



# Greater than the sum of its parts: multimodality imaging in adults with congenital heart disease

Nicholas Szugye<sup>^</sup>

Department of Heart, Vascular & Thoracic, Division of Cardiology & Cardiovascular Medicine – Pediatric Cardiology, Cleveland Clinic Lerner College of Medicine, Cleveland, OH, USA

*Correspondence to:* Nicholas Szugye, MD. Assistant Professor of Pediatrics, Department of Heart, Vascular & Thoracic, Division of Cardiology & Cardiovascular Medicine – Pediatric Cardiology, Cleveland Clinic Lerner College of Medicine, 9500 Euclid Avenue, M-41, Cleveland, OH 44195, USA. Email: szugyen@ccf.org.

**Abstract:** As the population of adults with congenital heart disease (ACHD) grows, there also grows an expanded need for non-invasive surveillance methods to guide management and intervention. A multimodal imaging approach layers complementary insights from echocardiography, computed tomography (CT), magnetic resonance imaging (MRI), and other modalities into a clinician's view of patient physiology. Merely applying strategies from acquired adult cardiac disease would be inadequate and potentially misleading. As data amasses in this small but growing population, investigators in the field of ACHD have discovered population-specific imaging biomarkers that identify deterioration and pivotal time points where intervention may reduce morbidity and mortality. Moreover, due to the variety of physiologies and the modest number of ACHD patients relative to that of adults with acquired heart disease, multicenter registries will be key in advancing research. The integration of well-defined imaging variables into these databases can help identify important biomarkers. Emerging technologies like computational fluid dynamics (CFD) and artificial intelligence (AI) are also primed to enhance imaging capabilities and clinical workflows, though require careful adaption as ACHD patients are not meaningfully represented in the training data for these technologies. Ultimately, a multimodal imaging approach is essential for optimizing care for ACHD patients, enabling personalized medicine where interventions can be performed before clinical deterioration occurs.

**Keywords:** Adults with congenital heart disease (ACHD); multimodal imaging; cardiac magnetic resonance imaging (CMR); cardiac computed tomography (CCT); congenital heart disease

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## Introduction

As outcomes for children born with congenital heart disease have improved, the number of adults with congenital heart disease (ACHD) has continued to rise. In the past decade, the number of ACHD has surpassed the number of children (1). As such, the natural history of this population is being revealed in real time. Surveilling the course of residual disease requires continued and close study

within our field. In this unique population, merely applying lessons learned from other populations, such as those with acquired adult cardiac disease, is an unacceptable solution, and one that would result in a mishandling of clinical data and improperly formed conclusions.

Indeed, a necessary goal in caring for the ACHD population is to identify signals of clinical deterioration and interventions that can minimize morbidity and mortality.

<sup>^</sup> ORCID: 0000-0002-4435-7891.

Here we review key examples and lessons learned from imaging biomarkers in multimodal imaging, which has seen tremendous growth in the past two decades (2). The 6<sup>th</sup> special issue on “Current Management Aspects of Adult Congenital Heart Disease (ACHD)” arrives at a pivotal moment, underscoring the indispensable role of multimodality imaging in the comprehensive care of ACHD patients.

Multimodality imaging refers to the integration of various imaging techniques—such as echocardiography, magnetic resonance imaging (MRI), and computed tomography (CT)—to provide a detailed and holistic view of cardiac anatomy and function. Each modality offers unique strengths and, when used synergistically, they enhance diagnostic accuracy, guide therapeutic interventions, and improve long-term management strategies. Following a brief review of these imaging modalities, key examples and practical considerations will be reviewed.

### The role of echocardiography

Echocardiography is the cornerstone of ACHD imaging, primarily due to its accessibility, cost-effectiveness, and ability to provide real-time functional and anatomical information. Transthoracic echocardiography (TTE) is particularly useful for routine follow-ups, offering critical insights into ventricular function, valvular abnormalities, and hemodynamic parameters. Its value as a screening test, though it is limited by poor acoustic windows in some patients, operator dependency, less detailed spatial resolution compared to MRI and CT. Often, cross-sectional imaging is needed to further refine and quantify abnormalities suspected on echocardiography.

