Pediatr Cardiol (2010) 31:1244–1248
DOI 10.1007/s00246-010-9782-x

CASE REPORT

4D Phase-Contrast Flow Cardiovascular Magnetic Resonance: Comprehensive Quantification and Visualization of Flow Dynamics in Atrial Septal Defect and Partial Anomalous Pulmonary Venous Return

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Received: 7 July 2010 / Accepted: 12 August 2010 / Published online: 17 September 2010

Abstract The case of an 8-year-old girl with atrial septal defect and associated anomalous pulmonary venous return is presented to illustrate the advantages of four dimensional flow (4D flow) over the current two dimensional flow (2D flow) in terms of time efficiency, easy planning, accurate and individual quantification of the blood sources contributing to the left-to-right shunting from one single acquisition, internal validation of flow measurement accuracy, possibility of reanalysis without rescanning in case of unexpected findings during the postprocessing, and comprehensive understanding of flow insight by use of particle tracing visualization.

Keywords Anomalous pulmonary venous return · Atrial septal defect · Cardiac magnetic resonance

Electronic supplementary material The online version of this article (doi:10.1007/s00246-010-9782-x) contains supplementary material, which is available to authorized users.

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Secundum atrial septal defects (ASDs) may be associated with partial anomalous pulmonary venous return [1]. Anomalous pulmonary venous drainage as an additional source of shunting in secundum ASD patients generally results in larger left-to-right shunting and greater risk for the development of pulmonary artery hypertension than observed in patients with only secundum ASD [7, 8].

Current planning for surgical correction usually relies on delineation of the cardiovascular morphology and shunting evaluation possible with cardiac magnetic resonance (CMR) [2]. Conventional two dimensional phase-contrast CMR (2D flow) is frequently used for shunting determination by subtraction of the pulmonary (Qp) to aortic flow (Qs), which yields the absolute amount of left-to-right shunting (Qp–Qs) [2]. The 2D flow also may depict the individual sources of shunt flow separately but at the expense of prolonged scan time. Therefore, such information usually is not obtained despite its relevance for surgical planning [3].

To illustrate an alternative concept of concise hemodynamic assessment by CMR, we present a case of a secundum ASD and partial anomalous pulmonary venous return for which we used a three-dimensional time-resolved, phase-contrast, flow-sensitive volume scan (four dimensional flow, 4D flow) covering the whole mediastinum. This report aims to prove the great potential of this novel 4D flow technique in the setting of multilevel pre-tricuspid left-to-right shunting in congenital heart diseases.

Case Report

An asymptomatic 8-year-old girl with suspicion of atrial-level shunting from a chest X-ray was referred to our pediatric cardiology unit for further workup. Her weight

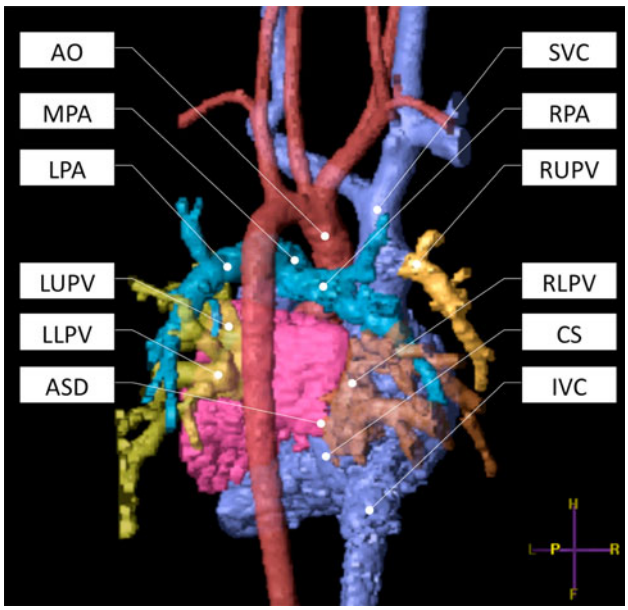

Fig. 1 Three dimensional anatomic shaded surface contrast enhanced magnetic resonance image. A posterior view of the cardiovascular segments where the 4D flow was assessed is shown. Note the partial anomalous right upper pulmonary vein return to the superior vein cava (SVC) and the position of the atrial septal defect (ASD). *AO* aorta; *CS* coronary sinus; *IVC* inferior vein cava; *LPA* left pulmonary artery; *LLPV* left lower pulmonary vein; *LUPV* left upper pulmonary vein; *MPA* main pulmonary artery; *RLPV* right lower pulmonary vein; *RPA* right pulmonary artery; *RUPV* right upper pulmonary vein

was 19 kg, and her height was 115 cm. Transthoracic echocardiography showed marked dilation of the right heart and pulmonary vessels due to an inferoposterior large secundum ASD but was unable to delineate fully the pulmonary venous drainage.

