



Inter- and Intra-Scanner Differences in Doppler Flow Measurements Using Three-Dimensional Printed Flow Phantom Model of the Carotid Artery in Preterm Infants

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ABSTRACT

This study compared flow measurements with three dimensional (3D) printed flow phantom models of the carotid artery of preterm infants using two commonly available brands of ultrasound scanners (scanner 1 and 2) in the neonatal unit. 3D printed flow phantoms with three different vessel diameters was used for

performing continuous and pulsatile flow measurements by 2 observers, blinded to phantom characteristics and each other's measurements. Agreement between observers were examined using Bland-Altman analysis. Of the 48 measurements, 62% were pulsatile flow measurements and majority (36(75%)) performed with phantom vessel diameter of 0.244 cm. Bland-Altman analysis for continuous flow measurements (n=18(38%)) using scanner 1, revealed observer 1 had mean (95% LOA) bias of 3.95 (-2.06 to 9.96) ml/min compared to 0.45 (-12.74 to 13.65) ml/min for observer 2. For scanner 2, bias was -2.42 (-12.18 to 7.34) ml/min for observer 1 and 0.54 (-17.00 to 18.09) ml/min for observer 2. Pulsatile flow measurements (n=30(62%)) using scanner 1, demonstrated that observer 1 had a bias of -0.63 (-3.82 to 2.57) ml/min compared to 0.82 (-5.88 to 7.52) ml/min for observer 2. Using scanner 2, bias was -2.49 (-6.18 to 1.21) ml/min for observer 1 and -2.60 (-7.95 to 2.75) ml/min for observer 2. Inter and intra-observer reliability was excellent for most pulsatile flow measurements. We found excellent inter and intra-observer reliability for majority of pulsatile flow measurements and lower variance for observer 1. Researchers and clinicians can use 3D printed flow phantoms for training and assessing operator capabilities using different ultrasound scanners.

Keywords: 3-dimensional, 3D printed flow phantom, inter scanner, carotid artery, preterm infant

INTRODUCTION

Optimal cerebral blood flow and oxygenation is integral to normal brain development. Infants receiving intensive care undergo invasive and non-invasive monitoring of several physiological parameters including cardiovascular[1, 2] markers. Studies have shown that incorporating these physiological variables into clinical care has been shown to be associated with improved outcomes.[3, 4] Doppler ultrasound of the carotid artery to interrogate cerebral blood flow measurements has been studied in term, preterm and extremely preterm newborn infants.[5, 6] A flow phantom model of the carotid artery in preterm infants built using polytetrafluoroethylene[7] was subsequently improved by developing a three-dimensional (3D) printed flow phantoms model of the carotid artery in preterm infants.[8, 9]

Flow phantoms are excellent tools used for simulation, and training clinicians and researchers.[10, 11] They are particularly useful for finetuning hand skills and improving hand eye coordination especially when dealing with small calibre vessels frequently encountered in preterm infants. In addition, the flow phantom eliminates the inherent physiological variability frequently seen in these infants. Doppler measurements are carried out using standard ultrasound scanners which are widely available in most neonatal intensive care units. Several models of ultrasound scanners are available to clinicians with which these measurements can be carried. The performance of these ultrasound machines can vary,[12] and we wanted to investigate how this 3D printed flow phantom model performed against multiple ultrasound scanners.

The aim of this work was to compare continuous and pulsatile flow measurements using 3D printed flow phantom models of the carotid artery in preterm infants using two commonly available brands of ultrasound scanners used in the neonatal intensive care unit.

METHODS

The phantom was designed and produced in the Clinical Physics Department of Barts Health NHS Trust.

Data collection for designing flow phantom

In order to determine the physical characteristics of the right common carotid artery in human preterm infants, data was collected from twenty-one randomly selected infants who were admitted to the tertiary level neonatal intensive care unit. As part of standard routine care, cerebral blood flow measurements were also performed in some infants as part of haemodynamic assessment when functional echocardiography and cranial ultrasound scans were performed. Some of the scans were obtained from infants who were recruited to a blood pressure study that had ethics committee approval (reference 12/LO/1553).[13]

Data used for designing flow phantom

From images obtained with a transducer placed over the anterior triangle of the neck, the following data were collected about the physical characteristics of the right common carotid artery (Figure 1):

d – cross sectional diameter of the blood vessel (cm)

Tp – proximal depth of the blood vessel from skin surface (cm)

Td – distal depth of the blood vessel from skin surface (cm)

L – distance between Tp and Td measuring points

Φ – angle formed between blood vessel and skin surface, calculated using the following formula;

$$\Phi = \tan^{-1} (Td - Tp) / L$$

Flow phantom production

Flow phantom design

All 3D printed components were developed using SolidWorks 3D CAD drawing software (Standard, SP1.0, 2018: Waltham, MA, USA) and printed on an Objet 260 Connex 3D printer (Stratasys, Eden Prairie, MN, USA).

