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Evaluation of blood flow distribution asymmetry and vascular geometry in patients with Fontan circulation using 4-D flow MRI

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Abstract

Background—Asymmetrical caval to pulmonary blood flow is suspected to cause complications in patients with Fontan circulation. The aim of this study was to test the feasibility of 4-D flow MRI for characterizing the relationship between 3-D blood flow distribution and vascular geometry.

Objective—We hypothesized that both flow distribution and geometry can be calculated with low interobserver variability and will detect a direct relationship between flow distribution and Fontan geometry.

Materials and methods—Four-dimensional flow MRI was acquired in 10 Fontan patients (age: 16±4 years [mean ± standard deviation; range 9–21 years]). The Fontan connection was isolated by 3-D segmentation to evaluate flow distribution from the inferior vena cava (IVC) and superior vena cava (SVC) to the left and right pulmonary arteries (LPA, RPA) and to characterize geometry (cross-sectional area, caval offset, vessel angle).

Results—Flow distribution results indicated SVC flow tended toward the RPA while IVC flow was more evenly distributed (SVC to RPA: 78%±28 [9–100], IVC to LPA: 54%±28 [4–98]). There was a significant relationship between pulmonary artery cross-sectional area and flow distribution

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Compliance with ethical standards

Conflicts of interest None

(IVC to RPA: $R^2=0.50$, $P=0.02$; SVC to LPA: $R^2=0.81$, $P=0.0004$). Good agreement was found between observers and for flow distribution when compared to net flow values.

Conclusion—Four-dimensional (4-D) flow MRI was able to detect relationships between flow distribution and vessel geometry. Future studies are warranted to investigate the potential of patient specific hemodynamic analysis to improve diagnostic capability.

Keywords

Cardiovascular magnetic resonance; Children; Congenital heart disease; Fontan; Four-dimensional flow magnetic resonance imaging; Heart

Introduction

Hypoplastic left heart syndrome and other disease constellations with a functionally univentricular circulation are among the most severe forms of congenital heart disease. These patients undergo a series of multistaged palliative vascular surgical procedures to achieve the Fontan circulation in which systemic venous return is routed directly to the lungs [1, 2]. The single ventricle physiology is characterized by the direct connection of blood flow from the inferior vena cava (IVC) and superior cava (SVC) to the left and right pulmonary arteries (LPA, RPA). Despite growing surgical success, it remains unclear why some patients go on to develop “failing Fontan physiology” while others remain asymptomatic [3–5].

Asymmetrical blood flow distribution at the Fontan connection is suspected to cause arteriovenous malformations in the lung vasculature, leading to negative outcomes. Several studies provide evidence for this mechanism and demonstrated that more evenly distributed delivery of hepatic venous blood directed to the left and right lung through the IVC results in decreased Fontan complications [6–9]. Blood flow at the Fontan connection has previously been studied in vivo by multiple techniques [10–15], including whole-heart 4-D flow MRI data [16–21] and computational fluid dynamics.

A number of studies based on in vitro flow models [22, 23] or patient-specific computational fluid dynamics [24–29] have shown that the surgically constructed Fontan connection geometry may be a major contributing factor to the resulting flow distribution. However, previous studies relied on model systems or did not include a complete assessment of Fontan geometry and flow in the same patient. Because this is a feasibility study, we were interested to test whether our newly developed methods can also detect these relationships. The aim of this study was thus to quantify both 3-D blood flow distribution and vascular geometry in vivo in Fontan patients based on a single 4-D flow MRI measurement. Three-dimensional pathlines, emitted from regions in the IVC and SVC, were employed for the quantification of Fontan flow distribution. In addition, 4-D flow derived 3-D phase contrast MR angiograms were used to assess parameters of Fontan geometry. We hypothesized that both flow distribution and geometry can be calculated with low interobserver variability and will detect a direct relationship between flow distribution and Fontan geometry.