A CMR study performed with the patient under general anesthesia confirmed normal systemic venous connections to the dilated right atrium and the large secundum ASD. Findings showed left pulmonary veins draining to the left atrium. However, CMR demonstrated anomalous drainage of the right upper pulmonary vein to the superior vena cava (SVC) and of the right lower pulmonary vein to the right atrium (Fig. 1).

CMR Flow Scanning

The flow rates in the thoracic vessels of the reported patient were quantified using two different approaches, conventional 2D flow and a novel 4D flow sequence, to compare the results and relative merits of each approach.

2D Flow

Six separate free-breathing 2D phase-contrast magnetic resonance imaging (MRI) flow sequences (repetition time [TR], 4.4 ms; echo time [TE], 2.4 ms; flip angle, 10°; temporal resolution, 15–19 ms; spatial resolution, 2.5 × 2.5 × 6 mm; two numbers of excitation, velocity-encoded value, 100–250 cm/s as appropriate) were performed, with an overall total scan time of 16 min. The 2D flow quantitative analysis was performed on an extended MR Workspace, version 2.5.3.1 (Philips Medical System, Best, The Netherlands), and the results are shown in Table 1. The absolute amount of left-to-right shunt was indirectly calculated by subtraction of the pulmonary (Qp) to the aortic (Qs) flow.

Table 1 2D and 4D quantitation of flow dynamics and time results

	2D flow (l/min/m^2)	4D flow (l/min/m^2)
Pulmonary flow (Qp)[a]	6.54–6.85	6.20–6.40
Superior vein cava[b]	–	0.78
Inferior vein cava	–	0.80
Coronary sinus	–	0.18
Right upper pulmonary veins[c]	–	1.65
Right lower pulmonary veins	1.73	1.94
Atrial septal defect	–	0.85
Main pulmonary artery	6.85	6.30
Right pulmonary artery	3.93	3.79
Left pulmonary artery	2.61	2.61
Systemic flow (Qs)[d]	1.75–1.8	1.56–1.69
Left upper pulmonary veins[e]	2.61	1.25
Left lower pulmonary veins[f]		1.30
Aorta	1.75	1.56
Shunt flow		
Qp:Qs	(3.63–3.91):1	(3.66–4.10):1
Qp–Qs	4.74–5.1	4.51–4.81
Total scan time (min)	16:41	12:20

[a] 4D and 2D flow quantification expressed in l/min/m^2. Qp summarizes all the blood sources contributing to the pulmonary blood flow. Analogously, Qs lists the blood sources for the systemic flow

[b] The Qp interval is derived from the main pulmonary artery flow, the sum of the right and the left pulmonary arteries, and the sum of all the blood sources before the pulmonary valve (superior vein cava, inferior vein cava, coronary sinus, right pulmonary veins and atrial septal defect)

[c] The superior vein cava flow is calculated before the joining of the right upper pulmonary vein

[d] The 2D flow plane at the level of the right pulmonary veins to the atrium junction could not assess the right upper pulmonary vein

[e] The Qs interval is derived from the aortic flow and the net calculation of left pulmonary veins—atrial septal defect

[f] The left upper pulmonary veins could not be quantified independently in 2D flow because the plane was too close to the left atrium

4D Flow

The 4D flow scan used a free-breathing segmented k-space sequence with a TR of 4.8 ms, a TE of 2.7 ms, a flip angle

of 15°, a temporal resolution of 25 ms, and a spatial resolution of 2.5 × 2.5 × 2.5 mm. The protocol used only one number of excitation and a sensitivity encoded (SENSE) factor of 2 to achieve a scan time of 12 min covering the whole mediastinum. No respiratory motion correction was deemed necessary under conditions of general anesthesia. The velocity fields were mapped in the three spatial dimensions, with a velocity-encoded value set at 250 cm/s for each direction. The 4D flow data was analyzed on GTFlow, release 1.4.6 (GyroTools, Zurich, Switzerland) for quantitative and visual analysis, as described on the following discussion.