Three 3-chamber models were developed (Figure 2A-B), with each chamber having a vessel of different Φ and d. The phantom model encasement was 3D printed using VeroWhitePlus, which is a rigid general-purpose material. The dimensions of the phantom (15.0 x 5.5 cm, 9.0 cm height) were compatible with typical transducers used in neonatal intensive care. Vessel supports protruded from either side of the chambers, with a central channel to hold the 3D printed neonatal carotid artery. These supports maintained the vessels at the correct position, relative to the phantom surface. Various phantom vessel internal diameters were used (0.158, 0.196 and 0.244 cm) at a Φ of 10°, 15° and 20°. The internal base of the phantom, consisted of an angled and soft surface made from Agilus30Black (rubber like material), to minimise reflections of the ultrasound energy back to the transducer.

Each vessel was 3D printed using a digital material mixture of VeroWhitePlus and Agilus30Black. The digital material was the result of combining these two materials, in specific concentrations to create a composite material with hybrid characteristics. The vessels used in this study had a Shore-A: 95 hardness value on the Durometer Shore hardness scale, with a wall thickness of 0.5mm. The Shore A scale measures the hardness and flexibility of a wide range of materials.

The vessels were encased in an agar and glycerol-based tissue mimicking material (TMM).[14] The phantom vessel was embedded in the TMM at a depth of 1.0 cm from the phantom surface to the upper point of the tubing. The top of the phantom was sealed with a 0.1 cm layer of low-density polyethylene (LDPE) plastic (PSG Group Ltd, London, UK), this minimised desiccation, and thereby increasing phantom lifetime. Each vessel was printed with two removable formers (made from VeroWhitePlus) which were positioned centrally in the vessel. The formers could be carefully removed from each vessel. The purpose of the formers was to minimise the quantity of support material to be removed after printing. Subsequently, precision ground rods of increasing diameter were inserted through the vessel, to provide assurance that no residual support material was left in the vessels. Additionally, the rods provided assurance the vessel lumens were of the correct specified dimensions.

Testing the flow phantom

The flow phantom was set up in the neonatal unit where the ultrasound scanner was housed. Blood mimicking material (Model 707, ATS Laboratories, Norfolk, VA USA) with a density of $1004 \pm 10 \text{ kg/m}^3$ was run through the model. The flow was adjusted by varying the height of the reservoir containing the blood mimicking fluid or by adjusting the outflow valve attached to the end of the line. This produced continuous flow through the circuit. Pulsatile flow, simulating physiological flow, was achieved by incorporating a peristaltic pump (Watson Marlow, model MHRE 72) into the circuit. The pump was run at speeds that produced a pulsatile flow of 120–150 pulses per minute in keeping with the physiological heart rates in premature infants. Continuous flow measurements were carried out using the 0.244 cm lumen diameter flow phantom whereas pulsatile flow measurements were carried out using the 0.158 cm, 0.196 cm and 0.244 cm lumen diameter flow phantom.

The calibration of the blood mimicking flow was achieved by the measurement of the accumulation of the fluid mass over the flow measurement period. The mass of the fluid was simply measured by its collection into a container placed on a sensitive load cell (Compression Load Cell, model 1004, Tedea Huntleigh) that acted to dynamically measure the accumulative mass of the blood mimicking fluid. The load cell output was measured as one arm of a classical resistance bridge circuit set within a full bridge module (National Instruments NI 9237). The module was connected via a USB link to a monitoring laptop that was running data acquisition and visualisation software LabVIEW real-time software (v. 14.0.1, National Instruments, Newbury, UK).

Ultrasound scanners used for flow measurements

Two ultrasound scanners were used to carry out the flow measurements. Phillips iE33 ultrasound system (Bothwell, USA) (scanner 1) was the initial scanner present in the neonatal unit and the one that all the investigators were familiar with. The GE Vivid S70N (GE Healthcare, UK) (scanner 2) was the newer scanner acquired by the unit a few months prior to this study being carried out. All measurements were performed with a 7-15 MHz 'hockey-stick' linear array probe (footprint of 1 cm by 3.2 cm) using the Phillips iE33 ultrasound system (Bothwell, USA) (scanner 1) and the 8-18 MHz 'hockey-stick' linear array probe (footprint of 1.2 cm by 3.5 cm) using the GE Vivid S70N (GE Healthcare, UK) (scanner 2).

