Abstract

Multidimensional blood flow imaging with magnetic resonance (MRI) has rapidly evolved over the last decade. The technique, often referred to as *4D Flow*, can now reliably image the heart and principal vessels of the chest in 15 minutes or less. In addition to dynamic three-dimensional flow visualization, a range of unique quantitative *hemodynamic markers* can be calculated from 4D Flow data. We will introduce some of the more promising of these hemodynamics markers including pulse wave velocity, pressure, turbulent kinetic energy, wall shear stress, and flow eccentricity.

Evaluation of a range of thoracic pathologies has been explored with 4D Flow and many applications have been proposed. We will review the potential clinical applications of 4D Flow in four broad contexts: the aorta, the pulmonary artery, acquired heart disease, and complex congenital heart disease. Promising preliminary results will be highlighted, including the use of abnormal systolic blood flow to risk stratify patients for progressive valve-related aortic disease, turbulent kinetic energy to directly assess of the hemodynamic impact of a stenotic lesion, and altered intracardiac flow to identify early heart failure. We will discuss ongoing research efforts in the context of the larger clinical goals of 4D Flow: the use of unique hemodynamic markers to 1) identify cardiovascular disease processes early in their course before clinical manifestation so that preemptive treatment can be undertaken, 2) refine the assessment of cardiovascular disease so as to better identify optimal medical or surgical

therapies and 3) enhance the evaluation and monitoring of the hemodynamic impact of different treatment options.

Introduction

Magnetic resonance imaging (MRI) is routinely used for assessment of the heart and great vessels. Precise anatomic imaging is the goal of most clinical evaluation. However with recent advances in phase contrast (PC) MRI, a range of hemodynamic analysis is now possible that better evaluates the fundamental purpose of the cardiovascular system: the effective and efficient pumping of blood to the lungs and the body. MR blood flow imaging is starting to be used clinically to augment traditional anatomic evaluation. The purpose of this review is to introduce advanced MR flow imaging and to discuss its application and potential benefits for thoracic imaging.

Conventional two-dimensional (2D) cine PC-MRI, also referred to as velocity-encoded cine (VEC) MRI, has several current applications in the chest. Its principal asset is that it allows reliable quantification of pathologies that are only qualitatively evaluated by echocardiography. Examples of this quantitative assessment include regurgitant fractions across incompetent valves, intracardiac shunt ratios (i.e., Qp/Qs), differential pulmonary blood flow, and coronary sinus flow reserve. Congenital heart disease may require a combination of these analyses, as well as other specialized applications for evaluation of complex anatomy and pathology.

Three-dimensional (3D) cine PC-MRI (*4D Flow*) affords several advantages over 2D cine PC-MRI. 4D Flow allows volumetric flow imaging in a single acquisition, whereas 2D cine PC-MRI is limited to a prospectively determined imaging plane. Abnormal flow that may not be initially apparent can be analyzed retrospectively from the volumetric dataset. Furthermore, complex blood flow is revealed as it unfolds in multiple dimensions over time. Flow related parameters, also referred to as *hemodynamic markers*, can be calculated to provide a fuller understanding of the pathological role of abnormal flow. While some of these parameters can be derived from 2D cine PC-MRI, 4D Flow allows for comprehensive analysis at any location within the dataset. We will discuss a range of hemodynamic markers and their potential clinical applications.

The clinical application of 4D Flow is not without challenges. Scan time has long been the major limitation, with scans taking upwards of one hour. However, an array of new techniques has greatly reduced scan time, with studies now routinely completed in 15 minutes or less. Examples of time-saving techniques include data undersampling in combination with parallel imaging and compressed sensing reconstructions.[1, 2] Other examples include alternative data acquisition approaches such as radial or spiral trajectories through k-space.[3] [4] Novel respiratory gating techniques and advancements in hardware such as high channel count receiver coils can further reduce scan time. Data processing is another significant challenge of 4D Flow. Reconstructing data, navigating complex 3D datasets, segmenting anatomic regions of interest and calculating hemodynamic parameters are currently time consuming and require

specific operator skills. Specialized software is required and is often cumbersome to use. Perhaps the most significant limitation, however, is the lack of proven clinical applications where 4D Flow outperforms other types of imaging. The identification of such applications can be expected to lead to the development of tailored analysis packages.