Materials and methods

Study cohort

Ten patients (age: 16 ± 4 years [mean $\pm$ standard deviation; range 9–21 years]) with Fontan circulation (7 extracardiac, 3 lateral tunnel) were scanned using 4-D flow MRI from February 2012 to August 2015 (Table 1). The MRI interval from Fontan completion was 13 ± 4 years (mean $\pm$ standard deviation; range: 7–18) years). Institutional review board approval was obtained for this HIPAA-compliant study and informed consent was obtained from all participants for this prospective evaluation.

MR imaging

All measurements were performed using 1.5-T MRI scanners (Avanto and Aera; Siemens, Erlangen, Germany). All patients underwent standard-of-care cardiac MRI with administration of contrast agent (0.12 ml/kg gadofosveset trisodium; Lantheus Medical Imaging, Inc., North Billerica, MA), as well as electrocardiographic and respiratory navigator-gated 3-D time-resolved phase contrast MRI with 3-D velocity encoding (4-D flow MRI) [30]. Imaging parameters for 4-D flow MRI were as follows: spatial resolution= $1.9\text{--}3.6 \times 1.6\text{--}2.5 \times 1.9\text{--}3.3$ mm³, whole-heart coverage (field of view= $250\text{--}320$ mm $\times$ 180–280 mm, slab thickness=96–145 mm), temporal resolution=32.2–44.0 ms, TE=2.4–2.9 ms, TR=4.6–5.5 ms, flip angle=7–15°, bandwidth=455–800 Hz/pixel and velocity sensitivity (venc)=0.8–1.5 m/s. The use of GRAPPA with acceleration factor (R=2) was utilized for 6 patients and then k-t (spatio-temporal) GRAPPA (generalized autocalibrating partially parallel acquisitions) (R=5) became available for 4 patients [31, 32].

Data analysis

Preprocessing and 3-D segmentation of Fontan connection—Four-dimensional flow MRI data processing included corrections for Maxwell terms, eddy currents and velocity aliasing as previously described [33, 34]. To obtain a depiction of cardiovascular geometry, a time-averaged 3-D phase contrast angiogram (PC-MRA) was calculated [35]. Commercial software (Mimics Innovation Suite; Materialise, Leuven, Belgium) was used to generate a 3-D segmentation of the Fontan connection as shown in Fig. 1. The 3-D segmentation of the Fontan connection was applied as a mask to the measured 4-D velocity field and only voxels within the Fontan volume were considered for further analysis.

3-D blood flow visualization—To distinguish between flow from the upper and lower body, two subvolumes were separated from the Fontan volume for IVC and SVC flow emitter volumes (yellow and blue regions, respectively in Fig. 1). For 3-D visualization of Fontan hemodynamics, time-resolved 3-D pathlines were emitted from equidistantly positioned points within the IVC and SVC emitter volumes with a density of 30 emitter points per cm³. Three-dimensional pathlines were released into the velocity field masked by the Fontan volume to visualize the spatial distribution and dynamics of 3-D blood flow over two heartbeats, giving ample time for pathlines to reach both pulmonary arteries (Fig. 1) (EnSight; CEI, Apex, North Carolina, USA).

An interactive video of 3-D blood flow was visually assessed by two independent cardiovascular MRI physicians, blinded to each other's grading results (C.K.R. with 15 years and J.D.R. with 7 years of experience in cardiovascular imaging, respectively). General findings were noted and locations of vortex flow were reported where spinning flow patterns were present. Qualitative caval flow distributions to the LPA and RPA were rated on a scale of 0%–100% in 10% increments. Preferred caval flow was determined by the flow asymmetry or difference between flow distribution to the left and right with absolute difference 20% considered a visually evident split (60%:40% or 40%:60%) and preferential RPA/LPA or LPA/RPA flow ratio of 1.5. Comparably, previous MRI studies [15, 18] have shown average total pulmonary blood flow splits favoring the RPA with RPA/LPA flow ratios of 1.2 to 1.7. To enable this assessment, the interactive video allowed for IVC or SVC flow to be shown as animated (for noticing vortex flow) or static (showing all generated pathlines, for determining preferential flow).