### Advancements in cardiac MRI (CMR)

CMR has emerged as a gold standard for detailed anatomical and functional assessment in ACHD. Its ability to provide high-resolution images without ionizing radiation makes it ideal for serial evaluations and lifelong monitoring of ACHD patients. CMR is particularly valuable in quantifying ventricular volumes and vascular flow, and myocardial tissue characterization offering comprehensive insights that are critical for pre-surgical planning and post-surgical follow-up. Stress CMR can detect perfusion differences in populations such as those with sequelae of Kawasaki disease, anomalous origin of the coronary arteries, or surgeries requiring coronary translocation. Four-dimensional (4D) flow is an advanced CMR sequence where blood flow is mapped in

three orthogonal directions to produce a three-dimensional (3D) flow vector at each voxel (vector field) throughout the cardiac cycle (time is the 4<sup>th</sup> dimension). Flow can be measured post-hoc in any plane rather than limiting flow analysis to pre-defined planes designated during the MRI scan. Additionally, flowlines can be assessed for qualitative or quantitative assessment of nonlaminar and stenotic areas. This is particularly useful in the complex flow patterns, flow restriction, and energy loss seen in anatomies such as in a Fontan conduit or a systemic venous baffle (3-6).

### The precision of cardiac CT (CCT)

CCT, with its excellent spatial resolution, plays a vital role in the anatomical delineation of complex congenital anomalies, valvar structure and coronary artery anatomy, and pre-interventional planning. Technological advancements have significantly reduced radiation exposure, making it a more viable option for repeated imaging when necessary. Likewise, significant metallic hardware compromises CMR image quality, requiring CCT for anatomic and functional assessment. Additionally, the superior spatial resolution of CCT is ideal for virtual and 3D model creation (7).

### Nuclear imaging

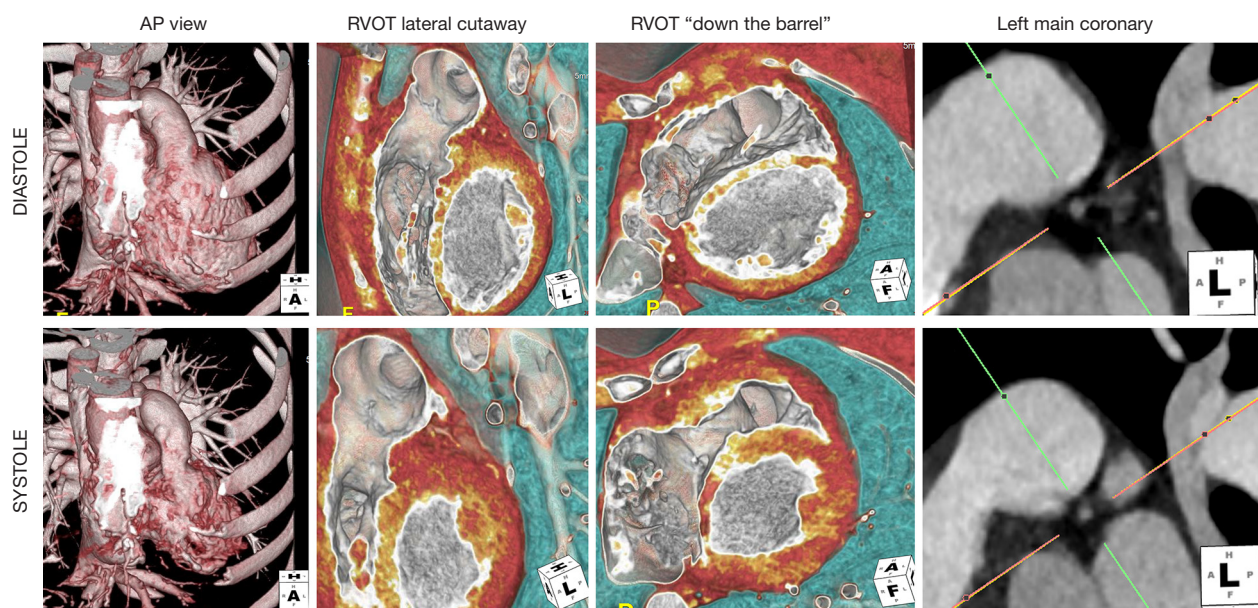
Nuclear imaging techniques, including single-photon emission CT (SPECT) and positron emission tomography (PET), provide functional information that complements anatomical imaging. These modalities are particularly useful in assessing myocardial perfusion and viability, but also the detection of infective endocarditis (8).