4D Flow MRI

4D Flow refers to time-resolved volumetric, three-directional PC-MRI. Whereas conventional 2D cine PC-MRI allows for mapping of velocity in a single prospectively chosen plane, 4D Flow enables complete evaluation of time-varying blood flow through a volume of interest. Typical spatial and temporal resolutions are about 1.5-3.0 mm and 35-60 ms, respectively. Hundreds of heartbeats are required for collection of a full 4D Flow dataset, making real-time or breath-hold acquisitions unfeasible. Data is acquired during free-breathing with respiratory gating employed to alleviate motion artifacts.

Only a fraction of the complete data set is acquired during each heartbeat. Data acquisition is synchronized to the cardiac cycle with ECG-gating to create a cine series of images. Prospective gating triggered at defined points in the cardiac cycle allows for different segments of k-space to be acquired individually until completely filled. However, prospective gating does not permit acquisition of a complete cardiac cycle and variability in cardiac cycle length limits the utility of prospective gating during late diastole. Retrospective gating, in contrast, allows

for complete coverage of the cardiac cycle. Image data and ECG-signal are acquired continuously and a full k-space is retrospectively assembled. In reconstruction, each acquired cardiac cycle is individually stretched to minimize the impact of beat-to-beat variations.

4D MRI Flow Visualization – Vector Plots & Particle Traces

There are various post-processing methods to visualize multidirectional blood flow data. Visualization techniques include vector plots or particle trace methods such as streamlines and pathlines.[5, 6] A vector plot is represented as arrows corresponding to velocity for points within a region of interest in the volumetric dataset, and is typically color-coded according to speed. Streamlines are lines plotted through a flow field at a single time point aligned tangent to the instantaneous velocity vectors. It should be noted that streamlines do not represent the actual path of blood flow. Such analysis must be performed with pathlines, which are calculated by integrating the vector field over time to demonstrate virtual particle trajectories. Pathlines have traditionally been colored according to flow speed, but alternative color-coding according to point of origin or departure can intuitively highlight specific flow features.[7, 8] Other visualization methods include isosurfaces or volume renderings, which are useful for visualizing scalar fields such as pressure, vorticity and turbulent kinetic energy (TKE).

Hemodynamic Markers

In addition to visualizing complex cardiovascular flow, 4D Flow data can be used to calculate a range of hemodynamic markers. The many opportunities for quantitative data analysis may be the principal clinical value of 4D Flow. Recent studies have started to explore the clinical utility of these hemodynamic markers in thoracic imaging for early identification of disease and risk-stratification for progression. In this section, we will introduce some of the more promising hemodynamic markers.

Hemodynamic Markers – Flow Volume

Flow volume is the most commonly measured hemodynamic variable, used for such things as quantifying stroke volume and shunt ratios. The clear advantage of 4D Flow is that assessment can be performed for any vessel within the volumetric acquisition. With conventional phase contrast analysis, in contrast, a specific vessel needs to be targeted prospectively at the time of imaging. Following segmentation of the vessel lumen, the flow rate at a given time point is calculated as the average through-plane velocity multiplied by the cross-sectional area of the vessel. The total volume of flow through a vessel is obtained by integrating flow rate over time.

Hemodynamic Markers – Flow Eccentricity

Normal flow in the ascending aorta and pulmonary artery exhibits a *parabolic* velocity profile with the highest velocity in the center of the vessel. Valvular and vascular disease has been shown to skew this velocity profile in many contexts, resulting in eccentric flow with high peripheral velocities. Quantification of this abnormal eccentric flow may identify patients at risk of pathological vascular remodeling. One quantitative approach for the ascending aorta is to measure the angle of eccentric blood flow between the left ventricular outflow tract and aortic root.[9] A simpler and potentially more robust approach is to measure the displacement of systolic flow relative to the vessel centerline.[10]

Hemodynamic Markers – Pulse Wave Velocity

Pulse wave velocity (PWV) is a measure of the rate of transmission of the systolic pulse through a vessel. It is calculated from the transit time of the systolic impulse wave over a known vascular distance. This can be performed with ultrasound (e.g., global carotid-femoral measurement) or MRI. Clear advantages of MRI are that it is not limited by the geometric assumptions of ultrasound and that regional analysis is possible.[11] 4D Flow affords some potential advantages including better estimation of PWV in tortuous anatomy, and has been shown to correlate well with conventional 2D approaches for estimating PWV.[12, 13]