Ultrasound image optimisation used for flow measurements

After placing an adequate amount of water-based ultrasound jelly on the flow phantom, the cross-sectional view of the vessel was obtained represented by the presence of 2 echogenic areas in the vessel wall (Figure 3A-B). These brighter areas were seen when the scan plane was perpendicular to the vessel, representing the stronger reflections from ultrasound striking a surface at right angles, and confirming that a perpendicular measurement of diameter was being performed. The zoom function in the ultrasound machine was utilised to increase image size. Focus range was adjusted to include the whole vessel and the midpoint of the focus was aligned to the midpoint of the vessel. The scanner gain settings were adjusted to an appropriate level to visualise the vessel lumen. The image was frozen and scanner calipers were placed on the leading edge and the centre to measure the vessel diameter as these parameters have been shown to reflect the most accurate lumen diameter.[8] The probe was rotated by 90 degrees to align it parallel to the tubing housed in the chamber. A generous amount of ultrasound jelly was used to obtain the lowest possible angle of insonation. Continuous and pulsatile flow measurements were carried out. Pulsatile flow mimicking physiological levels was achieved using a peristaltic pump as previously described.[7]

Flow measurements using the phantom

Flow volume (Q) was calculated using the following formula;

$$Q = IWMV * (\pi d^2 / 4) \text{ in ml/min}$$

where $IWMV$ is intensity weighted mean velocity (cm/s) and d is cross-sectional diameter of the vessel lumen (cm).

Therefore, diameter is an important parameter as measurement errors can square when calculating flow. We extensively studied ideal diameter measurement points in 3D printed flow phantoms and demonstrated that the centre to leading edge measurements reflected the lumen diameter accurately.[8] Furthermore, follow up studies measuring flow using these diameter measurements points were also performed.[9] In this study, continuous flow followed by pulsatile flow measurements (Figure 4A-D) were performed by multiple observers SP (observer 1, with more than 10 years of experience) and ASA (observer 2, with more than 1 year of experience) who were blinded to each other's measurements and to the characteristics of the chamber (vessel diameter and Φ). All intra-observer comparisons were performed contemporaneously.

Reproducibility

Reproducibility of the various parameters used for flow measurements were carried out by both observers. The observers were blinded to each other's measurements. Inter and intra observer measurements were carried out using scanner 2 only. We have previously carried out multiple intra observer measurements using scanner 1.[7-9]

Statistical analysis

Data was summarised using mean (standard deviation) for normally distributed data. The correlation between observers was examined and validity of measurements was examined using Bland-Altman plot and expressed as difference in percentage.[15] The absolute difference between actual lumen diameter and mean diameter measurements of observers was calculated for measurements performed using the most frequent flow phantom. Reliability between

observers was checked using intra class correlation (ICC) using 2-way mixed ANOVA with observers being fixed factors and measurements being random factors.[16, 17] The coefficient of variation (mean SD/Mean)*100 was also calculated as an additional measure of agreement and results expressed as percentage. The grading of strength of correlation was assessed using previously described methods.[18] All statistical analyses were performed using IBM SPSS v27 (Chicago, IL, USA) and GraphPad Prism version 9.2.0.

RESULTS

Vessel diameter measurements

Among the 48 measurements performed, 36 (75%) were performed on flow phantoms with a lumen diameter of 0.244 cm. Scanner 1 was used in 16 (33.3%) measurements whereas scanner 2 was used for 32 (66.6%) measurements. Vessel diameter measurements were similar between both observers (Table 1). For the flow phantom with lumen diameter of 0.244 cm, using scanner 1, the mean (SD) absolute difference between lumen diameter and measured diameter was 0.003 (0.002) cm and 0.006 (0.005) cm for observer 1 and 2 respectively. Whereas, using scanner 2, the mean (SD) absolute differences were 0.003 (0.004) cm and 0.010 (0.005) cm for observer 1 and 2 respectively. The mean bias (95% limits of agreement) using scanner 1 and 2 were lower for observer 1 when compared to observer 2 (Figure 5).

Vessel flow measurements

Continuous flow measurements (n=18 (38%)) were performed by both observers using both scanners. Using scanner 1, observer 1 had a mean (95% limits of agreement) bias of 3.95 (-2.06 to 9.96) ml/min compared to 0.45 (-12.74 to 13.65) ml/min for observer 2 (Figure 5). Using scanner 2, mean (95% limits of agreement) were -2.42 (-12.18 to 7.34) ml/min for observer 1 and 0.54 (-17.00 to 18.09) ml/min for observer 2.

Pulsatile flow measurements (n=30 (62%)) were performed by both observers using both scanners. Using scanner 1, observer 1 had a mean (95% limits of agreement) bias of -0.63 (-3.82 to 2.57) ml/min compared to 0.82 (-5.88 to 7.52) ml/min for observer 2 (Figure 5). Using scanner 2, mean (95% limits of agreement) were -2.49 (-6.18 to 1.21) ml/min for observer 1 and -2.60 (-7.95 to 2.75) ml/min for observer 2 (Table 2).