Blood flow distribution quantification—Analysis planes were placed in the LPA and RPA (Fig. 1) and flow distribution (d) was quantified by counting the number of pathlines (p) reaching the specified destination plane (LPA or RPA) normalized to the total number reaching both planes over the course of two heartbeats (Matlab; The MathWorks, Natick, Massachusetts, USA).

$$d_{IVC_LPA} = \frac{p_{IVC_LPA}}{p_{IVC_RPA} + p_{IVC_LPA}} \times 100\%$$

$$d_{IVC_RPA} = \frac{p_{IVC_RPA}}{p_{IVC_RPA} + p_{IVC_LPA}} \times 100\%$$

$$d_{SVC_LPA} = \frac{p_{SVC_LPA}}{p_{SVC_RPA} + p_{SVC_LPA}} \times 100\%$$

$$d_{SVC_RPA} = \frac{p_{SVC_RPA}}{p_{SVC_RPA} + p_{SVC_LPA}} \times 100\%$$

Data analysis – characterization of Fontan geometry

To assess Fontan connection geometry, the Fontan volume was interpolated to refine the intervals of the volumetric grid by a factor of 2. Next, a centerline calculation was performed using the fast marching distance transform [36] to extract vessel centerlines along the Fontan pathway (baffle or conduit carrying IVC flow), SVC, RPA and LPA as shown in Fig. 2 (Matlab; The MathWorks, Natick, Massachusetts, USA). The centerline of the Fontan volume was used to guide placement of analysis planes in the Fontan pathway, SVC, LPA and RPA, normal to the centerline and close to the Fontan connection (EnSight; CEI, Apex, North Carolina, USA). The RPA plane was placed in the proximal RPA. The LPA plane was placed in the neo-LPA (segment leftward of the Glenn and Fontan anastomoses and

proximal to the stump of the main pulmonary artery). The SVC plane was placed distal to the azygous vein insertion and proximal to the RPA anastomosis. The Fontan pathway plane was just proximal to the neo-LPA anastomosis. Based on vessel centerlines and analysis planes, the following measures of Fontan geometry were obtained:

Cross-sectional Area: The intersection between the LPA and RPA analysis planes and the Fontan volume determined the cross-sectional area (Fig. 2).

Caval Offset: The center of analysis planes was used to measure the offset between the SVC and Fontan pathway along the right-left and anterior-posterior orientations (Fig. 2). The offset was considered positive when the Fontan pathway was to the left and posterior of the SVC.

Vessel Angle: The centerline of the Fontan volume showed bifurcation points where the SVC and Fontan pathway centerlines divided into two branches. These bifurcation points, along with the center of analysis planes, were used to measure vessel angles (Fontan pathway-LPA, Fontan pathway-RPA, SVC-LPA, SVC-RPA) (Fig. 2).

Data analysis – interobserver variability

To test interobserver variability, plane placement by a second observer, blinded to findings from the first observer, was additionally performed for the calculation of metrics of Fontan geometry and the quantification of flow distribution. The observers were V.C. with 1 year and K.J. with 3 years' experience of 4-D flow MRI analysis, respectively. This study was performed in the first eight of ten patient data sets. The remaining two data sets were acquired after the initial observer study was completed. At that time, the second observer was no longer available to perform analysis.