PWV reflects vascular stiffness, which increases with age and numerous physiological, genetic and cardiovascular risk factors. It is an independent predictor of mortality and has been shown to have a better predictive value for cardiovascular events than Framingham risk factors.[14] In addition to this general cardiovascular risk-stratification, PWV has been reported to predict progression in specific disease states.[15, 16]

Hemodynamic Markers – Pressure

Pressure gradients are commonly employed to estimate severity of obstruction across a narrowed vessel or stenotic valve. Catheter based measurements are the gold standard, but are invasive. Imaging can be used to evaluate pressure by measuring the peak velocity associated with an obstruction and transforming it into an estimate of the peak pressure gradient using the modified Bernoulli equation. This analysis is typically performed with Doppler ultrasound, though MRI does offer advantages in anatomic regions where acoustic windows are limited.

More precise measurement of local pressure differences is now possible with MRI. Using the Navier-Stokes equation, the velocity vector field that 4D Flow provides can be used to calculate relative pressure differences and generate 3D pressure maps.[17, 18] One assumption of this approach is non-turbulent flow, which makes the technique of only limited value for many important obstructive lesions where turbulence is present, including valvular stenosis and aortic

coarctation. Intracardiac flow, however, has minimal turbulence and is thus a promising application for pressure mapping.

Hemodynamic Markers – Turbulence

Turbulence refers to chaotic flow with apparently random fluctuations in velocity. It stands in distinct contrast to the ordered, typically laminar flow of the normal cardiovascular system, and is seen with many forms of cardiovascular disease. 4D Flow has recently been extended to permit estimation of turbulence intensity and turbulent kinetic energy (TKE).[19, 20] The technique is based on a MRI signal model that describes how the distribution of velocities within a voxel is related to the overall signal amplitude.[21] Validation studies have demonstrated good agreement with reference methods.[19, 22] Turbulence mapping has potential for a range of applications including the identification of vascular regions at risk for endothelial cell damage and thrombus formation, and estimation of pressure loss in areas of vascular narrowing, valvular stenosis or regurgitation, as well as in patients with prosthetic heart valves.[20, 23]

Hemodynamic Markers – Wall Shear Stress

Wall shear stress (WSS) is the frictional force on the endothelium resulting from flowing blood. It is defined as the product of the dynamic viscosity and the near-wall velocity gradient, or wall shear rate. The near-wall gradients captured by 4D

Flow have been used to estimate WSS. MRI typically underestimates actual WSS due to limited spatiotemporal resolution as well as segmentation errors and partial volume effect.[24] [25] So while the absolute MRI measurements of WSS are of limited value, relative measurements may be of clinical use for identifying regions of abnormal hemodynamic stress. For example, a steep near-wall velocity gradient has been shown to result in a relative increase in WSS in the context of eccentric systolic flow with aortic valve disease.[26] [27] Areas of abnormal WSS have been shown to predispose to atherosclerosis, plaque rupture and vascular remodeling.[28, 29] [30]

Hemodynamic Markers – Flow Connectivity and Distribution

Pathlines have traditionally been used for dynamic flow visualization, but are also valuable for quantitative analysis of flow connectivity. As pathlines can be traced both forwards and backwards in time, they can unveil the point of departure (i.e., “where did you come from”) or destination (i.e., “where are you going”) for individual virtual blood particles. This can be used to classify various subcomponents of flow within complex regions such at the ventricles, or to determine the distribution of flow into branching vessels.[7, 8] [31] Streamlines should not be used for these purposes when there is pulsatile flow as they reflect the instantaneous flow field.

Clinical Applications

4D Flow can now reliably image the heart and principal vessels of the chest in a reasonable scan time. Evaluation of a range of pathologies has been explored and many clinical applications have been proposed. Promising preliminary results suggest that 4D Flow may play a unique role in better understanding how altered flow interrelates with adverse vascular remodeling and progression of cardiovascular disease. In this section, we will review potential clinical applications of 4D Flow in four broad contexts: the aorta, the pulmonary artery, acquired heart disease, and complex congenital heart disease. Emphasis will be placed on specific applications where quantitative flow markers have been correlated with key clinical endpoints.

Aorta

Aortic pathology is typically evaluated with computed tomography (CT) in the acute setting. MRI plays a role in surveillance imaging and can precisely determine aortic dimensions or the extent of aortic dissection without radiation exposure. The current anatomy-based approach to evaluating aortic disease, however, overlooks the considerable role that hemodynamics play in vascular homeostasis. Abnormal aortic flow may not just reflect anatomic alterations, but instead have a causative role in disease progression.