Inter observer reliability

Inter observer reliability for both observers using ICC(3,1)[16, 18] was 'almost perfect' [17] grade for majority of the parameters in pulsatile flow measurements when compared to continuous flow measurements. The coefficient of variation using scanner 1 was 0.7% for observer 1 and 3.2% for observer 2. The coefficient of variation using scanner 2 was 1.6% for observer 1 and 4.5% of observer 2 (Table 1).

Intra observer reliability

Paired measurements several flow parameters were carried out by both observers using scanner 2 only. Intra observer reliability using ICC (3,1)[16, 18] was 'almost perfect' for majority of the pulsatile flow measurements when compared to continuous flow measurements (Table 2). The mean intra observer coefficient of variation for diameter measurements for observer 1 was 1.5% and that of observer 2 was 3.1%.

DISCUSSION

We carried out a range of continuous and pulsatile flow measurements using a 3D printed flow phantom models of the common carotid artery in preterm infants. We examined several parameters involved in calculating flow measurements using two commonly available brands of ultrasound scanners found in neonatal units and also performed reliability studies which demonstrated excellent reliability for the majority of measurements.

Glossy finish 3D printed flow phantoms were used as it is easier to eliminate the residual support material resulting in a uniform vessel margin. The leading edge to centre points were used for diameter measurements as this has been shown to accurately reflect lumen diameter in this material.[8] This has been an issue with the prototype of this flow phantom and therefore every care was taken to produce clear vessel margin and therefore reduce the error in diameter estimation.

We found reliability was much better for the majority of the parameters used to measure flow using pulsatile flow when compared to continuous flow. The continuous flow measurements (n=18) were performed first followed by pulsatile flow measurements. One possible explanation is that the observers performed continuous flow measurements first followed by pulsatile flow measurements, they became more proficient with the pulsatile flow measurements with time and also became more accustomed with the new ultrasound scanner. Another potential reason is with pulsatile flow, observers were more familiar with pulsatile flow in newborn infants and found it easier to identify and measure the most distensible diameter of the vessel during each pulsatile flow. Pulsatile flow produced in these studies were similar to physiological rates found in extremely preterm infants.

Observer 1 was found to have smaller differences between measured and actual flow measurements (for both continuous and pulsatile flow) with both scanner 1 and 2 when compared to observer 2. In addition, the coefficient of variation for observer 1 was lower than that of observer 2 for all measurements. This could be attributed to observer 1 experience and being more familiar with performing such measurements. High levels of operator experience has been shown to reduce the variation in cardiovascular measurements in multiple settings.[19, 20] For observer 1, the bias in pulsatile flow measurements were similar using scanner 1 and 2. This could indicate a different ultrasound scanner may play less of a role than operator experience in measurement variations when performing such measurements.

We found excellent intra and inter observer reliability for the majority of the pulsatile flow measurement parameters in this study. Additionally, the CoV for both ranged between 0.7% to 4.5%. These values were similar to our previous work[7, 9] and lower than those performed in newborn infants.[5, 6] Other studies using 3D printed vascular models for different purposes found similar values.[21, 22]

This study is not without limitations. We only examined a small number of 3D printed materials for production of flow phantoms. However, we used materials with lower Shore values and found practical difficulty in eliminating all the support material debris from the vessel lumen which could affect the volume of fluid flowing through the flow phantom.[23] Secondly, we did not explore the aging effects of the flow phantom model in this study. Though we produced several versions of the flow phantom, measurements were carried out within a couple of

months of production and these were not extensively used. Lastly, we did not perform intra observer reliability studies using scanner 1 at the same time. This is due to the large number of reliability work reported using scanner 1 in 3D printed flow phantoms[7-9] and other materials such as polytetrafluoroethylene.[7]

This study examined several parameter of flow measurements by two observers using multiple ultrasound scanners. Future work in this area should explore the effects of long-term impact and phantom fatigue on flow measurements. We used a tested method for accurate reflection of lumen diameter using 3D printed materials and thereby reducing the chance of errors in diameter estimation, an integral part of flow measurement. Pulsatile flow measurements, involving physiological heart rates were studied and these showed excellent inter and intra observer reliability and should be used for training clinicians and researchers in performing flow measurements and honing their skills before attempting to carry out flow measurements in extremely preterm infants.

CONCLUSION

Similar measurements were found between observers for the majority of measurements. Observer experience and pulsatile flow measurements were associated with lower variance when using different brands of ultrasound scanners. Realistic 3D flow phantoms are an excellent training and simulation tool for clinicians and researchers to gain experience and hone practical skills before attempting cerebral blood flow measurements in extremely preterm infants.