Quantitative 4D Flow Analysis

Free offline plane reformatting permits accurate quantification of through-plane flow in any vessels of interest within the scanned volume, no matter how tortuous this vessel might be. The relevant flow information in this case was obtained directly by interrogating 12 vessels of interest, as detailed in Table 1. This allowed for individual quantification of the shunting contribution (e.g. each pulmonary vein was separately assessed, as were the aortic and right and left pulmonary flows) and internal validation of flow measurements (e.g., right pulmonary artery [RPA] + left pulmonary artery [LPA] = main pulmonary artery [MPA]; SVC + inferior vena cava [IVC] = aortic flow; see Discussion section).

4D Flow Particle Trace Visualization

Particle traces are path lines that an imaginary particle would follow over time [12]. Each line represents the theoretical course that erythrocytes would follow within the given cardiovascular anatomy when the measured 4D velocity distribution information is applied. With a plane of interest selected, imaginary particles are released in the chosen cardiac phase and then followed through the cardiac cycle. Particles are released in both the systemic and pulmonary veins (Fig. 2 and additional Video 1), showing the sources of left-to-right shunting at three different levels: (1) from the right upper pulmonary vein to the SVC through the wall septal defect (Fig. 2a), (2) from the right lower pulmonary vein to the right atrium due to the malalignment of the interatrial septum (Fig. 2b), (3) from the left atrium to the right atrium shunt through the ASD (Fig. 2c). Increased pulmonary flow, quantified individually as shown Table 1, can thus be visualized in a more comprehensive way (Fig. 3), allowing a more intuitive understanding of the shunting pathophysiology (see additional Video 2).

Discussion

Multilevel pre-tricuspid shunting such as that with sinus venous or secundum ASD combined with partial anomalous pulmonary venous return may result in later development of pulmonary artery hypertension [9], atrial arrhythmia, and congestive heart failure [6]. Surgery involving redirection of the anomalous pulmonary venous flow to the left atrium and closure of the ASD is not exempt from risks such as late SVC or pulmonary vein stenosis and sinus node dysfunction [10]. Knowledge of the flow in the different vessels contributing to the left-to-right shunting may be helpful in surgical decision making to address whether the individual contribution to the total shunting flow justifies the risk of the chosen surgical repair method.

In the reported case, we used both 2D and 4D flow to assess hemodynamics. Good agreement of flow measures was observed between the two techniques, as shown in Table 1. However, the 4D flow approach proved to be

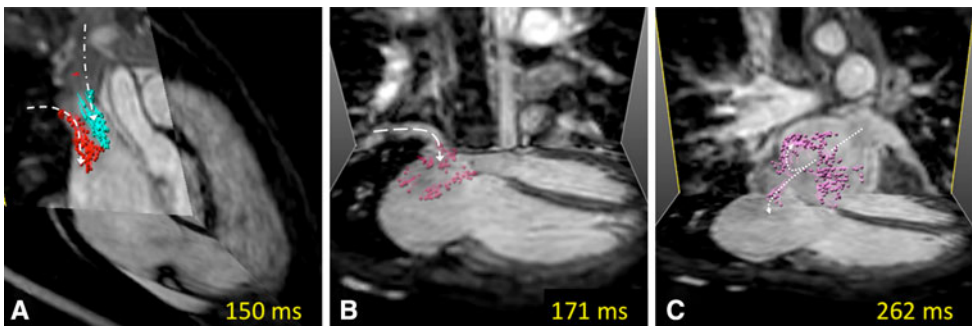

Fig. 2 Visualization of 4D flow particles. **a** Particles released in the superior vein cava (SVC, *turquoise, dash-dotted line*) and the right upper pulmonary vein (RUPV, *red, dashed line*). The left to right shunting is clearly visualized as the particles from the RUPV mix with the particles from the SVC and drain into the right atrium. **b** The particles released in the right lower pulmonary vein (RLPV, *deep purplish red, long-dashed line*) drain into the right atrium, contributing to the left-to-right shunting. **c** The particles released in the left pulmonary veins (*pink, dotted line*) hit the atrial septum but some of them shunt through the ASD to the right atrium (Color figure online)