Valve-Related Aortic Disease

Ascending aortic disease has been linked to aortic valve disease through the long-observed phenomenon of *post-stenotic dilation*. A clear association between aortic and valve disease is recognized with bicuspid aortic valve (BAV), a common congenital abnormality seen in up to 2% of people. Aortic dilation is common with BAV, but the causal effect of hemodynamic factors remains unclear and there is considerable evidence of an underlying connective tissue disorder that contributes.[32] Abnormal flow patterns, however, are frequently seen with BAV.[26] While echocardiography is widely used for evaluation of BAV, MRI has a unique role in assessing these abnormal flow patterns and their hemodynamic impact on the ascending aorta.

4D Flow reveals characteristic alterations in aortic flow with BAV that are seen even in the absence of aortic aneurysm or stenosis. Helical systolic flow in often seen with peak velocities peripherally and relatively lower velocities at the vessel center. This flow pattern is associated with eccentric systolic flow jets that result in focal wall shear stress alterations where aneurysms are known to form with BAV.[27, 33, 34] Different jet orientations have been identified that correlate with type of valve leaflet fusion.[26] These findings contribute to the understanding of valve-related aortic disease and the broader significance of abnormal flow patterns. They suggest a new risk stratification tool based on 4D Flow for identifying patients at risk for development or progression of aortic dilatation and possibly dissection with BAV and aortic valve disease in

general.[33] Preliminary data show a good correlation between the degree of eccentric systolic flow with BAV and progressive aortic dilation.[34]

Aorta – Coarctation

Aortic coarctation refers to a congenital aortic obstruction, typically at the aortic hiatus. Patients need lifelong surveillance imaging due to the high rate of complications even if the lesion is successfully repaired. MRI has become the imaging modality of choice for aortic coarctation as it offers both anatomic and functional assessment without ionizing radiation. Minimal cross-section area is the best anatomic variable for predicting a significant coarctation. Functional assessment includes estimation of pressure gradients with the modified Bernoulli equation, collateral flow calculation and assessment of flow versus time profiles in the descending aorta. Collateral flow develops to maintain distal perfusion beyond the coarctation through vessels that bypass the obstruction. Collateral flow is quantified by comparing flow immediately distal to the coarctation to that at the level of the diaphragm. Normal flow should drop over this interval as blood exits through intercostal vessels, but will increase if collateral flow is present.[35] Flow versus time profiles can also be useful for identifying a significant coarctation. Delayed return of flow to baseline after systole with persistence of flow into diastole is indicative of hemodynamically significant obstruction.[36, 37]

The utility of 4D Flow evaluation in the setting of aortic coarctation has been demonstrated prior to and following endovascular or surgical repair.[38]

4D phase contrast MRI correlates very well with conventional 2D cine PC-MRI in assessing collateral flow.[39] 4D Flow also offers information beyond flow quantification. Downstream abnormal flow patterns are seen including vortical flow in regions of post stenotic dilatation and marked helical flow with angulated aortic arch anatomy, which is associated with exercise-induced hypertension.[39, 40]

Marfan Syndrome

Marfan syndrome is an inherited connective tissue disorder. Degeneration of the aortic media places patients at substantially increased risk for aortic dilatation, dissection and rupture. Diseased segments of the aorta with Marfan syndrome have been shown to be measurably stiffer using pulse wave velocity (PWV). Moreover, PWV can predict progressive aortic dilatation and assess treatment response.[15, 41, 42]

Medical treatment typically includes β-adrenergic blockers, which can slow the rate of aortic dilatation and complications, presumably by reducing the impact of hemodynamic drivers of disease.[43] Abnormal flow patterns have been observed in Marfan patients at relatively early stages of disease using 4D Flow, but have yet to be incorporated into a coherent model of disease progression.[44] 4D Flow has a distinct advantage for evaluation of Marfan patients in being able to measure the local or regional PWV in addition to other regional hemodynamic markers. The detection of focally increased PWV and/or altered systolic flow may

identify patients at elevated risk for aortic dilatation and dissection, as well as better monitor for treatment response.