Data analysis – comparison with net flow

To test the reliability of using pathlines to quantify flow distribution, net flow (Q) was measured at analysis planes in each Fontan vessel (SVC, IVC, RPA, LPA) and two comparisons were performed:

1. *Pathline based net flow vs. measured net flow*—the calculated net flow (QP) to each pulmonary artery, determined by flow distribution (d) and measured net flow (Q) in the IVC and SVC, was compared to the measured net flow in each pulmonary artery.
 - a. $QP_{LPA} = d_{IVC_LPA} \times Q_{IVC} + d_{SVC_LPA} \times Q_{SVC}$ vs. Q_{LPA}
 - b. $QP_{RPA} = d_{IVC_RPA} \times Q_{IVC} + d_{SVC_RPA} \times Q_{SVC}$ vs. Q_{RPA}
2. *Flow distribution from pathlines vs. flow distribution from net flow*—the contribution of the IVC and SVC were combined (as if they were one feeding vessel) and the flow distribution determined by pathlines ($d_{IVC,SVC}$ from the number of pathlines, p) was compared to the flow distribution determined by the measured net flow (dQ) for each pulmonary artery.

$$\begin{aligned} \text{a.} \quad d_{LPA} &= \frac{p_{IVC_LPA} + p_{SVC_LPA}}{p_{IVC_LPA} + p_{IVC_RPA} + p_{SVC_LPA} + p_{SVC_RPA}} \times 100\% \quad \text{vs.} \quad dQ_{LPA} = \frac{Q_{LPA}}{Q_{LPA} + Q_{RPA}} \\ \text{b.} \quad d_{RPA} &= \frac{p_{IVC_RPA} + p_{SVC_RPA}}{p_{IVC_LPA} + p_{IVC_RPA} + p_{SVC_LPA} + p_{SVC_RPA}} \times 100\% \quad \text{vs.} \quad dQ_{RPA} = \frac{Q_{RPA}}{Q_{LPA} + Q_{RPA}} \end{aligned}$$

Statistics

All numbers are reported as mean $\pm$ standard deviation [range]. Caval flow distributions to the RPA and LPA were compared using paired Wilcoxon signed-rank test. Interobserver agreement for the visual rating of flow distribution was evaluated using Cohen's kappa and agreement with quantitative measures assessed by Pearson's coefficient (r). To study relationships between flow distribution and geometry, linear regression was performed and relationships with $P < 0.05$ considered significant. To evaluate interobserver agreement for quantification of Fontan geometry and flow distribution, Bland-Altman analysis [37] was used to find the mean difference ($\bar{d}$) as well as limits of agreement ($\bar{d} \pm 1.96 * d_{std}$ standard

deviation of the differences). Also, average observer disagreement ($\frac{1}{n} \sum_{i=1}^n \left| \frac{d_i}{\text{mean}_i} \right|$) was calculated. All statistical analysis was performed using R: A language and environment for statistical computing (R Foundation for Statistical Computing, Vienna, Austria. <http://www.R-project.org/>).

Results

3D visualization of Fontan hemodynamics

Segmentation and blood flow visualization was completed in all patients and results are shown in Fig. 3. Images represent time-integrated 3-D pathlines (cumulative blood flow over two cardiac cycles for all released pathlines) originating from the SVC (blue traces) and IVC (yellow traces). See Supporting Video S1 for an example of time-resolved 3-D blood flow visualization.

Due to vortex flow in the SVC for patient 4 (Fig. 3), pathlines were generated from emitter volumes in the brachiocephalic veins (feeding the SVC), instead of the SVC volume, in order to ensure IVC flow entering the vortex was not counted as SVC flow. Flow was visualized using pathlines generated over three heartbeats for this patient to give additional time for vortex flow to reach either side. Patient 6 showed an additional vessel (a large hemiazygous vein) feeding the Fontan connection at a location close to the SVC and then draining predominantly to the LPA. Flow from the hemiazygous vein was tagged separately for flow visualization (shown in lighter blue in Fig. 3 and denoted as HA).

Flow distribution

Caval flow distribution results showed preferences in IVC flow: to the left in five patients, to the right in three patients and neither in two patients; and SVC flow: to the left in one patient, to the right in eight patients and neither in one patient. Therefore, among these patients, SVC flow distributions tended toward the right (RPA: $78 \pm 28\%$, LPA: $22 \pm 28\%$, $P = 0.04$) while IVC flow was more evenly distributed (RPA: $46 \pm 28\%$, LPA: $54 \pm 28\%$,

$P=0.69$) (Table 2). There was good agreement between observers for visually categorizing flow preference as left, right, or none ($\kappa=0.77$). Correlation analysis indicated excellent agreement between quantified flow asymmetry and visual ratings ($r=0.94$, $P<0.0001$). The observers qualitatively assessed IVC flow preference to opposite sides in one patient (patient 9). Both observers qualitatively assessed IVC flow preference to the opposite side of the measured value in one patient (patient 4).