### Cardiac catheterization and angiography

Invasive catheterization-based angiography, once the primary tool for cardiac imaging, remains a vital tool in specific scenarios in ACHD, particularly in cases where a hemodynamic assessment and interventional procedure are concurrently needed. The spatial and temporal resolution of invasive angiography surpasses that of even CCT (spatial resolution 0.16 mm; temporal resolution 1–10 ms) and provides imaging of an isolated vessel segment within the limits of orthographic projection (9).

### Intracardiac echocardiography (ICE)

ICE is used in specific interventional settings for ACHD.



**Figure 1** Volume rendering images of a patient with TOF from a 4D CT enabling both diastolic and systolic measurements. The proximity of the left main coronary artery to the pulmonary root is shown in the far-right frame. AP, anteroposterior; RVOT, right ventricular outflow tract; A, anterior; H, head; L, left; F, foot; P, posterior; R, right; TOF, tetralogy of Fallot; 4D, four-dimensional; CT, computed tomography.

ICE offers real-time, high-resolution images of intracardiac structures from within the heart, providing superior guidance during catheter-based interventions. It allows for precise visualization of device placements, assessment of valve function, and detection of complications during and after procedures. Also, it can be used for detection of endocarditis when transesophageal echo is inadequate or contraindicated (10).

## Select cardiac defects

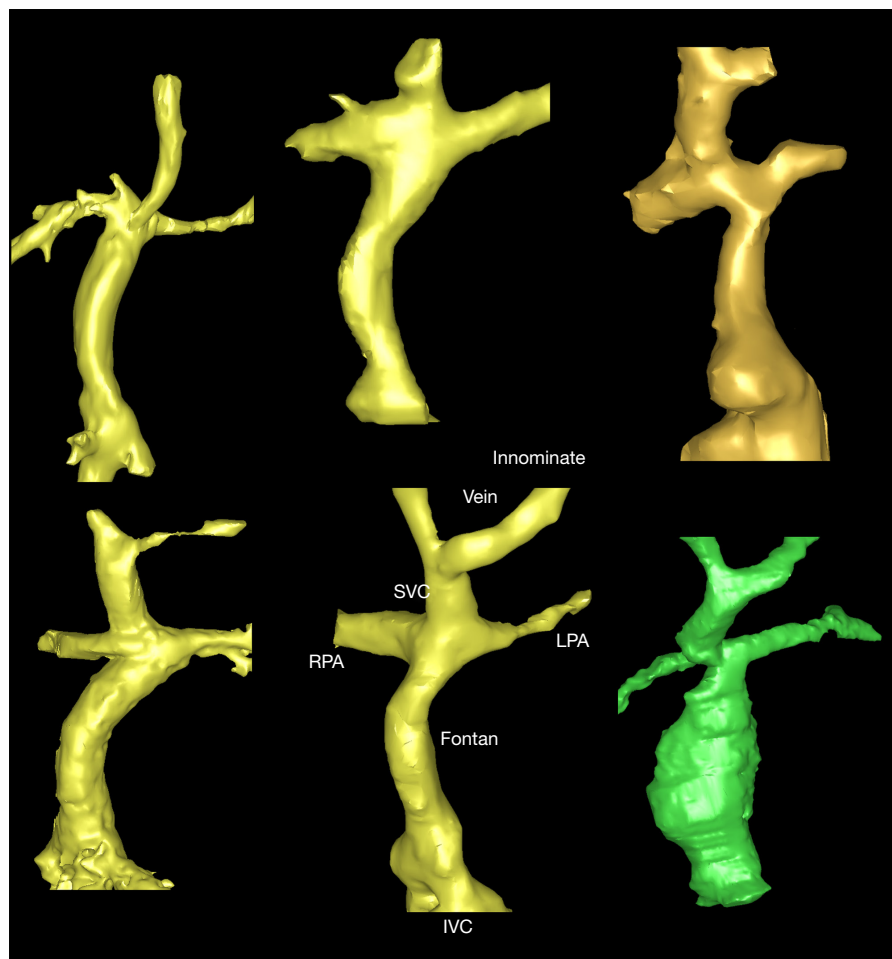
### *Tetralogy of Fallot (TOF)*

CMR is the standard of care for quantification of right ventricular size and function in patients with TOF, with current guidelines recommending serial CMR every 3 years in stable patients (11). Bokma *et al.* are the first to show a mortality benefit in pulmonary valve replacement, particularly in patients who underwent proactive pulmonary valve replacement guided by CMR volume and function data (12). A combination of CMR and CT provides complementary data in preparation for transcatheter pulmonary valve replacement (13). CMR provides functional information, flow data, and prognostic

value as to the long-term benefit of valve replacement. For example, higher burden of right ventricular late gadolinium enhancement prior to pulmonary valve replacement imparts a higher risk of deleterious post-valve replacement volume changes (14). Whereas 4D CT (full cardiac cycle CT images) provides detailed anatomy of the landing zone within the right ventricular outflow tract (15) as well as anatomic detail of the coronary arteries to assess the risk of coronary artery compression, as shown in the example in Figure 1 (13).

