Central Venous Catheter malfunction in children: a bioengineering approach

Authors: Claudia Bruno[1], Rayan Moumneh[1], Emilie Sauvage[2], Lynsey Stronach[3], Kathryn Waters[3], Ian Simcock[3,4], Owen Arthurs[3], Silvia Schievano[2,3], Claudio Capelli[2,3], Rukshana Shroff[1,3]

Institutional affiliations:
1 Institute of Child Health, University College London (London, UK)
2 Institute of Cardiovascular Science, University College London (London, UK)
3 UCL Great Ormond Street Hospital for Children (London, UK)
4 NIHR Great Ormond Street Hospital Biomedical Research Centre (London, UK)

Central venous catheters (CVCs) are commonly used in children for maintenance hemodialysis (HD) even though they are known to have a high complication rate with poor blood flow, thrombosis and infections (1,2) compared to arteriovenous fistulas. It is not known if specific features of the CVC design contribute to the high complication rate. Computational fluid dynamics (CFD) is an engineering tool to predict fluid flow inside a geometry such as a vessel or a medical device and for in silico measurements of hemodynamics parameters which are difficult or impossible to replicate *in vivo* or *in vitro*. Geometries of different dimensions and sizes can be compared to determine the factors that improve or reduce optimal blood flow.

In this multidisciplinary study, we investigate flow characteristics in pediatric CVCs combining computational simulations and clinical data to provide a comprehensive fluid dynamics characterization of different CVC designs for pediatric applications.

Four models of CVCs that are routinely used across Europe were recreated from microCT scans and studied within appropriate-sized anatomical models by means of numerical simulations (Ansys Fluent, Ansys Inc., *Canonsburg, PA, USA*). The four CVCs, which differed in design of lumen, tip and configuration of side-holes were: Tesio 6.5F, Hemo-Cath 8F, Pediatric Split Cath 10F and Split Cath III 14F (MedCOMP, *Harleysville, PA, USA*). Computational analyses showed that after CVC insertion, the velocity of blood flow increased due to a reduced vessel lumen (Figure 1A-a), therefore increasing shear stress on the vein wall (Figure 1A-b). A maximum three-fold increase of shear stress was recorded with the 10F model. With smaller CVC models asymmetric eddies were identified (Figure 1A-c). Similar changes in hemodynamics due to the catheter placement are shown to increase the risk of venous thrombosis in adult HD patients (3). When the catheters were used in arterial configuration, blood entered the lumen mainly through the most proximal side-holes, regardless of the CVC design and size. The presence of a low velocity zone (Figure 1A-d), due to the relatively lower blood flow through the tip, was observed in all CVC designs. This might trigger platelet activation and consequent blood clotting (4). Similar to previous computational studies (4), shear stress levels were measured at the arterial tip of the catheters. Regions close to the proximal side-holes recorded the highest shear stresses (Figure 1A-e) with maximum values between 105.25 to 255.43Pa. For comparison, in physiological conditions blood shear stresses ranges from 0.1 to 1Pa in veins, 5Pa in arteries and 6Pa in arterioles (5). Large areas of stagnation were recorded in the 6.5F model. The arterial lumen of the Hemo-Cath (8F) recorded the highest percentage of shear stress

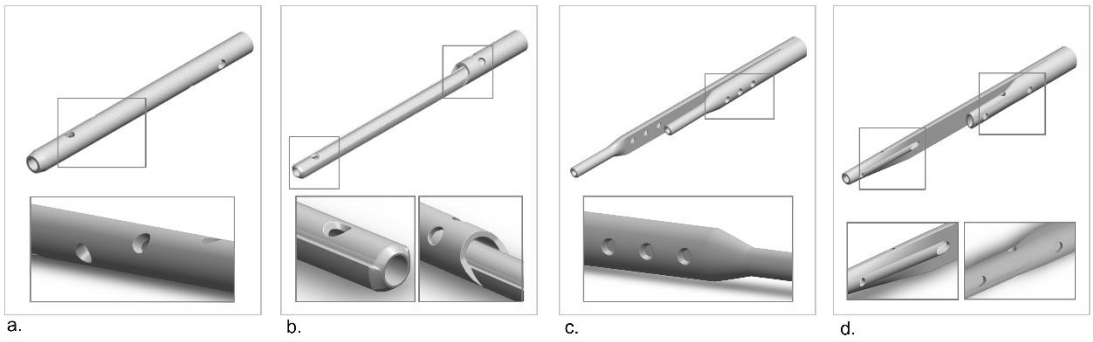
above the 10Pascal threshold defined by Mareels et al. in 2007 (4). The average shear stress values were comparable among the four models.

