamics using computational simulation are correlated with histopathological evaluation of in-stent restenosis, intimal hyperplasia or plaque buildup at bifurcation points. If this can be validated, in the future individual predictive risk scores could be calculated by such testing for different stent designs and bifurcation techniques. Figure 4 is an example of a patient-specific computational model that demonstrates the Medina classification, significance of the side branch disease and the suitability, and potential success of a TAP technique in obtaining optimal coverage of the diseased segments (Courtesy of Yiannis Chatzizisis).

Conclusion

Modern day technology has allowed precise and detailed prediction of the interaction of devices and the different anatomies. Simulation, 3D printing, bench testing, and computational analyzes have all contributed to the refinement of operator skills, procedural techniques, and the development of newer iterations of devices. As these tech-

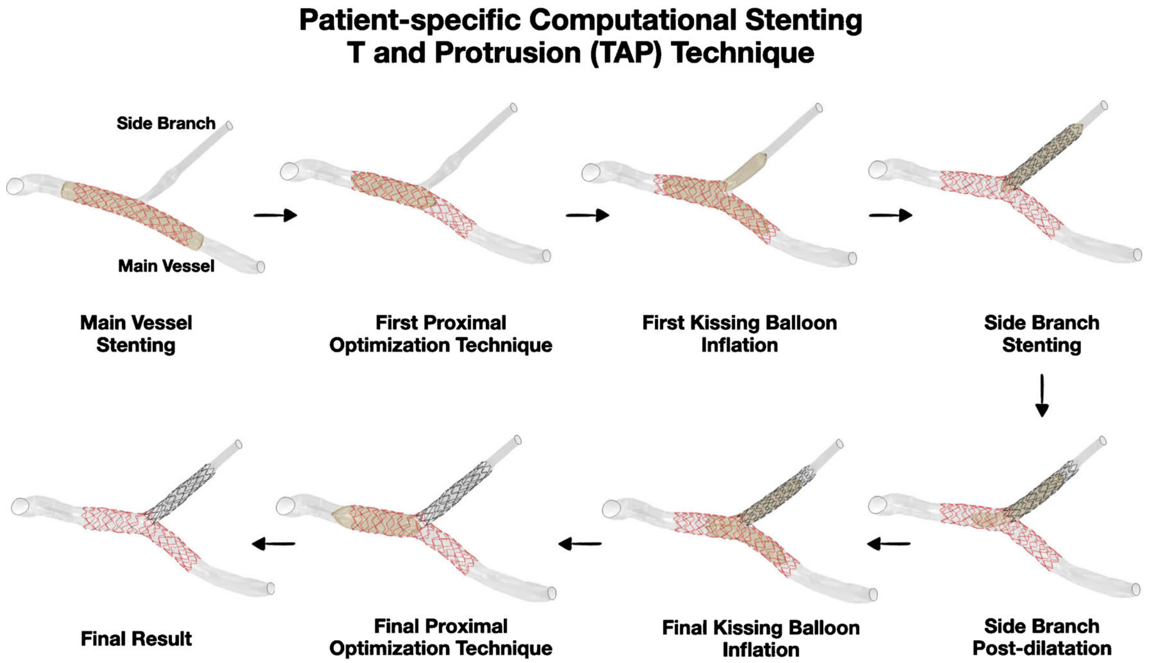

Fig. 4 A patient-specific computational model demonstrating the Medina classification of the bifurcation disease and predicted success of the TAP technique to adequately scaffold the side branch and main vessel (Courtesy of Yiannis Chatzizisis)

nologies mature and become validated, they will contribute further to the growth of interventional, structural, and coronary interventions.

Declarations

Conflict of Interest None of the authors have any relevant conflicts of interest. This manuscript was not funded.

References

Papers of particular interest, published recently, have been highlighted as:

- • Of importance
- •• Of major importance

1.• Vukicevic M, Mosadegh B, Min JK, Little SH. Cardiac 3D printing and its future directions. JACC Cardiovasc Imaging. 2017 Feb;10(2):171-184. doi: 10.1016/j.jcmg.2016.12.001. PMID: 28183437; PMCID: PMC5664227. **Provides a thorough summary of the 3D Printing technology.**

2.•• Harb SC, Rodriguez LL, Vukicevic M, Kapadia SR, Little SH. Three-Dimensional Printing Applications in Percutaneous Structural Heart Interventions. Circ Cardiovasc Imaging. 2019 Oct;12(10):e009014. doi: 10.1161/CIRCIMAGING.119.009014. Epub 2019 Oct 9. **Provides an overview of the clinical utilities of 3D printed models.**

3. Alasnag M, Sweidan R, Nosir Y, Bokhari F, Al-Shaibi K. 3-Dimensional modeling to plan tricuspid valve in valve in a patient with a permanent dual-chamber pacemaker. HeartRhythm Case Rep. 2020 Jun 5;6(9):588-590. doi: 10.1016/j.hrcr.2020.05.021. PMID: 32983872; PMCID: PMC7498512.

4. Alasnag M, Al-Nasser I, Poqueddu M, Ahmed W, Al-Shaibi K. 3D model guiding transcatheter aortic valve replacement in a patient with aortic coarctation. *JACC Case Rep.* 2020;2:352–7.