### *Fontan circulation*

A growing population of patients with Fontan physiology require meticulous follow-up to monitor the function of their unique circulatory system. In addition to an annual echocardiogram, CMR every 2–3 years is recommended to provide detailed assessment of the Fontan pathway for obstructions and baffle leaks, ventricular volumes, and function (16). In the past decade, there has been increased interest in noninvasive assessment of collateral burden by CMR (17), with particular attention toward short-term morbidity and mortality relative to high collateral burden. As long-term data of this analysis accumulates in the ACHD



**Figure 2** 3D surface rendered images of six examples of the Fontan circuit. The renderings at the right upper and lower spaces are examples of lateral tunnel Fontans and the remaining renders are of extracardiac conduit Fontans. SVC, superior vena cava; RPA, right pulmonary artery; LPA, left pulmonary artery; IVC, inferior vena cava; 3D, three-dimensional.

Fontan population, it is anticipated that prognostic data may be drawn from this imaging biomarker. Alongside the circulatory system, lymphatic imaging has been an area of investigation and imparts prognostic information (18). More complex flow data with 4D flow energetics have found to correlate with exercise capacity (5). *Figure 2* demonstrates the variety of Fontan circuit morphologies that can be seen with CMR.

#### ***Aortic coarctation***

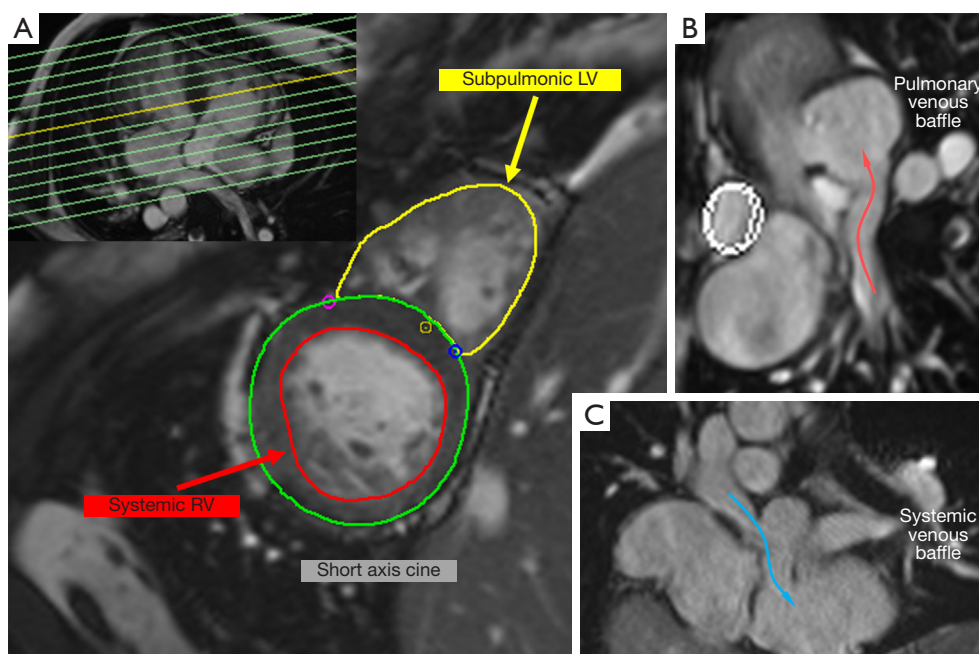
The thoracic anatomy of ACHD patients imparts limited echocardiographic windows, obliging cross-sectional imaging for detailed anatomic assessment. CMR angiography and CCT are both useful for monitoring the aorta for aneurysm

formation and re-coarctation, with the latter providing better spatial resolution. In addition to an anatomic assessment at rest, the dynamic changes that occur at increased cardiac output provide a better understanding of the hemodynamic effect of residual coarctation on a patient's daily activities. Stress CMR of the aortic arch flow individually assesses a patient's hemodynamic response to exercise that is nearly physiologic (19-21). CMR with 4D flow is being investigated to noninvasively detect difference in flow geometry, wall stress, and pressure gradient to predict which patients may benefit from intervention (21-23).

