Comprehensive Analysis of Total Cavo-Pulmonary Connection Hemodynamics with In Vivo and In Vitro 4D Flow MRI and Computational Fluid Dynamics

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Target audience: Those interested in 4D Flow MRI and patient-specific physical and numerical models for assessing congenital heart disease.

Introduction: Altered hemodynamics in total cavo-pulmonary connection (TCPC), a palliation of single ventricle defects, results in long-term complications, such as decreased exercise capacity, arrhythmia, and ventricular failure[1]. Patient-specific anatomy hinders a general solution for all patients. Although 4D Flow MRI has been used to assess flow in TCPC *in vivo*, this approach is limited in its ability to predict flow behavior under extreme conditions or to evaluate effects of varying surgical procedures. Computational fluid dynamics (CFD), or numerical modeling, helps understand hemodynamic phenomena and to virtually explore variations in physiological conditions, anatomy and tissue properties. Limitations due to simplifications and insufficient validation have hindered the clinical use of this potentially powerful tool [2]. ***The purpose of this study*** was to develop an experimental 4D Flow MRI setup as verification of a corresponding CFD model of TCPC. This study serves as a first step to bridge CFD and in vivo 4D Flow MRI for better TCPC understanding and treatment.

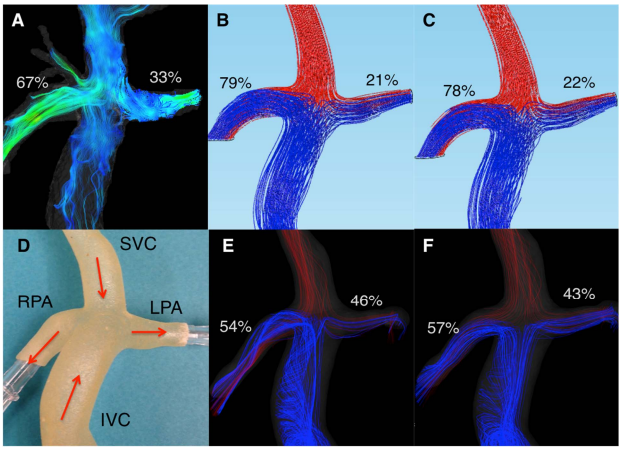

Figure 1: 4D Flow MRI on a 2YO extra-cardiac TCPC patient compared to patient-specific physical and CFD models. **A.** *In vivo* velocity color-coded streamlines. **B.** *In silico* results at baseline flow (1 L/min). **C.** *In silico* results at increased flow (1.8 L/min). **D.** Patient-specific physical model fabricated from MRI using SLS. **E.** *In vitro* results at baseline flow. **F.** *In vitro* results at increased flow. For B, C, E and F, blue and red streamlines represent IVC and SVC flow, respectively. Flow into each PA is shown as percent of the total outflow.

Methods: ***In vivo***: 4D Flow MRI was performed in extra-cardiac (2yM) and atrio-pulmonary (32yF) TCPC subjects following an IRB-approved protocol. 4D flow MRI (PC VIPR) imaging parameters were: imaging volume: 32x32x24cm, 1.25mm acquired isotropic spatial resolution, TR/TE=6.4/2.2ms, VENC = 200cm/s (extra-cardiac) and 100cm/s (atrio-pulmonary) [3]. Vessel segmentation was performed (MIMICs, Materialise, Leuven, Belgium) from PC angiograms; visualization and quantification were performed in EnSight (CEI, Apex, NC). TCPC anatomy was isolated and converted to a three-dimensional (3D) geometry (Mimics), which was used for: 1) a selective laser sintering (SLS) system to build a physical model (Nylon 11) and 2) CFD analysis. ***In vitro:*** The physical model was connected to a perfusion system (Stockert SIII Heart-Lung Machine), which circulated water at two different rates for each model (1 and 1.8 L/min for the extra-cardiac TCPC and 3 and 4.5 L/min for the atrio-pulmonary TCPC models). Flow was pumped through the IVC and SVC and drained through the RPA and LPA. Models were imaged using the same in vivo 4D Flow MRI protocol followed by image processing as described. ***In silico:*** CFD models were developed to simulate the in vitro system, discretizing the geometries with tetrahedral element meshes. Properties for water were defined (density 1000 kg/m^3, viscosity 0.001 Pa*s). No-slip (zero velocity) was implemented at rigid vessel walls. Inflow conditions for CFD were based on *in vitro* measurements. Velocity fields and streamlines were calculated.

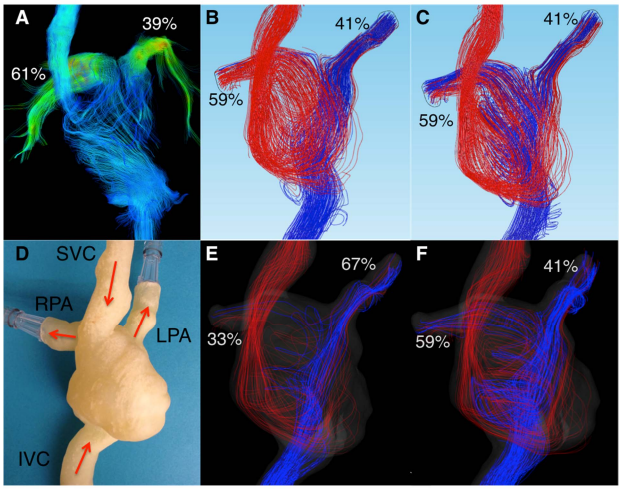

Figure 2: 4D Flow MRI in a 30YO atrio-pulmonary TCPC patient compared to patient-specific physical and CFD models. **A.** *In vivo* velocity color-coded streamlines. **B.** *In silico* results at 3 L/min. **C.** *In silico* results at 4.5 L/min. **D.** Patient-specific physical model fabricated from MRI using SLS. **E.** *In vitro* results at 3 L/min. **F.** *In vitro* results at 4.5 L/min. For B, C, E and F, blue and red streamlines represent IVC and SVC flow, respectively. Flow into each PA is shown as percent of the total outflow.

Results and Discussion: Results for *in vivo* and *in vitro* 4D Flow MRI and CFD measurements show comparable velocities and pulmonary flow distribution in both extra-cardiac (Fig.1) and atrio-pulmonary (Fig.2) TCPC. Interestingly, relative *in vitro* RPA and LPA flow distribution changed at different flow rates, while CFD predicted minimal change in relative distribution in the extra-cardiac TCPC and no change in relative distribution in the atrio-pulmonary TCPC. Although these methods are somewhat limited by the assumption of rigid vessel walls, these conditions were the same for both *in vitro* and *in silico* studies. This highlights the benefit of using patient-specific *in vitro* models to study the potential effects of changing physiological conditions on the hemodynamics of TCPC and for validation of CFD analysis. Future work will focus on improvement of *in vitro* designs and on quantitative assessment of flow and energy through the TCPC.

Summary: A comparison between *in vivo*, *in vitro* and *in silico* experiments was done in two patients with TCPC. The combinations of patient-specific *in vitro* and *in silico* models offer the ability to control hemodynamic parameters that are not possible to control *in vivo*. These models also serve as validation methods for the *in vivo* MRI measurements.

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References: [1] Khairy P. 2008; [2] de Zélicourt DA. 2012; [3] Johnson KM. 2010