Vessel Segmentation with 4D Flow MRI for the Characterization of Blood Mixing in Single Ventricle Patients after the Fontan Procedure

Kelly Jarvis[1], Susanne Schnell[1], Ramona Lorenz[2], Alejandro Roldan[3], Kevin Johnson[3], Maya Gabbour[4], Joshua D Robinson[4,5], Cynthia Rigsby[1,4], and Michael Markl[1]
[1]Radiology, Northwestern University Feinberg School of Medicine, Chicago, IL, United States, [2]Radiology, University Medical Center Freiburg, Freiburg, Germany, [3]Radiology and Medical Physics, University of Wisconsin School of Medicine and Public Health, Madison, WI, United States, [4]Medical Imaging and Cardiology, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, United States, [5]Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL, United States

Purpose and Target Audience: This study explores the use of 3D segmentation techniques in combination with 4D flow MRI analysis for the characterization and quantification of blood mixing at the Fontan connection in vivo. This information will be most beneficial to clinical and basic science researchers in the fields of congenital heart disease (specifically single ventricle physiology) and cardiovascular MRI with velocity encoding.

Introduction: Single ventricle physiology is one of the most severe forms of congenital heart disease. Patients undergo multiple surgical interventions including the Fontan procedure (caval venous return is routed directly to the pulmonary arteries). Despite apparent surgical success, some patients develop 'failing Fontan physiology'. Asymmetric distribution of protein-rich venous blood from the caval to the pulmonary system is suspected to cause arteriovenous malformations, leading to negative outcomes [1-2]. Previously, "blood mixing" at the Fontan connection (upper and lower venous blood distribution to the left and right pulmonary arteries) has been studied by visualizing particle traces from analysis planes in whole heart 4D flow MR data [3]. However, previous analysis techniques did not systematically constrain the analysis to the Fontan connection and were limited by artifacts due to partial volume effects and incomplete separation of neighboring vessels. In this study, we aim to isolate flow at the Fontan connection by integrating anatomical image segmentation into the 4D flow MR analysis work flow for improved flow visualization and mixing quantification.

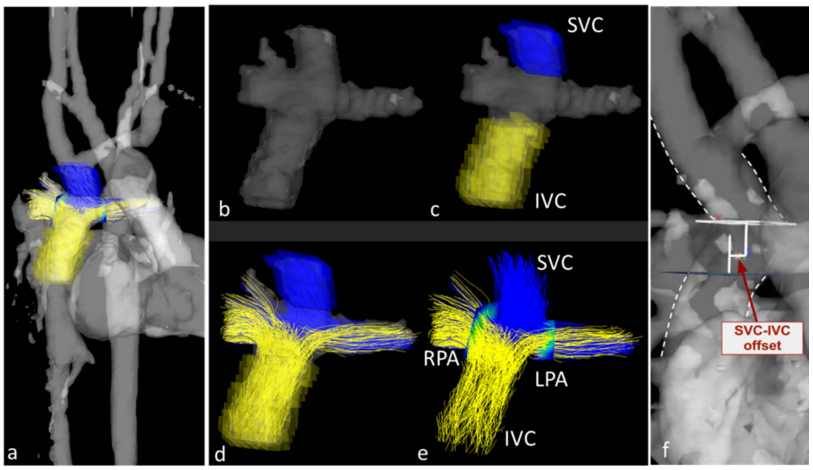

Figure 1 – 3D PC-MRA data (gray-shaded iso-surface in **a**) as derived from 4D flow MRI was used to segment the Fontan circulation (**b**) as well as sections of the IVC (yellow volume in **c**) and SVC (blue volume in **c**). Pathlines were generated from IVC and SVC volumes and color coded by vessel of origin (**d**). The number of intersections between pathlines and analysis planes positioned in the LPA and RPA were counted to quantify blood mixing (**e**). An example of SVC-IVC offset estimation is shown (**f**). All images are from subject 1.