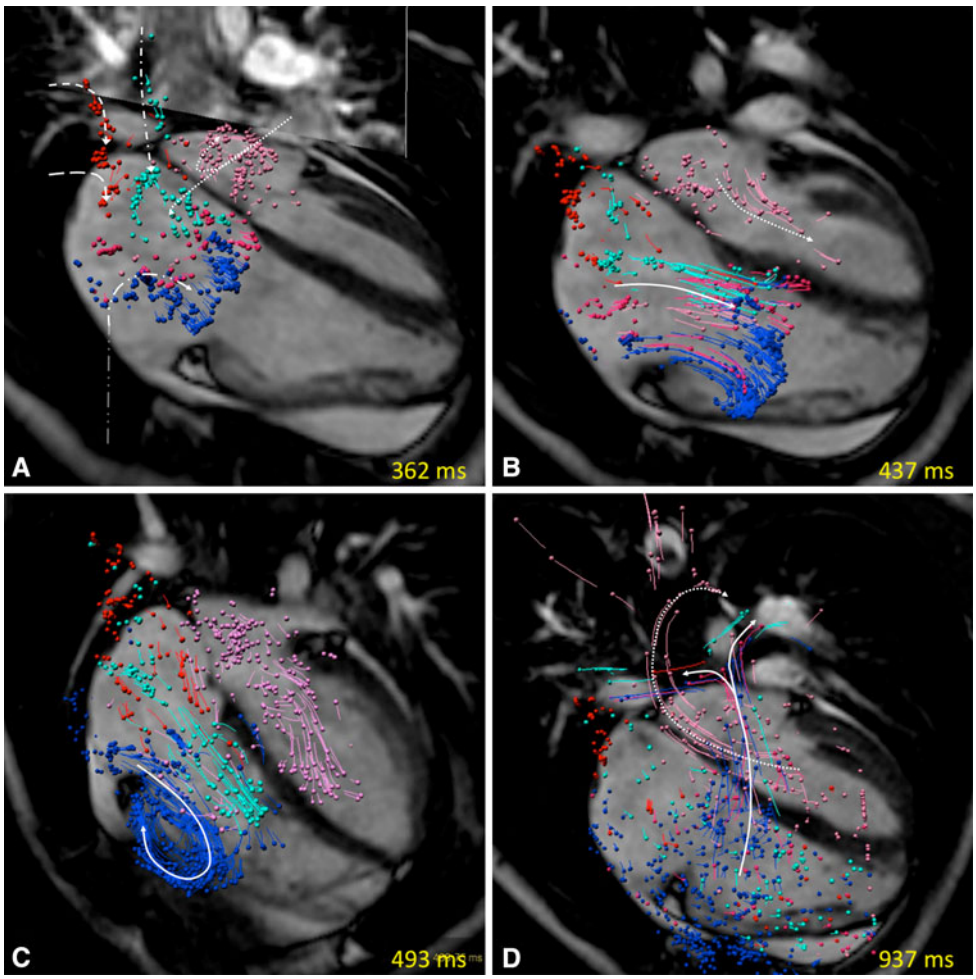

Fig. 3 Visualization of 4D flow particles during two consecutive heartbeats. **a** Ventricular diastole. Particles are released in the superior vena cava (SVC, *turquoise, dash-dotted line*), right upper pulmonary vein (RUPV, *red, dashed line*), right lower pulmonary vein (RLPV, *deep purplish red, long-dashed line*), inferior vena cava (IVC, *navy blue, dash-dot-dotted line*), and left pulmonary veins (*pink, dotted line*). **b** In the early diastole, a rapid ventricular filling occurs. **c** The left-to-right shunt results in a right-sided heart volume overload. Flow vortices contributing to the right ventricle remodeling may be first visualized in 4D flow. **d** During the subsequent heartbeat, the pulmonary flow overload is easily visualized as the mixing of desaturated (*bluish, solid line*) and saturated (*reddish, dotted line*) particles in the pulmonary arteries, whereas no desaturated particles are seen in the aorta (Color figure online)

much easier and more time efficient because it was able to yield direct quantification of shunting sources, internal validation, and unique information from particle tracing, all from a single scan, as shown in the following discussion.