Relationship between flow distribution and Fontan geometry

Vascular connection geometries varied among patients, as shown in Fig. 4. Linear regression analysis (Fig. 5) revealed a statistically significant relationship for IVC flow distribution to the RPA as a function of the RPA cross-sectional area (IVC to the RPA: $R^2=0.50$, $P=0.02$) and for SVC flow distribution to the LPA as a function of the LPA cross-sectional area (SVC to the LPA: $R^2=0.81$, $P=0.0004$). No other statistically significant relationships were found (Table 3). Potential trending relationships were found for caval offset as a function of caval flow distribution asymmetry (SVC: $R^2=0.35$, $P=0.07$) and SVC flow distribution to the LPA as a function of the angle between the SVC and the LPA ($R^2=0.36$, $P=0.06$). The remaining regressions showed P -values ranging from 0.25 to 0.86.

Interobserver variability

Results of the Bland-Altman analysis (Fig. 6) demonstrated good agreement for flow distribution, angle measurements and cross-sectional area with small bias between observers and an average observer disagreement of 5%, 2%, and 8%, respectively. Caval offset measurements showed a bias of 0.5 mm between observers and the average observer disagreement was 29%.

Comparison to net flow

Flow distribution reliability, evaluated by comparing *pathline based net flow vs. measured net flow* and *flow distribution from pathlines vs. flow distribution from net flow*, showed good agreement (Fig. 7) with small bias (0.3 ml/cycle and 2.3%, respectively). Correlation values were $r=0.99$, $P<0.0001$ and $r=0.91$, $P<0.0001$, respectively.

Discussion

Our study demonstrates the feasibility of 4-D flow MRI for the targeted evaluation of Fontan circulation hemodynamics including the visualization of complex blood flow patterns by emitting pathlines from IVC and SVC volumes, the quantification of blood flow distribution and the assessment of vascular geometry. The methods presented demonstrate low interobserver variability for flow distribution and geometry measures and good agreement when comparing flow distribution to net flow. These methods enable the comprehensive analysis of patients with Fontan circulation and the ability to detect relationships between flow and geometry.

Recent literature [25–28] for Fontan flow evaluation involves computational fluid dynamics modeling of blood flow, including 3-D patient-specific models of the vasculature and boundary conditions from phase contrast MRI. Instead, we employed 4-D flow MRI to

obtain three directional velocity components with volumetric coverage of the heart and surrounding vessels. While this approach requires longer scan times (average 10 min added to clinical scan) and has lower spatial and temporal resolution, visualization and quantification by 4-D flow MRI is based entirely on velocity data measured in vivo (e.g., pathlines are calculated directly from the acquired 3-D velocity data fields) and without the need for numerical flow simulation.

Previous work by Bachler et al. [20] utilizing whole-heart 4-D flow MRI included a validation study in healthy controls for using time-resolved 3-D pathlines emitted from regions of interest to quantify flow distribution. The results in our study extend those findings demonstrating good agreement in Fontan patients between flow distribution and net flow measurements and between observers. Previous MRI studies have found IVC flow preference to the LPA and SVC flow preference to the RPA [12, 20]. Similarly, we found more patients with IVC flow preference to the LPA than to the RPA and with SVC flow preference to the RPA than the LPA. Also, SVC flow showed a significant trend toward one side versus the other among patients. However, our results exhibited a wide range of values, emphasizing the need for comprehensive and individualized evaluation for patients with Fontan circulation.