#### ***Systemic right ventricle (RV)***

For patients with a systemic RV, as seen in conditions





**Figure 3** Selected images from a CMR of a patient with a systemic RV demonstrate ventricular functional assessment and anatomic assessment of the venous baffles. (A) Still frame of cine imaging used for volumetric assessment of a systemic RV (red) and subpulmonic LV (yellow), the reference four-chamber image is shown in the top left corner. (B) Pulmonary venous baffle. (C) Systemic venous baffle. LV, left ventricle; RV, right ventricle; CMR, cardiac MRI; MRI, magnetic resonance imaging.

like congenitally corrected transposition of the great arteries (ccTGA) or after atrial switch procedures for D-transposition of the great arteries (D-TGA), CMR provides reliable quantification of ventricular size and function (*Figure 3A*), as well as myocardial fibrosis, which provides prognostic information to the care team. An indexed RV end-diastolic volume of  $\geq 130$  vs.  $<130$  mL/m<sup>2</sup> imparts a 10-year survival of 70% vs. 100% in atrial switch patients and 62% vs. 100% (24). In patients with ccTGA, repair or replacement of a regurgitant systemic atrioventricular (AV) valve before the right ventricular ejection fraction falls below 40% better preserves systemic RV function at 1-year post-repair (25). Additionally, systemic RV function by MRI can inform the timing of cardiac resynchronization therapy in ccTGA patients with heart failure (26). Both CMR and CT can be used for the assessment of venous baffles (*Figure 3B,3C*) (27).

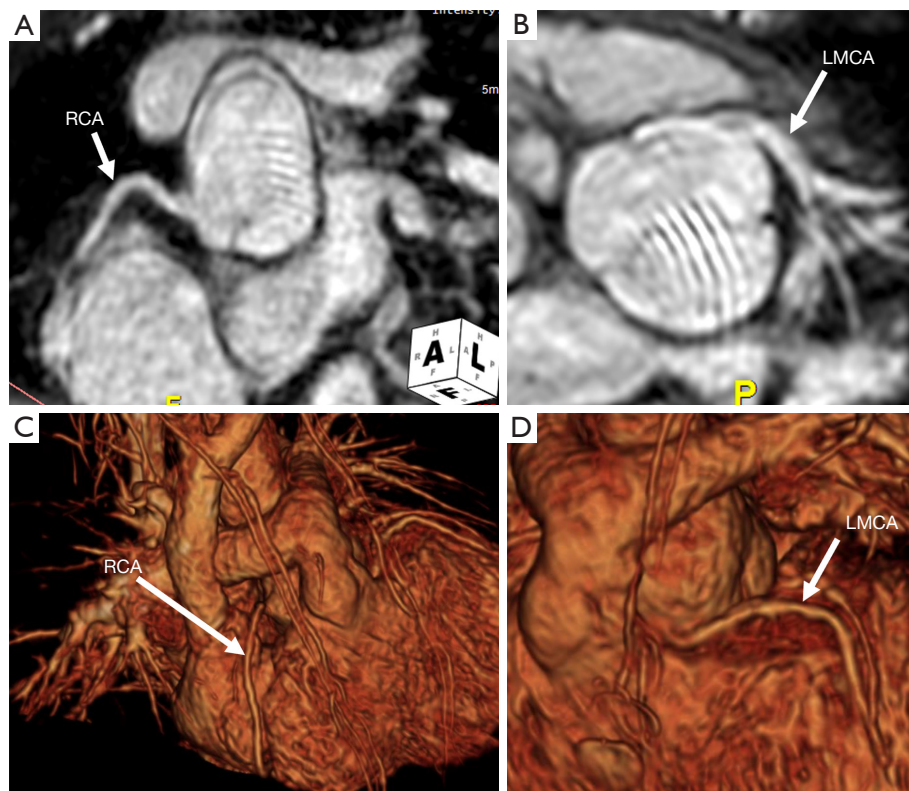
#### ***Transposition of the great arteries (TGA) with arterial switch operation***

In patients with D-TGA following the arterial switch

operation, regular surveillance with echocardiography provides information on ventricular function and valvar regurgitation. Following the Lecompte maneuver, echocardiographic imaging of the pulmonary arteries is limited and CMR is shown to have increased sensitivity for the detection of focal stenoses (28). Likewise, the neo-aortic root is prone to dilation resulting in neo-aortic regurgitation over time (29). In addition to the assessment of pulmonary arteries and the neo-aortic root, CMR can be used to assess re-implanted coronary arteries (see *Figure 4*) and perfusion defects relating to coronary anomalies in select individuals (30). CCT can be used for higher resolution anatomic evaluation of the coronary arteries, neo-aortic root, and pulmonary arteries.