Direct Quantification of Shunt Sources by 4D Flow

Direct quantification of the different sources contributing to the pulmonary overflow can be achieved by conventional 2D phase-contrast MRI, as previous studies have shown [4, 11]. However, this procedure is not performed routinely because the numerous scans required are difficult to plan, resulting in a prolonged scan time. In the reported case, this involved six 2D flow scans and a total scanning time of 16 min (Table 1). In contrast, the single 4D flow acquisition required less scanning time (12 min). Furthermore, the planning of the 4D flow scan was very easy and fast because it required only positioning of a sagittal volume box around the mediastinum containing the cardiovascular structures of interest (Fig. 1).

Internal Validation Using 4D Flow

From a single-flow scan, the total pulmonary flow (Qp), the total systemic output (Qs), and the left-to-right shunting can be internally validated for flow measurement accuracy, as shown in Table 2 [7].

Novel Findings During Offline Postprocessing

It is not unusual that during the offline analysis, new diagnostic findings in the anatomic pictures are discovered. For the reported patient, this was the case with the anomalous right upper pulmonary venous return to the SVC. With 2D flow, if the additional vascular anomalies are not identified at the time of the MRI scan, then retrospective reanalysis to determine flow within those vessels is not possible. In contrast, a 4D flow scan contains all the structures of interest within the scanned volume, and any new vessel plane can be analyzed easily offline, including retrospective reanalysis of the volume.

Table 2 Internal validation using 4D flow

Sources of blood flow	Flow (l/min/m^2)
Q_P = MPA = RPA + LPA = (RUPV + RLPV) + (LUPV + LLPV)	
MPA	6.30
RPA + LPA	6.40
(RUPV + RLPV) + (LUPV + LLPV)	6.14
Q_S = AO = SVC + IVC = (LUPV + LLPV) – ASD	
AO	1.56
SVC + IVC	1.58
(LUPV + LLPV) – ASD	1.70

From a single flow scan, the total pulmonary flow (Qp), the total systemic output (Qs), and the left-to-right shunt can be internally validated. The total left-to-right shunting (Q_P–Q_S) as determined by different arrangements of measurements of either Q_P or Q_S is approximately 4.51–4.81 l/min/m^2. This represents a shunting portion of 71% to 76% of Q_P and a Q_P/Q_S ratio of (3.7–4.1):1

ASD atrial septal defect; *AO* aorta; *CS* coronary sinus; *IVC* inferior vein cava; *LPA* left pulmonary artery; *LLPV* left lower pulmonary vein; *LUPV* left upper pulmonary vein; *MPA* main pulmonary artery; *RLPV* right lower pulmonary vein; *RPA* right pulmonary artery; *RUPV* right upper pulmonary vein; *SVC* superior vena cava

4D Particle Tracing

Additional particle tracing information provided by 4D flow may prove helpful for understanding the fluid–solid interactions possibly involved in the mechanics of right ventricle dilation, as can be intuited from the vortices generated in the right ventricular inflow (Fig. 3c). In general terms, understanding of intraventricular flow dynamics is likely to shed further light on mechanisms of ventricular remodeling and subcompartment adaptation to pathologic loading conditions. This may be even more useful in conditions such as those involving tetralogy of Fallot with chronic pulmonary regurgitation [5].

In summary, optimal planning of interventional strategies for patients with ASD and associated pulmonary venous return depends on accurate flow quantification and precise delineation of the anatomy. In our opinion, 4D flow shows advantages over the current 2D flow in terms of time efficiency and ease of planning, accurate individual quantification of the various sources contributing to the left-to-right shunting from a single flow scan, internal validation of flow measurement accuracy, possibility of reanalysis without rescanning in case of unexpected findings during postprocessing, and novel insights from particle-tracing visualization.

Acknowledgment This work was supported by EuHeart, Virtual Physiological Human network of excellence (FP7/2007-2013) under grant agreement no. 224495.

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