Computational fluid dynamics studies [25, 28] have linked vessel size with blood flow characteristics at the Fontan connection. We also detected statistically significant relationships linking pulmonary artery size with flow distribution. Previous Xenon-133 perfusion, in vitro and computational fluid dynamics studies [11, 22, 27, 28] have implicated the importance of anastomosis side and caval offset in affecting flow distribution. Similarly, we found a potential trending relationship as the caval vessel moved farther to one side, so did the flow distribution asymmetry. When evaluating the association between flow and vessel angle, we hypothesized that we would find increasing flow directionality as the angle between the caval vein and the pulmonary artery increased toward 180°. And, we did find a potential trending relationship for the SVC-LPA angle. We are interested in understanding the nature of these relationships, such as why when there were two variables that were possibly correlated (SVC to LPA flow distribution vs. the LPA area and SVC to RPA flow distribution vs. the RPA area), that only one of them was correlated. We hypothesize the complex hemodynamics at the Fontan connection, with potentially vortex flow and colliding flow pathways, may contribute to this result. Thereby, SVC-LPA flow may correlate with LPA area but SVC-RPA flow may not correlate with the RPA area. Further study in a larger cohort is warranted.

Flow distribution visual ratings matched well with quantified values but the limitations of pathline visualization should be considered when interpreting flow distribution results. An overall approach involving both quantification and clinical visual assessment would be ideal. In addition to being susceptible to flow artifacts, pathline calculations are sensitive to the influence of measured velocity noise propagating throughout cardiac time steps [38]. In cases of large vortex formation and complex flow through long channels, there may not be enough pathlines reaching the desired analysis planes to make an accurate distribution assessment. This was the main reason for comparing our flow distribution results (determined by counting pathlines) to net flow as a validation step. In the future, this may be

further addressed by the systematic assessment of the influence of noise on pathline calculation and flow distribution quantification.

Even in this small cohort, vascular structure was highly variable, including patients with lateral tunnel and extracardiac Fontan connections, connections located close to pulmonary artery branches, additional feeding vessels and even dextrocardia. Nevertheless, the process for assessing flow distribution and geometry was highly automated, utilizing centerline calculation to reduce user-specific influence. As a result, the only measurement with sizeable differences between observers was the caval offset (on average 3 mm), limited by the spatial resolution of approximately the same size. Therefore, the average observer difference of the caval offset measurement is on the order of voxel size limiting the assessment of agreement to the spatial image resolution rather than to the interobserver difference. While it would be possible to achieve higher resolution by acquiring 4-D flow MRI with a smaller field of view, the benefit of imaging the entire volume is that the data can be utilized for comprehensive and retrospective assessment, instead of acquiring several 2-D phase contrast-MRI planes. This is particularly useful for patients with complex congenital heart disorders and multiple regions of pathology.

Analysis times are currently estimated to be between 2 to 4 h per patient. Variability in processing time depends mainly on the number of pathlines analyzed and the time needed for segmentation of the Fontan connection. Nevertheless, this is a limitation of the study. Future work is focused on improving and automating these new methods. It is encouraging that we can detect a wide range of flow distributions, as well as relationships between flow distribution and geometry, such that we may one day be able to systematically characterize variations in Fontan geometry and comorbidity with other heart defects. In the future, we would like to apply these methods to a larger cohort that may be divided into various homogenous groups for comparison.

Conclusion

Four-dimensional flow MRI enables the comprehensive and individualized analysis of complex flow pathways and vascular geometries in patients with Fontan circulation. Using these methods, we can detect relationships between flow distribution and Fontan vessel geometry. Further investigation in a larger cohort is needed to ensure reliability and to evaluate the ability of these techniques to improve diagnostic capability and patient care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Fig. 1.