CONTRIBUTORS

SP, AS, ASA JR, MB, SK researched literature and conceived the study. SK, SP, AS, ASA, JR collected data for designing the flow phantom. SP, SK, AS, ASA JR, MB designed the flow phantom and JR and MB built the flow phantom. SP, AS, ASA, and SK did the data analysis. SP wrote the first draft of the manuscript. AS, ASA, JR, MB and SK wrote the final version of the manuscript. All authors reviewed and approved the final version of the manuscript.*

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TABLES AND FIGURES

Table 1. The various continuous and pulsatile flow parameters measured by both observers using scanner 1 and 2 along with inter observer reliability measurements. IWMV – Intensity weighted mean velocity

Type of flow	Type of scanner	Parameter	Observer 1 (SSP) Mean (SD, 95% CI)	Observer 2 (ASA) Mean (SD, 95% CI)	Inter observer reliability ICC (95% CI)
Continuous	Philips iE33 (Scanner 1) (n=3 each observer)	Vessel diameter (cm)	0.241 (0.001, 0.237 to 0.244)	0.247 (0.004, 0.236 to 0.257)	-0.113 (-0.311 to 0.832)
		IWMV (cm/s)	11.4 (4.1, 1.3 to 21.5)	10.3 (4.6, -1.1 to 21.8)	0.886 (-0.055 to 0.997)
		Angle of insonation (degrees)	61.3 (1.2, 58.5 to 64.2)	61.3 (2.3, 55.6 to 67.1)	-
		Calculated flow (ml/min)	31.2 (11.5, 2.6 to 59.7)	29.4 (12.9, -2.5 to 61.4)	0.928 (0.003 to 0.998)
	General Electric S70N (Scanner 2) (n=6 each observer)	Vessel diameter (cm)	0.241 (0.003, 0.237 to 0.244)	0.244 (0.011, 0.235 to 0.256)	0.476 (-0.333 to 0.902)
		IWMV (cm/s)	12.0 (3.8, 8.1 to 15.9)	10.4 (1.7, 8.6 to 12.2)	0.244 (-0.555 to 0.838)
		Angle of insonation (degrees)	57.3 (2.1, 55.2 to 59.5)	59.7 (2.1, 56.5 to 60.8)	-
		Calculated flow (ml/min)	32.7 (10.1, 22.1 to 43.2)	29.6 (7.3, 21.9 to 37.3)	0.278 (-0.689 to 0.858)
Pulsatile	Philips iE33 (Scanner 1) (n=5 each observer)	Vessel diameter (cm)	0.215 (0.039, 0.167 to 0.263)	0.214 (0.042, 0.161 to 0.267)	0.986 (0.878 to 0.999)
		IWMV (cm/s)	10.8 (4.9, 4.6 to 16.9)	10.1 (3.7, 5.6 to 14.7)	0.923 (0.526 to 0.991)
		Angle of insonation (degrees)	60.4 (1.7, 58.3 to 62.5)	61.6 (2.2, 58.9 to 64.3)	-
		Calculated flow (ml/min)	21.3 (1.5, 19.5 to 23.1)	20.2 (2.8, 16.8 to 23.7)	-0.153 (-1.075 to 0.781)
	General Electric S70N (Scanner 2) (n=10 each observer)	Vessel diameter (cm)	0.215 (0.038, 0.188 to 0.242)	0.211 (0.034, 0.187 to 0.236)	0.954 (0.838 to 0.988)
		IWMV (cm/s)	11.7 (4.5, 8.5 to 14.9)	11.8 (3.6, 9.2 to 14.3)	0.913 (0.687 to 0.978)
		Angle of insonation (degrees)	54.6 (2.1, 53.1 to 56.1)	56.3 (1.3, 55.4 to 57.2)	-
		Calculated flow (ml/min)	23.4 (2.6, 21.5 to 25.3)	23.5 (3.2, 21.2 to 25.8)	0.450 (-0.272 to 0.833)

Table 2. Measurements performed using General Electric Vivid S70N (scanner 2) by two observers and the intra observer variability