Aortic Dissection

Type A aortic dissection is an emergency requiring surgical management. There is little role for MRI or complex flow imaging. However, Type B dissection is commonly managed medically with frequent surveillance imaging and variable clinical outcome. Currently, aortic size is the main imaging parameter used to guide intervention in patients with Type B dissection. Other imaging features may be important as well. For example, partial false lumen thrombosis is associated with poor prognosis. It is thought to restrict outflow from the false lumen and result in higher pressures and consequently increased disease progression.[45] Given the implication that hemodynamics are central to disease progression in patients with chronic Type B dissection, 4D Flow could play a pivotal role in their clinical monitoring. Recently, complex flow features including the degree of helicity within the false lumen have been correlated with interval expansion rates.[46] This suggests a clear role for 4D Flow in identify patients at risk for aortic expansion and rupture that may influence the timing of intervention.

Pulmonary Artery

Pulmonary arterial hypertension (PAH) is associated with substantial morbidity

and mortality. The diagnosis has traditionally relied on invasive measurement of mean pulmonary arterial pressure. Pulmonary arterial size measurements alone by CT and MRI are unreliable for identifying PAH, necessitating the use of more advanced imaging approaches. Doppler echocardiography is commonly employed, however 2D cine PC-MRI has been shown to be more comparable with right heart catheterization than echocardiography in estimating pulmonary flow including pulmonary artery stroke volume and systolic pressure.[47]

The pulmonary artery stiffens with PAH. This stiffness can be quantified with MRI using a range of measurements including pulsatility and compliance.[48] The reduced vascular compliance along with pulmonary artery dilatation contributes to retrograde pulmonary arterial flow seen in PAH. While a small amount of retrograde pulmonary flow is normal, PAH retrograde flow is substantial and predictably occurs earlier in the cardiac cycle. The timing of retrograde flow can effectively identify pulmonary hypertension and estimate the mean pulmonary arterial pressure.[49]

4D Flow can extend analysis of PAH beyond vessel stiffness and the timing and extent of regurgitant flow. Abnormal and characteristic complex flow patterns have been demonstrated in PAH. Systolic vortex flow in the main pulmonary artery is strongly correlated with manifest PAH, and the duration of vortical flow correlates with resting mean pulmonary artery pressure.[50] Additionally, diastolic flow duration along the anterior main pulmonary artery post pulmonary valve closure has been reported to be significantly longer in PAH than in latent PAH.[50] With visualization and quantification of these additional flow

features, serial 4D Flow may be able to monitor patients and detect disease progression in a way not possible with other modalities. This could be useful for guiding medical therapy and assessing treatment response.

Cardiac

Intracardiac blood flow patterns are complex and depend on many factors: the function of cardiac valves, myocardium, thoracic vessels, as well as the cardiac rhythm and 3D chamber geometry. Altered flow patterns can be demonstrated by echocardiography and MRI. However, echocardiography is limited by acoustic windows and to the assessment of flow in a single dimension. 2D cine PC-MRI is limited to the plane of acquisition and does not do justice to 3D flow features. 4D Flow affords a clear advantage in this regard, and has shown promise for the evaluation of valvular regurgitation and stenosis, as well as different forms of heart failure.

<u>Valve Disease</u>

Conventional 2D cine PC-MRI assessment of the cardiac valves is challenging. The valves move considerably during the cardiac cycle, requiring correction for through-plane valve motion. This is particularly true of the mitral and tricuspid valves. Retrospective 3D valve-tracking using a volumetric 4D Flow dataset can mitigate the effects of this motion. Good accuracy has been

demonstrated for mitral and tricuspid flow measurements, and simultaneous evaluation of all 4 valves has been proposed with a single acquisition.[51, 52] Another approach for evaluation of valve regurgitation that inherently accounts for motion is assessment of the associated flow turbulence. For example, the elevated turbulent kinetic energy (TKE) seen in the left atrium with mitral regurgitation has been shown to be proportional to regurgitant volume.[53]

Clinical assessment of valve stenosis also relies heavily on hemodynamic assessment. For aortic stenosis, maximum velocity, transvalvular gradient and continuity equation estimation of valve area are routinely studied with echocardiography. MRI has proven useful for estimation of the effective orifice area (EOA). A jet shear layer detection method using phase-contrast MRI data avoids the need for stroke volume measurements, and has been shown to be less variable than other approaches for EOA estimation.[54] The pressure loss caused by a stenotic valve is typically performed using the modified Bernoulli equation and the peak measured post-stenotic velocity. MRI compares well with echocardiography in this regard.[55] However, the modified Bernoulli equation is designed to estimate the peak pressure gradient rather than the true irreversible pressure loss. Consequently, it often misclassifies the true hemodynamic severity of a stenosis. MR-measured TKE has been show to correlate with irreversible pressure loss in aortic stenosis, and may represent the most direct means of measuring the true hemodynamic impact of a stenotic lesion.[23]