Methods: 4D flow MRI (spatial resolution = 2.2-3.3 x 1.8-2.5 x 2.8-4 mm^3, temporal resolution = 38.4-40.8 ms) with whole heart coverage was performed at 1.5T and 3T systems (Avanto, Trio, Siemens, Germany) in 7 patients (3 females 4 males, age 17 +/- 7, range 5-26) with extra-cardiac Fontan circulation. Time-averaged 3D phase contrast angiograms (PC-MRAs) were calculated using 4D flow MRI data to provide an enhanced depiction of cardiovascular geometry as shown in the gray-shaded portion of figure 1a. From PC-MRAs, three segmentation volumes (Figure 1) were generated for the Fontan connection as well as each feeding caval vein (Mimics Innovation Suite, Materialise, Belgium). The Fontan segment was separated from the PC-MRA using a combination of user guided segmentation techniques. The Fontan segment was further manually separated into volumes for superior (SVC) and inferior (IVC) caval veins. All three anatomical 3D segmentation masks (SVC, IVC, Fontan connection) were exported and registered to 4D flow data for analysis. Time-resolved particle pathlines were generated from segmentation volumes in the caval veins to illustrate the spatial distribution and dynamics of blood flow to the left and right lungs (EnSight, CEI, USA). Blood mixing was quantified by the number of pathlines reaching analysis planes in the left (LPA) and right (RPA) pulmonary arteries (Matlab, The MathWorks, USA). In addition, SVC-IVC offsets were estimated by the distance between vessel centerpoints as a measure of Fontan geometry.

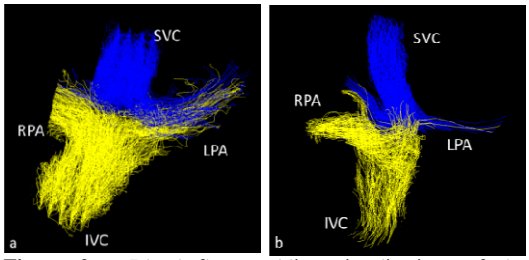

Figure 2 – Blood flow pathline visualizations of the segmented Fontan connection for asymmetric flow in (**a**) patient 4 and (**b**) patient 7. In both cases, flow from the IVC (yellow) is skewed toward the RPA. In patient 4, SVC pathlines (blue) tend toward the LPA; whereas in patient 7, SVC pathlines tend toward the RPA. Also in patient 7, flow pathlines to the LPA are few when compared to the RPA and are primarily from the SVC.

Results: The 3D segmentation successfully allowed for the specific assessment of Fontan hemodynamics compared to previously reported techniques. 3D visualization and quantification results for blood mixing at the Fontan connection varied substantially between patients (Table 1, Figure 2). Quantification of blood mixing showed that SVC flow was predominantly directed to the RPA in 3 patients, to the LPA in 2 patients and more evenly distributed (<20% difference) in the remaining 2 patients. For flow originating in the IVC, the situation was more homogenous and flow was primarily directed toward the RPA in 5 of 7 patients. Correlation analysis revealed a relationship between the asymmetry of flow distributions to the RPA and LPA (% difference in pathline distributions to RPA and LPA) and SVC-IVC offsets (IVC: r=0.74, p=0.06; SVC: r=0.42, p=0.34).

Conclusions: Integrating vessel segmentation into 4D flow MR provides an improved workflow that allows for a targeted evaluation of hemodynamics confined to the Fontan circulation. The analysis workflow developed in this study can be utilized in the future for vessel segmentations based on 2D or 3D CINE, combined with 4D flow velocity data. While the findings in this study did not confirm a statistical linear relationship between Fontan geometry (SVC-IVC offset) and blood distribution to the left and right lungs, results appear to be tending toward this relationship, particularly in the IVC. This study was limited by the number of subjects and the spatial and temporal resolution. In addition, SVC-IVC offsets are estimates and represent a simplified depiction of the Fontan geometry.

Patient Number	Blood mixing						Fontan geometry SVC-IVC Offset [mm]
	Flow originating in IVC			Flow originating in SVC			
	to LPA [%]	to RPA [%]	Diff [%]	to LPA [%]	to RPA [%]	Diff [%]	
1	21.2	78.8	57.7	45.2	54.8	9.5	5.4
2	43.1	56.9	13.8	40.9	59.1	18.1	1.8
3	15.4	84.6	69.2	12.7	87.3	74.7	2.5
4	36.4	63.6	27.3	87.6	12.4	75.3	3.4
5	13.7	86.3	72.5	98.3	1.7	96.6	10.2
6	97.6	2.4	95.2	0.7	99.3	98.7	8.3
7	1.4	98.6	97.1	32.8	67.2	34.3	7.9

Table 1 - For seven patients with Fontan circulation, the number of IVC and SVC pathlines reaching analysis planes in the LPA and RPA were normalized over the total number that reached either PA. The percent pathline distribution from the IVC and SVC to the LPA and RPA are shown as well as the offset estimation.

References: 1. Dasi LP, et al. *JTCS*. 2011;141:207-14. **2.** Shah MJ, et al. *Ann Thorac Surg*. 1997;63:960-3. **3.** Markl M, et al. *EJTCS*. 2011. 39:206-12.
Grant support by NIH R01HL115828, NUCATS Dixon Award