5. Farooqi KM, Saeed O, Zaidi A, Sanz J, Nielsen JC, Hsu DT, et al. 3D printing to guide ventricular assist device placement in adults with congenital heart disease and heart failure. JACC Heart Fail. 2016 Apr;4(4):301–11. https://doi.org/10.1016/j.jchf.2016.01.012.

6. Wang DD, Eng M, Kupsky D, Myers E, Forbes M, Rahman M, et al. Application of 3-Dimensional Computed Tomographic Image Guidance to WATCHMAN Implantation and Impact on Early Operator Learning Curve: Single-Center Experience. JACC Cardiovasc Interv. 2016 Nov 28;9(22):2329–40. https://doi.org/10.1016/j.jcin.2016.07.038.

7. Ooms JF, Wang DD, Rajani R, Redwood S, Little SH, Chuang ML, Popma JJ, Dahle G, Pfeiffer M, Kanda B, Minet M, Hirsch A, Budde RP, De Jaegere PP, Prendergast B, O'Neill W, Van Mieghem NM. Computed Tomography-Derived 3D Modeling to Guide Sizing and Planning of Transcatheter Mitral Valve Interventions. JACC Cardiovasc Imaging. 2021 Mar 11:S1936-878X(21)00146-7. doi: 10.1016/j.jcmg.2020.12.034. Epub ahead of print.

8. Wang DD, Qian Z, Vukicevic M, Engelhardt S, Kheradvar A, Zhang C, et al. 3D Printing, Computational Modeling, and Artificial Intelligence for Structural Heart Disease. JACC Cardiovasc Imaging. 2021 Jan;14(1):41–60. https://doi.org/10.1016/j.jcmg.2019.12.022 Epub 2020 Aug 26.

9.• Chatzizisis YS. Complex cardiovascular interventions: visualization, planning, outcomes. JACC Case Reports 2019;1:124-6. **Provides an example of the first cases when simulation was used to assist in cases.**

10.•• Antoniadis AP, Mortier P, Kassab G, Dubini G, Foin N, Murasato Y, et al. Biomechanical Modeling to Improve Coronary Artery Bifurcation Stenting: Expert Review Document on Techniques and Clinical Implementation. JACC Cardiovasc Interv. 2015 Aug 24;8(10):1281–96. https://doi.org/10.1016/j.jcin.2015.06.015 **Provides descriptive explanation of modeling for bifurcation stenting. Provides an overview of the utility of bench testing in bifurcation stenting**.

11.•• Iles TL, Burzotta F, Lassen JF, Iaizzo PA. Stepwise visualisation of a provisional bifurcation stenting procedure - multimodal visualisation within a reanimated human heart utilising Visible Heart methodologies. EuroIntervention. 2020;16:e734–7 **This is the main article describing the Visible Heart technology adopted by the consensus European Bifurcation Club document and used to train early career individuals**.

12.•• Burzotta F, Lassen JF, Lefèvre T, Banning AP, Chatzizisis YS, Johnson TW, et al. Percutaneous coronary intervention for bifurcation coronary lesions: the 15th consensus document from the European Bifurcation Club. EuroIntervention. 2021;16(16):1307–17. https://doi.org/10.4244/EIJ-D-20-00169 **This is the latest consensus document elaborated by the European Bifurcation Club**.

13. Sanchez JZ, Burzotta F, Valenzuela T, Lassen JF, Iles T, Iaizzo PA. Direct Visualization of TAVR-Related Coronary Artery Management Techniques in Reanimated Beating Hearts. JACC Cardiovasc Interv. 2021 May 10;14(9):e87–91. https://doi.org/10.1016/j.jcin.2021.02.045.

14. Park C, Fan Y, Hager G, Yuk H, Singh M, Rojas A, Hameed A, Saeed M, Vasilyev NV, Steele TWJ, Zhao X, Nguyen CT, Roche ET. An organosynthetic dynamic heart model with enhanced biomimicry guided by cardiac diffusion tensor imaging. Sci Robot. 2020 Jan 29;5(38):eaay9106. doi: 10.1126/scirobotics.aay9106. PMID: 33022595; PMCID: PMC7545316.

15. Genuardi L, Chatzizisis YS, Chiastra C, Sgueglia G, Samady H, Kassab GS, et al. Local fluid dynamics in patients with bifurcated coronary lesions undergoing percutaneous coronary interventions. Cardiol J. 2021;28(2):321–9. https://doi.org/10.5603/CJ.a2020.0024 Epub 2020 Feb 13.

16. Schultz C, Rodriguez-Olivares R, Bosmans J, Lefèvre T, De Santis G, Bruining N, et al. Patient-specific image-based computer simulation for theprediction of valve morphology and calcium displacement after TAVI with the Medtronic CoreValve and the Edwards SAPIEN valve. EuroIntervention. 2016 Jan 22;11(9):1044–52. https://doi.org/10.4244/EIJV11I9A212.

17. Rocatello G, El Faquir N, De Santis G, Iannaccone F, Bosmans J, De Backer O, et al. Patient-Specific Computer Simulation to Elucidate the Role of Contact Pressure in the Development of New Conduction Abnormalities After Catheter-Based Implantation of a Self-Expanding Aortic Valve. Circ Cardiovasc Interv. 2018 Feb;11(2):e005344. https://doi.org/10.1161/CIRCINTERVENTIONS.117.005344.