Type of Flow	Parameter	Observer 1 (SSP) (Mean (SD, 95% CI)		Observer 1 Intra observer reliability (95% CI)	Observer 2 (ASA) Mean (SD, 95% CI)		Observer 2 Intra observer reliability (95% CI)
		Measurement (a)	Measurement (b)		Measurement (a)	Measurement (b)	
Continuous (n=3 each observer)	Diameter (cm)	0.240 (0.003, 0.234 to 0.247)	0.241 (0.005, 0.229 to 0.252)	0.831 (-1.312 to 0.995)	0.245 (0.011, 0.219 to 0.271)	0.244 (0.014, 0.209 to 0.279)	0.439 (-2.332 to 0.983)
	IWMV (cm/s)	13.1 (3.6, 4.1 to 22.2)	10.9 (4.3, 0.2 to 21.5)	0.655 (-0.385 to 0.989)	10.6 (2.3, 4.8 to 16.4)	10.2 (1.4, 6.9 to 13.6)	-0.239 (-2.589 to 0.953)
	Angle (degrees)	57.3 (2.3, 51.6 to 63.1)	57.3 (2.3, 51.6 to 63.1)	-	58.7 (2.3, 52.9 to 64.4)	58.7 (2.3, 52.9 to 64.4)	-
	Flow (ml/min)	35.8 (10.2, 10.4 to 61.2)	29.5 (10.9, 2.3 to 56.7)	0.650 (-0.353 to 0.989)	30.2 (8.8, 8.3 to 52.2)	29.0 (7.4, 10.5 to 47.5)	-0.136 (-2.602 to 0.959)
Pulsatile (n=5 each observer)	Diameter (cm)	0.217 (0.040, 0.167 to 0.267)	0.213 (0.039, 0.164 to 0.261)	0.991 (0.800 to 0.999)	0.209 (0.036, 0.165 to 0.253)	0.214 (0.037, 0.167 to 0.259)	0.957 (0.718 to 0.995)
	IWMV (cm/s)	11.4 (4.7, 5.6 to 17.2)	12.0 (4.8, 6.1 to 17.9)	0.960 (0.739 to 0.996)	11.5 (2.9, 7.8 to 15.2)	12.0 (4.5, 6.5 to 17.6)	0.919 (0.501 to 0.991)
	Angle (degrees)	54.4 (2.3, 51.5 to 57.3)	54.8 (2.2, 52.1 to 57.5)	-	55.8 (0.4, 55.2 to 56.4)	56.8 (1.6, 54.8 to 58.8)	-
	Flow (ml/min)	23.2 (3.5, 18.9 to 27.5)	23.6 (1.9, 21.3 to 25.9)	0.613 (-0.578 to 0.953)	22.8 (3.4, 18.5 to 27.0)	24.2 (3.2, 20.3 to 28.2)	0.530 (-0.383 to 0.936)