Fontan blood flow distribution for patient 5, a 16-year old boy status post extracardiac Fontan. The Fontan volume was separated from the 3D PC-MRA and divided into IVC and SVC flow emitter volumes (a). Pathlines were emitted from the IVC and SVC volumes and color-coded by flow origin (b–d) with resulting pathlines shown with the 3-D PC-MRA (gray-shaded isosurface) for anatomical reference (e). The number of intersections between pathlines and analysis planes positioned in the LPA and RPA were counted to quantify blood flow distribution (f). A supplemental video of flow visualization is also provided (Supporting Video S1). *IVC* inferior vena cava, *LPA* left pulmonary artery, *PC-MRA* phase contrast MR angiogram, *RPA* right pulmonary artery, *SVC* superior vena cava,

Fig. 2.

To characterize vessel geometry in each patient (a) the centerline was calculated from the Fontan volume. Analysis planes (b) were placed normal to the centerline and close to the connection to find the center of the plane (for all vessels) and measure cross-sectional area (for pulmonary arteries). Caval offset (c) was measured by the distance in the RL or AP direction between the center of the Fontan pathway and SVC planes. Vessel angle (d) was measured for Fontan pathway-LPA, Fontan pathway-RPA, SVC-LPA and SVC-RPA using the center of analysis planes and the centerline bifurcation points. To illustrate, Fontan

pathway-RPA and Fontan pathway-LPA angles are shown. All images are of patient 1, a 20-year old male status post lateral tunnel Fontan. *AP* anterior-posterior, *FP* Fontan pathway, *LPA* left pulmonary artery, *RL* right-left, *RPA* right pulmonary artery *SVC* superior vena cava,

Fig. 3.

Three-dimensional blood flow visualization of the segmented Fontan connection (a–j: patients 1–10) in anterior (*left*) and posterior (*right*) views. Pathlines are color-coded by flow origin (yellow – IVC, dark blue – SVC, light blue – hemiazygous vein) feeding the Fontan connection. Areas of vortex flow are noted. *IVC* inferior vena cava, *LPA* left pulmonary artery *RPA* right pulmonary artery, *SVC* superior vena cava

Fig. 4.

Geometry results for (a–j: patients 1–10). Left: The centerline was calculated from the Fontan volume and the cross-sectional areas of the pulmonary arteries were measured. Right: Enlarged view of analysis points (green – vessel points and orange – bifurcation points) were used to measure vessel angle. Results are from observer 1. *FP* Fontan pathway, *HA* hemiazzygous arch, *IVC* inferior vena cava, *LPA* left pulmonary artery, *RPA* right pulmonary artery, *SVC* superior vena cava

Fig. 5.

Linear regression results. (a) SVC flow distribution to the LPA as a function of LPA cross-sectional area, (b) IVC flow distribution to the RPA as a function of RPA cross-sectional area, (c) SVC flow distribution to the LPA as a function of SVC-LPA vessel angle and (d) IVC and SVC flow asymmetry vs. caval offset RL. *IVC* inferior vena cava, *LPA* left pulmonary artery, *RL* right-left, *RPA* right pulmonary artery, *SVC* superior vena cava

Fig. 6.

Bland-Altman plots for the interobserver study for (a) flow distribution and (b–d) geometry measurements. Both the RL and AP caval offset measurements were included (b). All vessel angles (the Fontan pathway-RPA, Fontan pathway-LPA, SVC-RPA and SVC-LPA) were included (d). *AP* anterior-posterior, *FP* Fontan pathway, *LPA* left pulmonary artery, *obs* observer, *RL* right-left, *RPA* right pulmonary artery, *SVC* superior vena cava

Fig. 7.