#### ***Sinus venosus defect***

Sinus venosus defects require detailed imaging to evaluate the anomalous pulmonary venous connections. Echocardiography provides qualitative assessment of right heart size and function but is inadequate to fully map the venous system. CCT and CMR provide precise anatomical



**Figure 4** Transposition of the great arteries status post-arterial switch operation and LeCompte maneuver. CMR multiplanar reformats of the coronary arteries of (A) the RCA and (B) the LMCA. 3D volume renderings of (C) the RCA and (D) the LMCA. RCA, right coronary artery; A, anterior; H, head; L, left; F, foot; P, posterior; R, right; LMCA, left main coronary artery; CMR, cardiac MRI; MRI, magnetic resonance imaging; 3D, three-dimensional.

details needed for surgical planning, with CMR providing the additional advantage of direct measurement of the shunt fraction [pulmonary-to-systemic flow ( $Q_p:Q_s$ ) ratio] (31). In poor surgical candidates for open heart repair of superior sinus venosus repair, transcatheter-covered stent closure is an alternative method (32). This innovative approach requires precise anatomic mapping and often 3D printing or virtual reality examination of the atrial and venous anatomy for pre-procedural planning (33,34). *Figure 5* shows an example of a CT and surface-rendered 3D model used for pre-procedural planning.

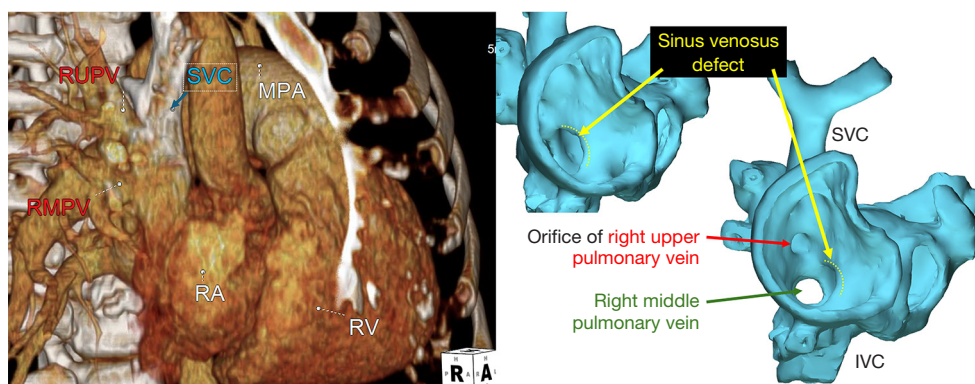
### The future of multimodal imaging

Though the ACHD population is growing, the population size is modest relative to adult patients with acquired heart disease. Multicenter registries hold promise to drive research forward in a complex and diverse population (35). As such, attention needs to be paid to the inclusion of

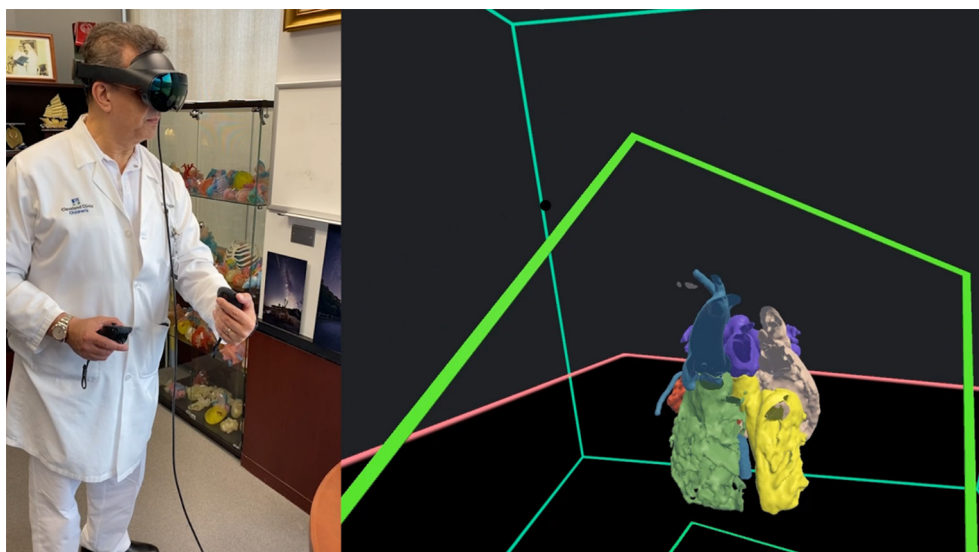
imaging variables in multicenter registries. The inclusion of more granular imaging variables with consistent definitions into large-scale databases will make the detection of potent imaging biomarkers more realizable.