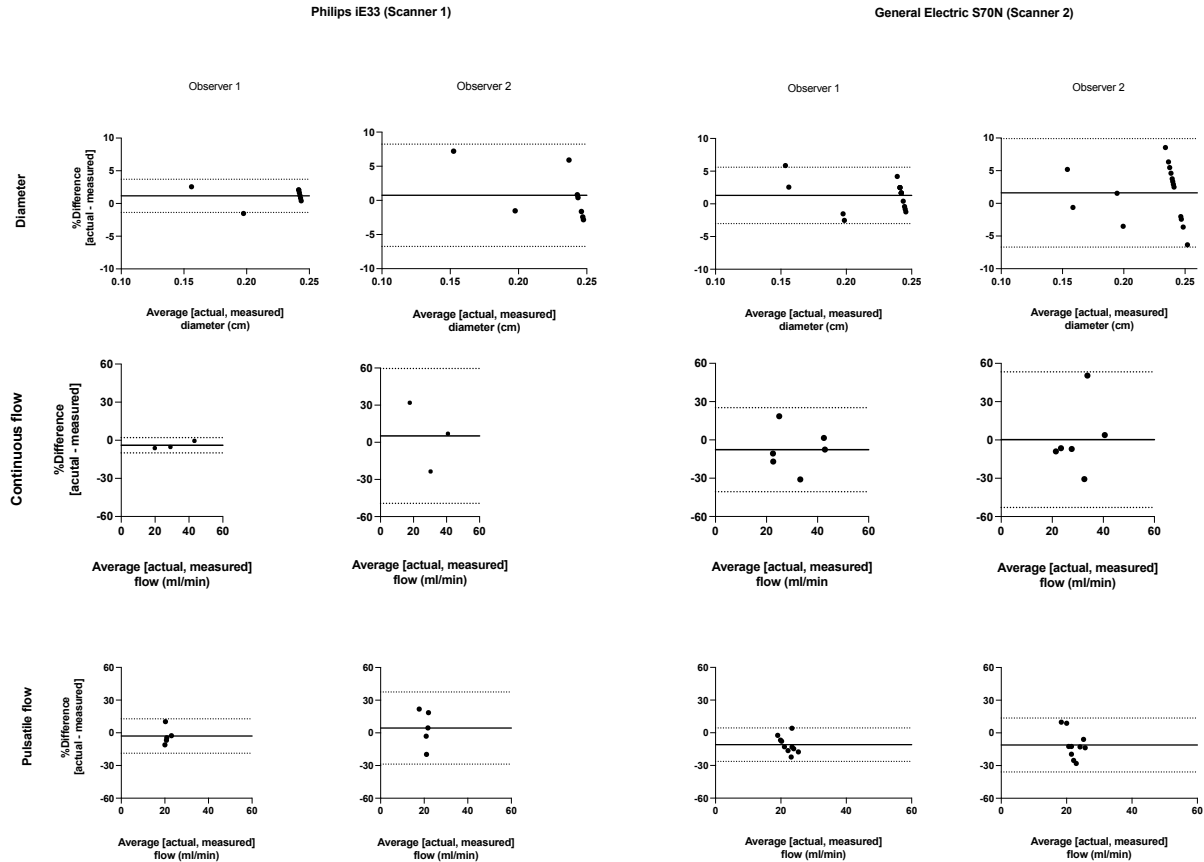


Figure 5. Bland-Altman plots for diameter measurements, continuous and pulsatile flow measurements carried out by two observers using scanners 1 and 2. Solid lines represent mean bias and dashed lines represent upper and lower 95% limits of agreement

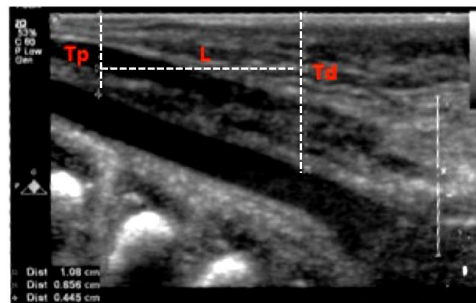


Figure 1. Ultrasound of the right common carotid artery in a preterm human infant, where Tp is the proximal depth of the vessel from the skin surface, Td is the distal depth from the skin surface and L is the distance between Tp and Td

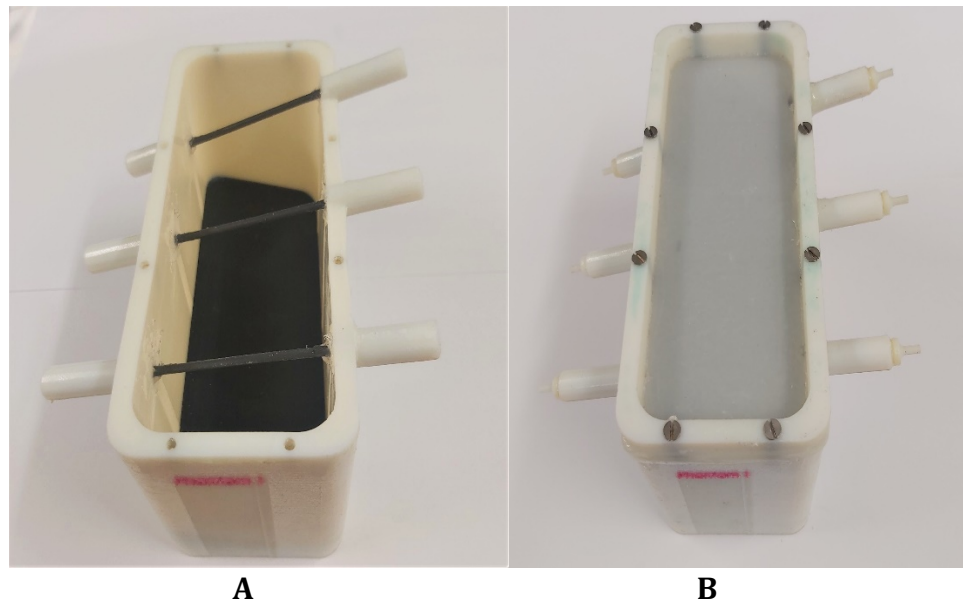


Figure 2: (A) Three-chamber phantom flow model – all components shown were 3D printed. (B). Phantom model filled with tissue mimicking material (TMM) and covered with low density polyethylene (LDPE) plastic

