4D flow RM imaging: a new diagnostic tool for congenital heart disease

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Abstract: Purpose. To demonstrate the utility of 4D flow MR imaging for analyzing blood flow patterns and flow distribution in patients with congenital heart diseases. Methods: Six patients with congenital heart diseases were scanned using a standard cardiac MRI protocol, according to their condition. Additionally, 2D flow sequences of the great vessels, and a 4D flow sequence covering the entire heart were acquired. Flow patterns were visualized by using vector fields, streamlines and particle traces. Results: 4D flow technique depicted vortices and helical flow in the pulmonary artery of most patients, as well as in the aorta and superior vena cava of one patient with corrected aortic coarctation and a levoatrial cardinal vein. Conclusion: 4D flow MR imaging enables the identification of flow patterns difficult to detect with other diagnostic modalities. Comprehensive evaluation of flow patterns might help to understand the hemodynamic consequences of congenital heart diseases and their surgical procedures.

Keywords: 4D flow, Congenital heart defect, Flow patterns, Magnetic resonance imaging.

Resumen: Objetivo. Demostrar la utilidad de 4D flow para el análisis de patrones y distribución de flujos en pacientes con cardiopatías congénitas. Métodos: Seis pacientes con cardiopatías congénitas fueron escaneados con un protocolo de resonancia magnética cardíaca estándar. Además se incluyeron secuencias de flujo 2D en los principales vasos del tórax y una secuencia 4D flow que cubría todo el corazón. Para la visualización de los patrones de flujo se emplearon vectores de velocidad, líneas de flujo y trazadores de partículas. Resultados: 4D flow reveló vórtices y hélices en la arteria pulmonar de la mayoría de los pacientes, y en la aorta y vena cava superior de un paciente con coartación aórtica reparada y vena cardinal levoatrial. Conclusiones: 4D flow permite identificar patrones de flujo en pacientes con cardiopatías congénitas, difíciles de observar con otros métodos diagnósticos. La evaluación de patrones de flujo podría contribuir a comprender las consecuencias hemodinámicas de diferentes cardiopatías congénitas.

Palabras claves: 4D flow, Cardiopatía congénita, Patrones de flujo, Resonancia magnética.


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Introduction
Cardiac magnetic resonance (CMR) imaging is a useful complementary tool for the diagnosis of patients with congenital heart disease (CHD)(1). This technique has replaced other imaging modalities, thus becoming the gold standard procedure for assessment and/or monitoring of some CHD, such as Tetralogy of Fallot or single ventricle.
CMR imaging is an ideal diagnostic procedure for pediatric patients with CHD, since many of them present complex cardiovascular anatomies and require numerous tests to monitor their condition and treatment. The technique offers important advantages: it is noninvasive, uses neither ionizing radiation nor iodinated contrast media. It also allows an accurate analysis of anatomy and quantification of cardiovascular function and flows.
In CMR the most widely used technique for quantification of cardiovascular flows is the two-dimensional (2D) phase-contrast imaging. This method allows
velocity encoding of hydrogen protons (spins) present in the patient (particularly in the blood) through the application of bipolar magnetic field gradients\(^2\). These bipolar gradients transform the velocity of the spins. The magnitude of the observed phase is proportional to the area of gradients, the time required to application of gradients, and particularly, to the velocity of the spins. These gradients may be applied to encode velocity in any spatial direction. For cardiac blood flow quantification, a sequence perpendicular to the target vessel is usually acquired, with bipolar gradients applied in the same direction as slice selection gradients. Cardiovascular flow curves are obtained by selecting a region of interest in the desired vessel. The average velocity multiplied by ROI yields the amount of blood flow at a certain phase of the cardiac cycle. The total volume of blood flowing through that vessel during the cardiac cycle is obtained by adding blood flows registered during all stages of the cardiac cycle. This technique is widely used and has been validated in patients with CHD\(^3-4\). However, data acquisition is difficult; it requires an experienced user to determine the location of sequences, and if the plane is not completely perpendicular to the analyzed vessel, flows may be underestimated\(^5-6\). 4D flow technique is an extension of the 2D phase-contrast MRI that allows obtaining the velocity of the spins in all directions and throughout the complete cardiac cycle\(^7-9\). Although this technique has proven very useful for understanding certain cardiovascular conditions, it has not gained widespread application in clinical practice. This is mainly due to long data acquisition times, and to the difficulty in processing and interpreting data. In recent years, faster magnetic resonators along with exceptionally user-friendly image processing softwares have given this technique a renewed value as a useful method for understanding the dynamics of blood flow. Most investigations on blood flow have focused on the understanding of aortic hemodynamics under different conditions\(^3,10-13\). However, little research on the application of this technique in patients with CHD has been conducted.