Each of the modalities discussed is reliant on operator experience and comfortability of technologists, sonographers, post-processors, and clinicians. A critical mass of ACHD pathology is needed at a given center to produce expertise over time. Advanced education and institutional partnerships may help raise the level of performance by concentrating care at more competitive centers (36).

Computational fluid dynamics (CFD) is a mathematical technique to quantify and characterize fluid flow through anatomy using sophisticated software. CFD has been used to simulate blood flow through patient-specific 3D virtual models predominantly on a research basis (37-39), though viable commercial systems have emerged in recent years. For example, CT fractional flow reserve is an established method of simulating coronary flow using CFD an adult



**Figure 5** On left, a volume rendered image of a sinus venosus defect. The RUPV and RMPV drain into the SVC. The RA, RV, and MPA are also demonstrated. On the right, there is a surface rendered image of the systemic veins and atria, transected through the right atrium and at the mitral annulus. The relationship between the pulmonary vein orifice and the sinus venosus defect is demonstrated IVC. RUPV, right upper pulmonary vein; RMPV, right middle pulmonary vein; SVC, superior vena cava; MPA, main pulmonary artery; RA, right atrium; RV, right ventricle; A, anterior; H, head; L, left; F, foot; P, posterior; R, right; IVC, inferior vena cava.



**Figure 6** A cardiothoracic surgeon examines 3D heart model in virtual reality. A “cut-plane” is used to transect the model to examine the intracardiac relationships. 3D, three-dimensional.

coronary artery disease (40). This highlights the potential for practical clinical tools for assessing patient-specific blood flow in the ACHD population (7). For example, CFD has been used to simulate the blood flow in complex repairs such as in Fontan palliation, identifying modifiable areas of inefficient flow that may result in exercise differences (41,42).

Extended reality (XR; encompassing virtual, augmented, and mixed reality) is a method to transform real-world imaging data into a “digital twin” model for interaction

in a virtual environment. XR has been shown to improve surgical planning in patient undergoing workup for complex congenital heart disease repairs by creating a more intuitive experience for operators interacting with imaging data, as shown in *Figure 6* (43–47). Additionally, XR has been shown to aid in patient understanding of their own anatomy, particularly in patients transitioning from pediatric to adult congenital cardiology care (48). Lastly, artificial intelligence (AI) in imaging is a central area of interest and research in radiology and cardiology, using sophisticated computer



models trained on large datasets to perform tasks at or above human capacity (7). AI technology has been deployed into MRI scanners to enable more rapid imaging and post-processing software for automated image segmentation with a primary benefit of reducing analysis burden (49). AI models in adult cardiology have been created and successfully tested on multiple publicly available datasets of non-congenital heart disease (CHD) patients containing large numbers of scans, whereas the only publicly available MR dataset for CHD patients contains less than 100 subjects (50). As AI products are integrated into clinical workflows, special attention should be paid toward the false negative and positive disease detection seen in this population that may not be meaningfully represented in the training data.

## Conclusions

Multimodality imaging in ACHD is an imperative toolkit for patient management, offering a multifaceted view not attainable from single imaging techniques. A multimodal imaging approach provides information into the underlying physiology that, when synthesized by the cardiologist provides value that exceeds the sum of each constituent modality. An understanding of the advantages and disadvantages of each modality is needed to guide a diagnostic approach for each patient. As we advance into an era of personalized medicine, the integration of these imaging modalities will be pivotal in optimizing the care and outcomes of ACHD patients.

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