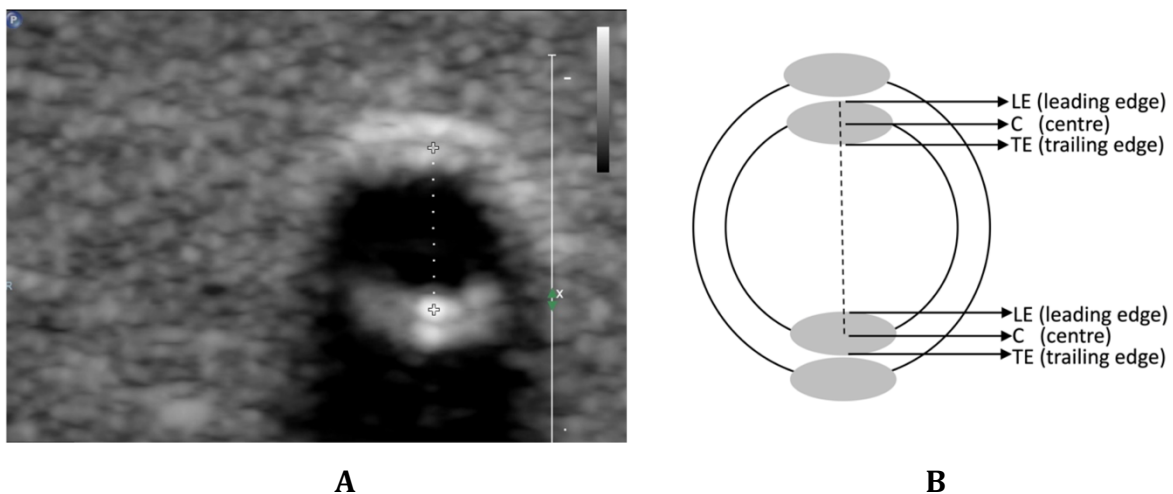
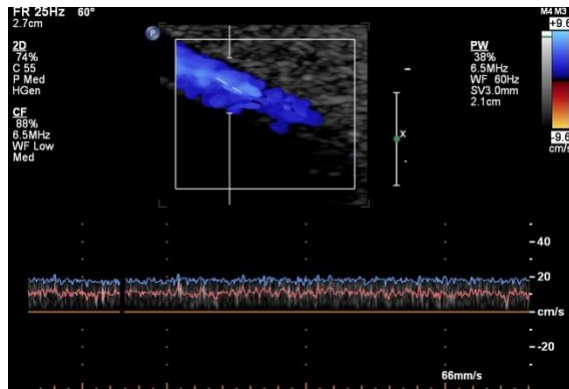
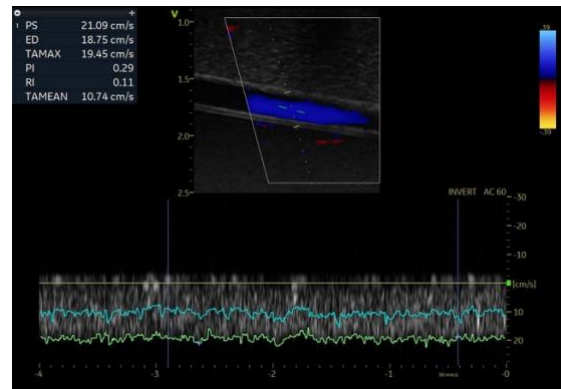


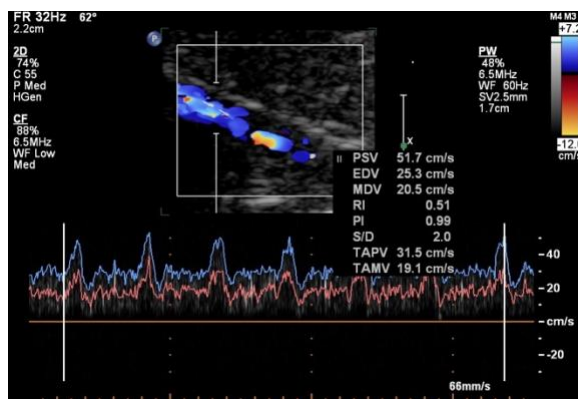
Figure 3. (A) Cross section of the vessel in the flow phantom. (B) Schematic illustrating the leading edge (LE), centre (C) and trailing edge (TE) of the echodensity from where measurements are taken



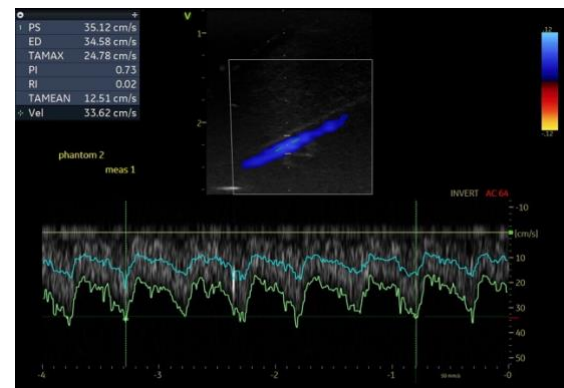
A



C



B



D

Figure 4. Doppler spectrograms obtained from scanner 1 for continuous (A) and pulsatile (B) flow measurements and from scanner 2 for continuous (C) and pulsatile (D) flow measurements