The aim of this paper is to demonstrate the usefulness of the 4D Flow imaging method in analyzing blood flow patterns and distribution in patients with CHD.

**Material and methods**

**4D flow Technique**

4D flow technique involves applying consecutive bipolar gradients for velocity encoding in three orthogonal directions. Like in 2D phase-contrast MRI, it is necessary to define the maximum velocity expected in the volume to be encoded. This parameter, referred to as VENC, can be defined independently for each direction. It is very important to get an accurately defined VENC, because if it is less than actual velocities, velocity measurements will be distorted. By contrast, if VENC is much greater than the actual velocity, measurements will be less accurate\(^11\), since discrimination between slightly different velocity magnitudes will be hindered.

4D flow imaging method allows acquisition of two different types of images, i.e., an anatomical image and a velocity encoded image, which in turn reveals three flow directions in three separate images (Figure 1).

The 4D flow sequence may be applied either in a single slice or in one volume. Volumetric whole-heart sequence takes about 10 to 15 minutes, even when using rapid acquisition techniques such as k-t SENSE and kt BLAST\(^14\). A Despite the long acquisition time this method can provide hemodynamic information about both the whole heart and great vessels in a single scan\(^15\), under the same physiological conditions.

Four-dimensional (4D) flow of the whole heart allows a posteriori data reorganizion in any direction; therefore, it is feasible to quantify blood flows of all large vessels present in the volume acquired. In addition to blood flow quantification, 4D-flow sequences enable semi-quantitative evaluation of flow patterns such as vorticity or helicity, determination of blood trajectory, calculation of cardiac shunts due to arterio-venous connections, and estimation of the wall shear stress in large blood vessels\(^16\).

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**Figure 1.** (A) Anatomical image, and 3 velocity-encoded images in 3 directions (b) Left to right, (c) bottom to top (d) and anteroposterior view. Zero velocity appears medium gray, whilst positive and negative velocities (depending on the direction previously established) are proportionally encoded in light and dark gray, respectively.
Data Acquisition

To demonstrate the usefulness of this technique, 6 patients with CHD (4 men and 2 women, mean age 19.3 years, range: 10-46 years) were scanned with a 1.5T Philips resonator (Philips Healthcare, Best, The Netherlands). Each patient underwent the standard protocol for RMC according to type of pathology; in most cases this included 2D phase-contrast sequences of the great vessels of the chest: Aorta (Ao), pulmonary artery (PA) and its main branches (APD API), inferior vena cava (IVC) and superior vena cava (SVC). Additionally, in each patient a 4D-flow sequence of the whole heart and of mediastinal great vessels was obtained with the following acquisition parameters: 50 slices, excitation angle of 6°, 38 ms of temporal resolution, spatial resolution of 2.5 mm, and VENC = 200-350 cm / s.

Analysis and quantification

For analysis of blood flow patterns various graphic tools were used: velocity vectors, flowlines or streamlines and particle tracers (Figure 2). To this end, a GT Flow software (Gyrotools LLC, Zurich, Switzerland) was used.

Velocity vectors

This method allows visualization of the velocity component parallel to the image plane. This data representation is useful for local analysis of vortices\(^\text{17}\).

Flowlines or streamlines

They represent imaginary lines oriented according to the blood velocity field in a given cardiac phase\(^\text{18}\). These imaginary lines provide a 3D perspective of the velocity vector, enabling creation of maps of blood connection; however, it is a mere static representation.

Particle tracers

Particle tracers enable to visualize the path that blood takes along the cardiac cycle\(^\text{19}\). This technique involves selecting a plane of interest and then drawing a region of interest (ROI) in a vessel from which fictitious particles will be emitted, which will be followed throughout the cardiac cycle.

Results

Diagnoses of study patients were as follows: 1) Partial anomalous pulmonary venous drainage (PA-PVD), and interauricular communication; 2) repair of aortic coarctation, and levoatrial cardinal vein (abnormal venous connection between the left atrium and left brachiocephalic vein); 3) and 4) pulmonary atresia, status post one and a half ventricle repair with Glenn anastomosis 5) Fontan-type repair; and 6) Transposition of the great vessels, status post arterial switch operation.

4D flow technique revealed blood flow patterns as vortices and helices in the pulmonary artery in most of the patients, and in the superior vena cava of one patient with levoatrial cardinal vein. In velocity vectors (Figure 3a) flow patterns are seen in patients undergoing one and a half ventricular repair and Glenn-type anastomosis during three cardiac phases. By using particle tracers it is possible to observe that vortices and retrograde flows occur in the pulmonary artery. Connectivity Maps (Figure 3b) also enabled visualization of these vortices as well as blood flow distribution from pulmonary artery into its branches. Surprisingly, in both patients with Glenn anastomosis most of the flow from SVC is diverted into the PA trunk as well as into the right ventricle during diastolic phases (Figure 4).