Heart Failure

Heart failure is a broad term that refers to the condition where the heart is unable to pump sufficient blood to meet the body's needs. It is associated with abnormal intracardiac blood flow.[56, 57] Quantitative analysis of intracardiac flow abnormalities can be achieved with 4D Flow. Such analysis may help fine-tune the identification and monitoring of these patients and direct efforts to restore efficient flow. For example, the blood that transits the left ventricle (LV) or right ventricle (RV) can be separated into four different functional components: 1) *direct flow* which enters and exits during a single heartbeat, 2) *retained inflow* which enters but does not exit, 3) *delayed ejection flow* which starts inside and exits on the subsequent heartbeat, and 4) *residual volume* that resides in the ventricle for more than one cardiac cycle.[8, 31, 58] Investigation of the relative percentages of these flow components, as well as the kinetic energy and momentum of the components, may allow for a refined analysis of the dynamics of ventricular filling and ejection.

Application of this analysis in patients with compensated heart failure has shown that 4D Flow can identify flow differences not seen with conventional hemodynamic assessment. Not only is the *direct flow* percentage diminished, but also the kinetic energy of the *direct flow* at end diastole is reduced. As a consequence, an increased workload is placed on the left ventricle to eject the same stroke volume.[59] These unique 4D Flow markers of inefficient intracardiac flow may have a role beyond the early identification and monitoring of cardiac dysfunction. They could also influence pacing strategies or heart rate targets where diastolic-systolic coupling is diminished. Furthermore, analysis of

the *residual volume* including its regional distribution and degree of stasis may be helpful in identifying areas prone to intra-chamber thrombus.

Diastolic Dysfunction

Isolated diastolic dysfunction is another promising target for 4D Flow. In ischemic disease, diastolic ventricular relaxation is impaired prior to loss of systolic function. In fact, up to half of patients with heart failure have normal left ventricular ejection fractions.[60] Invasive means of diagnosing diastolic dysfunction are impractical, while echocardiography is limited by the variables discussed above. 2D cine PC-MRI can assess diastolic function by measuring trans-mitral inflow (including E/A wave peak ratio) and deceleration time, as well as pulmonary vein flow.[61]

4D Flow may extend this analysis by detecting other flow features indicative of diastolic dysfunction. 2D MRI flow studies have demonstrated identification of impairment of the inflow jet before the ventricular apex with diastolic dysfunction.[62] Studies with animal models suggest additional flow aberrations with more severe ventricular dysfunction. A combination of pressure field calculation and pathline visualizations has been used to demonstrate disruption of the normal apical pressure gradient and diminished apically directed flow in animals with ventricular infarcts.[63] Detecting such flow alterations with 4D Flow may help to better identify early ventricular dysfunction.

Complex Congenital Heart Disease (CHD)

Congenital heart disease imaging is challenging because of complex anatomy and physiology. Imaging after surgical repair is even more difficult and requires a familiarity with surgical technique. In this section we will discuss a few of the more common types of complex congenital heart disease for which flow evaluation is useful: single ventricle physiology with Fontan palliation, anomalous pulmonary venous return, and Tetralogy of Fallot (TOF).

Imaging CHD often requires a multiple modality approach. Catheter angiography is often required, but is invasive and requires iodinated contrast and ionizing radiation. Echocardiography is almost universally used, but is restricted to available acoustic windows and has limited quantitative abilities compared to MRI. CT provides excellent anatomic assessment at the expense of radiation, but offers limited functional information. MRI is often employed for complex cases for its combination of anatomic and functional assessment. Flow quantification with conventional 2D cine PC-MRI typically requires multiple acquisition planes, which can be challenging, tedious and time-consuming. 4D Flow can comprehensively resolve complex blood flow in a single acquisition allowing the visualization and retrospective characterization of hemodynamic flow patterns otherwise not possible.[64] Capturing all flow data in a single acquisition has been shown to be faster than conventional 2D cine PC-MRI for the measurement of flow volumes in complex heart disease.[65] Furthermore, the 3D visualization of cardiac and

vascular anatomy and its relationship to thoracic structures may benefit in surgical planning and follow up.[66]