In a pilot study of children on HD we evaluated outcomes of 57 CVCs from time of insertion. All patients had one of the above four catheters depending on the size. Clinical observations showed that thrombosis (defined as the need for thrombolytic treatment at 3 consecutive HD sessions, or CVC removal due to occlusion) was the first type of CVC dysfunction in 92% of cases. At 90 days, the estimated thrombosis-free survival was 35%, 60% and 100% in the Hemo-Cath, Split Cath and Split Cath III groups respectively ($p = 0.013$). 89% of the CVCs removed presented at least one event of catheter dysfunction (defined as the composite end-point of thrombosis or infection). Infection and thrombosis were the main causes of CVC replacement, accounting for 30% and 27% of CVC removals, respectively. Dysfunction-free survival was 21%, 49% and 66% at 90 days in the Hemo-Cath, Split Cath and Split Cath III groups respectively (insufficient data was available for the Tesio). Although the smallest CVCs had the shortest dysfunction-free survival, this did not reach statistical significance ($p = 0.06$), implying that other, potentially modifiable, features of the CVC design may also play a role in determining catheter function. At the time of catheter dysfunction, the blood flow rate within the CVC was only 77% of the highest achievable flow ($p < 0.001$). Infection rates were comparable amongst groups.

Results from the computational study were in accordance with our pilot clinical data (Figure 1C). There was a significantly higher rate of thrombosis in the Hemo-Cath compared to the split tip models ($p = 0.013$), that could not be accounted for by the smaller lumen diameter of Hemo-Caths and was consistent with the computed shear stress: 43% of values were higher than 10Pascal against the 24% found in the Split Cath and 25% in the Split Cath III.

In conclusion, this proof-of-concept study identified critical fluid dynamics parameters of CVCs that correlated with adverse clinical outcomes. Findings will be verified in large multicentre clinical studies. Future work will use CFD to design new CVCs optimized for children.

A



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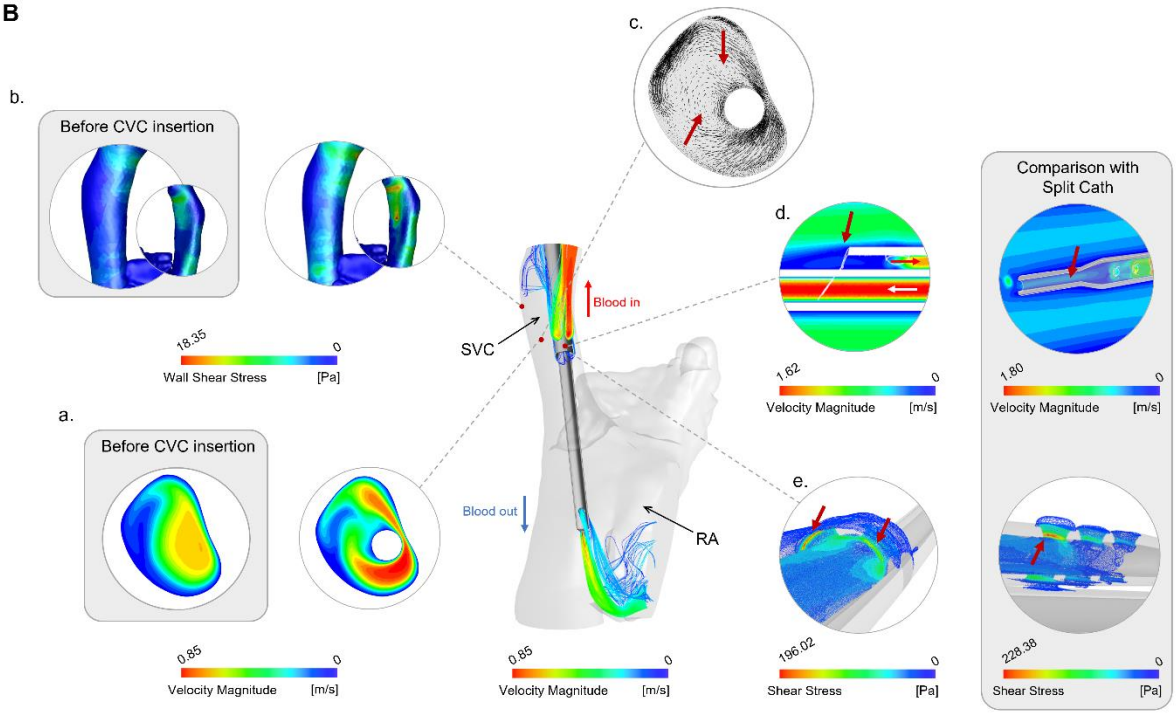