In Figure 5, a helical flow in the SVC of patient with repaired coarctation of the aorta and levoatrial cardinal vein secondary to communication between the left atrium and left brachiocephalic vein may be observed. In the same patient, a turbulent aortic flow in the repaired coarctation area was also observed (Figure 5b and 5c). It has been suggested that blood flow patterns similar to those detected in the aorta of this patient could contribute to subsequent development of aortic aneurysms\(^\text{20}\).
Figure 3. (A) Velocity vectors showing blood flow patterns in a patient who underwent Glenn anastomosis. Such vectors reveal vortices (arrows in columns 1, 2, and 3) in the pulmonary artery (PA) and retrograde blood flow during diastole (arrow in column 4). (B) Connectivity maps also show vortices (indicated by the arrow in all columns), and blood flow distribution of left pulmonary artery (LPA) and right pulmonary artery (RPA).

Figure 4. In patients with one and a half ventricle repair and Glenn anastomosis it was found that blood flow from the superior vena cava (SVC) mainly drains into the pulmonary artery (PA) and right ventricle (RV).

Discussion

Whole heart 4D Flow MRI not only allows the quantification of cardiovascular flows, but also makes it possible to analyze the complex blood flow dynamics. Through velocity vectors, flowlines or streamlines and particle tracers a qualitative and quantitative analysis of flow patterns and their distribution in the cardiac chambers and great vessels of patients with CHD is feasible.

In this group of patients, 4D flow imaging technique evidenced the presence of vortices in PA and SVC in one patient with left atrial cardinal vein. Abnormal aortic vortices in patient with repair of aortic coarctation as well as in patient with arterial switch were also detected. An important drawback of 4D-flow technique is the compensation for respiratory motion, i.e., the process to prevent or correct generation of artifacts in MR imaging caused by patients breathing. Some authors have demonstrated that some techniques for minimizing distortions caused by respiration are compatible with 4D flow MRI. Nevertheless, most of these methods use a respiration-triggered scan, which implies discarding data obtained from incorrect respiratory positions and performing a new acquisition of data. Consequently, this technique involves a significantly increased scanning time. In some patients with stenotic areas of the PA or the Ao, it is necessary to define a fairly high VENC to prevent errors of velocity quantification. Nevertheless, this is detrimental to the accuracy of measurements in vessels exhibiting low blood velocity. In children with high heart rates, standard 4D-flow temporal resolution (~38 ms) might be insufficient to detect short-duration blood flow patterns. This could affect assessment accuracy during peak systolic velocity. Pediatric cardiac structures are smaller, so it is necessary to improve...
the spatial resolution (of 1.5 mm3), thus increasing the scanning time. This is especially necessary for visualizing pulmonary veins difficult to be identified due to their small size.

By adding the 4D-flow sequence to the clinical protocol, scanning time increases by 10 to 15 minutes, which added to the 30-minute data processing time might be incompatible with clinical practice. This appears to be entirely impractical with children in critical conditions, who require general anesthesia and mechanical ventilation.

Automation of definition of ROI of great vessels and cardiac chambers could reduce this time considerably, making 4D-flow and 2D phase contrast MRI comparable in terms of acquisition times. Thus, 4D-flow sequence could replace 2D sequences, and therefore total test time could be reduced (22).

Application of 4D-flow MRI in different CHD could help to understand the relationship between hemodynamics and the behavior of vascular walls, i.e., the possibility of understanding not only the relationship between patients with bicuspid aortic valve and development of aortic aneurysms (23), but also development of aneurysms in patients undergoing aortic coarctation repair (20, 24, 25).

It has been documented that some patients with single ventricle after Fontan surgery have had a poor outcome after surgery. Although this diagnostic procedure has been applied over the last four decades, it remains controversial which is the most efficient pulmonary connection from a hemodynamic point of view. In this case, 4D-flow technique could reveal blood flow patterns and distribution in order to clarify this issue (26).

**Future Prospects**

New research works and developments in 4D-flow technique promise major advancements in the understanding of cardiovascular hemodynamics.

It is necessary to fully understand blood flow patterns in healthy volunteers in order to understand the blood flow dynamics in patients with CHD. Most studies in this area have focused on the Ao (10), describing a great variety of blood flow patterns.

Although not shown in this work, 4D-flow MRI also enables estimation of other parameters associated with the cardiovascular system, e.g., wall shear stress in blood vessels (27), creation of blood pressure maps (28), and new ways to quantify the helicity and vorticity of blood flows (16).

In conclusion, the 4D-flow technique represents a breakthrough for the understanding of cardiovascular blood flow dynamics in patients with CHD. New advances in both data acquisition and processing could become an important contribution for implementation of this technique in day-to-day clinical practice.

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