CHD – Fontan Circulation

In cases of complex CHD where only one functional ventricle exists, a Fontan palliation is often performed. The single functional ventricle is used to pump systemically, and systemic venous return is shunted directly to the pulmonary arteries via a total cavopulmonary connection (TCPC). Without the coordinated pumping of the right ventricle to deliver blood to the pulmonary arteries, some very complex flow patterns can develop. 4D Flow has proven very useful for visualizing the Fontan circulation.[67] [7, 64] Variable flow patterns are seen and correlate with the specific surgical technique used.[7, 64, 68]

4D Flow offers a comprehensive method for the evaluation and surveillance imaging of patients with Fontan anatomy. Fontan circulation is dynamic, changing over the life of the patient. Those with suboptimal Fontan hemodynamics demonstrate decreased IVC and progressively increased SVC flow.[69] The major potential of 4D Flow may lie in the assessment of differential pulmonary arterial flow. Determination of superior and inferior caval contribution of flow to each pulmonary artery can be achieved by quantitative pathline analysis.[7] Unequal distribution of blood flow is associated with pulmonary arteriovenous malformations in the lung that receives little IVC flow. Automated

quantification of the caval contribution of flow could augment the postsurgical evaluation of Fontan patients.

CHD – Shunts and Anomalous Pulmonary Venous Return

Echocardiography is commonly the first line investigation for shunts, with PC-MRI used as an adjunct modality for certain shunts that are difficult to see by echocardiography, and for its quantitative abilities. PC-MRI evaluation of flow dynamics commonly involves the calculation of pulmonary to systemic shunt ratios (Qp/Qs). A shunt ratio greater than 1.5 usually requires intervention.

4D Flow has been shown to identify intracardiac shunts with accuracy equal to echocardiography, and better than 2D cine PC-MRI. Extracardiac shunts can also be identified with sensitivity equal to that of echocardiography.[70] 4D Flow may have a unique role in the evaluation of complex, multilevel shunts. Quantification of each individual component of flow has been described with 4D Flow in the setting of anomalous pulmonary venous return and atrial septal defect (ASD).[71] Total and partial anomalous pulmonary venous return can be identified by MRI with depiction of both anatomic detail and shunt quantification. Compared to conventional MRI, 4D Flow allows for anomalous venous distinction from adjacent vessels without contrast and provides characterization of flow patterns, as well as the standard anatomic and shunt information.[72]

CHD – Tetralogy of Fallot

Tetralogy of Fallot (TOF) is the most common cyanotic congenital cardiac defect. MRI is routinely used for monitoring patients after surgical repair. Analysis includes assessment of right ventricular volumes and function, as well as quantification of pulmonary stenosis and regurgitation. Additionally, asymmetric pulmonary flow can be quantified, and may prompt endovascular intervention for pulmonary stenoses. 4D Flow has been used to characterize abnormal flow patterns throughout the right ventricular outflow tract and pulmonary circulation after surgical repair.[73, 74] Even in patients without residual pulmonary stenosis after repair, elevated peak systolic velocity and abnormal vortex flow in the main pulmonary artery have been demonstrated.[73] Given the previously demonstrated correlation between vortex flow and pulmonary hypertension, the presence of vortex flow in the TOF repair may offer a new risk stratification parameter beyond right ventricular function.

Summary of Future Prospects

4D Flow MRI is a rapidly advancing technique with great clinical potential. New acceleration techniques allow for data acquisition in 15 minutes or less. Complex flow visualization is evolving with consensus developing about the best ways to characterize abnormal flow features. A range of quantitative hemodynamic markers can be calculated that extend the diagnostic possibilities of the technique. Focused clinical applications are being explored with encouraging

preliminary results. 4D Flow evaluation of intracardiac flow may aid the diagnosis of diastolic dysfunction and early systolic heart failure. Valve-related aortic disease is another promising application with the degree of eccentric systolic flow shown to correlate with progressive aortic dilation in patients with BAV. Larger studies are needed to convincingly demonstrate the unique abilities of 4D Flow. One goal is to refine the assessment of cardiovascular disease so as to better identify responders to specific medical or surgical therapies. Another goal is to identify cardiovascular disease processes early in their course so that pre-emptive treatment can be undertaken.

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