Bland-Altman and correlation plots to test flow distribution values with net flow. **(a-b)**

Pathline based net flow vs. measured net flow and **(c-d)** flow distribution from pathlines vs. flow distribution from net flow. QP pathline based net flow, Q measured net flow, d flow distribution from pathlines, dQ flow distribution from net flow, d_{LPA} flow distribution to left pulmonary artery from pathlines, dQ_{LPA} flow distribution to left pulmonary artery from net flow

Table 1

Demographics and clinical history for patient cohort

Patient	Age	Sex	Clinical history
1	20	m	Tricuspid atresia, transposition of the great arteries s/p lateral tunnel Fontan
2	21	m	Congenitally corrected transposition of the great arteries, double outlet right ventricle s/p lateral tunnel Fontan
3	9	f	Pulmonary atresia with intact ventricular septum s/p extracardiac Fontan
4	17	m	Hypoplastic left heart syndrome s/p extracardiac Fontan
5	16	m	Situs inversus totalis, hypoplastic double outlet right ventricle s/p extracardiac Fontan
6	21	f	Heterotaxy syndrome, interrupted IVC with hemiazygous continuation to left SVC, double outlet right ventricle, unbalanced left ventricle dominant, atrioventricular septal defect s/p Kawashima operation and baffling of hepatic veins via lateral tunnel Fontan
7	13	m	Hypoplastic double outlet right ventricle, malposed great arteries, pulmonary atresia s/p extracardiac Fontan
8	11	f	Double-inlet left ventricle, pulmonary atresia with discontinuous branch pulmonary arteries s/p unifocalization, bidirectional Glenn and extracardiac Fontan
9	16	f	Tricuspid atresia s/p extracardiac Fontan
10	13	f	Double inlet single right ventricle with partial anomalous pulmonary venous return s/p Fenestrated extracardiac Fontan, subsequent fenestration closure

*f*female, *IVC* inferior vena cava, *m* male, *s/p* status post, *SVC* superior vena cava

Table 2

Summary of quantified results for flow and geometry

		Mean $\pm$ SD	[Range]
Flow distribution [%]	IVC to LPA	54 $\pm$ 28	4 – 98
	IVC to RPA	46 $\pm$ 28	2 – 96
	SVC to LPA	22 $\pm$ 28	0 – 91
	SVC to RPA	78 $\pm$ 28	9 – 100
Cross-sectional area [mm²]	LPA	170 $\pm$ 98	89 – 420
	RPA	222 $\pm$ 105	54 – 469
Caval offset [mm]	RL	3.7 $\pm$ 3.8	–1.1 – 12.3
	AP	–2.9 $\pm$ 4.3	–10.0 – 3.2
Inter-vessel angle [degrees]	FP to LPA	111 $\pm$ 26	67 – 163
	FP to RPA	97 $\pm$ 24	67 – 136
	SVC to LPA	95 $\pm$ 19	64 – 134
	SVC to RPA	106 $\pm$ 12	77 – 123

Results represent mean $\pm$ standard deviation for all patients. Measurements from both observers were averaged.

AP anterior-posterior, *FP* Fontan pathway, *IVC* inferior vena cava, *LPA* left pulmonary artery, *RL* right-left, *RPA* right pulmonary artery, *SD* standard deviation, *SVC* superior vena cava

Table 3

Flow distribution vs. Fontan geometry regression analysis

Flow Distribution Measure	Geometry Measure	R^2	P -value
% IVC to LPA	LPA cross-sectional area	0.01	0.78
% IVC to RPA	RPA cross-sectional area	0.50	0.02
% SVC to LPA	LPA cross-sectional area	0.81	0.0004
% SVC to RPA	RPA cross-sectional area	0.004	0.86
% IVC to LPA – % IVC to RPA	Caval offset RL	0.10	0.38
% SVC to LPA – % SVC to RPA	Caval offset RL	0.35	0.07
% IVC to LPA – % IVC to RPA	Caval offset AP	0.01	0.74
% SVC to LPA – % SVC to RPA	Caval offset AP	0.02	0.70
IVC to LPA	IVC-LPA	0.03	0.64
IVC to RPA	IVC-RPA	0.007	0.82
SVC to LPA	SVC-LPA	0.36	0.06
SVC to RPA	SVC-RPA	0.16	0.25

AP anterior-posterior, *FP* Fontan pathway, *IVC* inferior vena cava, *LPA* left pulmonary artery, *RL* right-left, *RPA* right pulmonary artery, *SVC* superior vena cava,