C

	Computational results					Clinical outcomes	
	Maximum blood velocity [m/s]		Shear Stress [Pa]			Survival at 90 days after insertion, N (%)	
Model	**Without Catheter**	**With Catheter**	**Maximum SS**	**Average SS**	**% SS > 10 Pa**	**Thrombosis-free**	**Dysfunction-free**
Tesio 6.5F	0.85	1.14	105	4.1	20	*Insufficient data*	*Insufficient data*
Hemo-Cath 8F	0.65	0.83	196	4.1	43	36	21
Pediatric Split Cath 10F	0.38	0.50	228	3.4	24	60	49
Split Cath III 14F	0.30	0.36	255	3.8	25	100	66

Figure 1 – (A) 3D models of the central venous catheters (CVCs) included in this study with magnification on the details of the side-holes: a. Tesio (6.5F); b. Hemo-Cath (8F); c. Pediatric Split Cath (10F); and, d. Split Cath III (14F). (B) Computational fluid dynamics to study changes in hemodynamics parameters in an anatomical model of the superior vena cava (SVC) and the right atrium (RA) in the presence of a Hemo-Cath 8F CVC and under clinical working conditions. Central picture: velocity pathlines for the Hemo-Cath 8F. Blood is aspirated from the arterial lumen in the SVC, while the venous lumen takes blood back to the RA. Lateral pictures illustrate several results from different sections of the geometry; colormaps are reported with the corresponding legend ranging from the minimum (blue) to the maximum (red) values measured. a. Velocity contours plotted at the cross section of the SVC, before and after CVC insertion. Blood velocity inside the vein increases in the presence of the catheter; increases range between 3% and 15% in average velocity and between 21% and 34% in maximum velocity; b. Wall shear stress plotted on the SVC (front and back views are shown). Increased shear stress is recorded after catheter insertion; the Pediatric Split Cath registered a 3-fold greater increase while in the remaining CVC models differences ranged between 40% and 48%; c. Asymmetric eddies (red arrows) are found in the SVC cross section when the catheter is placed inside the vein; d. A region of low velocity or blood stagnation is shown at the tip of the arterial lumen; e. Close up of the shear stress distribution in the region close to the arterial side-holes where higher values of shear stress are measured (red arrows). (Right panel) A region of blood stagnation can be also found in the Split Cath 10F (top) together with high shear stress levels in the region close to the most proximal arterial side-holes. (C) Table summarizing the most important results obtained from both the engineering simulations and the observations in clinical patients. Maximum blood velocity was measured at the smallest cross section of the vein before and after catheter placement while shear stress values were computed in a volume of fluid containing the arterial tip of the catheters. SS = Shear Stress

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References

1. Shroff R, Calder F, Bakkaloğlu S, Nagler E v., Stuart S, Stronach L, Schmitt CP, Heckert KH, Bourquelot P, Wagner AM, Paglialonga F, Mitra S, Stefanidis CJ: Vascular access in children requiring maintenance haemodialysis: A consensus document by the European Society for Paediatric Nephrology Dialysis Working Group. *Nephrology Dialysis Transplantation* 34: 1746–1765, 2019

2. Borzych-Duzalka D, Shroff R, Ariceta G, Yap YC, Paglialonga F, Xu H, Kang HG, Thumfart J, Aysun KB, Stefanidis CJ, Fila M, Sever L, Vondrak K, Szabo AJ, Szczepanska M, Ranchin B, Holtta T, Zaloszyc A, Bilge I, Warady BA, Schaefer F, Schmitt CP: Vascular Access Choice, Complications, and Outcomes in Children on Maintenance Hemodialysis: Findings From the International Pediatric Hemodialysis Network (IPHN) Registry. *American Journal of Kidney Diseases* 74: 2019

3. Park MH, Qiu Y, Cao H, Yuan D, Li D, Jiang Y, Peng L, Zheng T: Influence of hemodialysis catheter insertion on hemodynamics in the central veins. *Journal of Biomechanical Engineering* 142: 2020

4. Mareels G, Kaminsky R, Eloot S, Verdonck PR: Particle Image Velocimetry-validated, computational fluid dynamics-based design to reduce shear stress and residence time in central venous hemodialysis catheters. *ASAIO Journal* 53: 2007

5. Sheriff J, Bluestein D, Girdhar G, Jesty J: High-shear stress sensitizes platelets to subsequent low-shear conditions. *Annals of Biomedical Engineering* 38: 1442–1450, 2010