

Conventional echo color Doppler versus ULA-OP in the assessment of venous flow model

Valentina Tavoni,^{1,2} Francesco Sisini,^{1,2} Giovanni Di Domenico,¹ Nadiya Mohammed,¹ Giacomo Gadda,¹ Francesca Calderoni,¹ Mauro Gambaccini¹

¹Department of Physics and Earth Sciences; ²Vascular Diseases Center, University of Ferrara, Italy

Abstract

The quantification of venous flows can be obtained by multiplying cross sectional area, measured on a B-mode video-clip, by velocity values, obtained with Doppler measurements. The Doppler angle between ultrasound (US) line and blood flow requires a manual adjustment. Establishing this parameter is critical in order to calculate blood velocity. However, the operator dependency gives high variable results. It is worth noting that a new class of vector Doppler devices can enhance the accuracy and precision of measurements. Such technology uses a double US line that leads to automatically know the Doppler angle. By comparing in an *in vitro* model of venous flow conventional echo color Doppler (ECD) equipment with the new device, we found a better minimal difference between the latter and the nominal flow rate (20%). On the contrary, the comparison with conventional ECD showed a difference ranging between 2% and 43%, according to the possible settings of the equipment. Our study demonstrates a better accuracy of the experimental device with respect to conventional ECD in measuring the venous flow rate.

Introduction

Ultrasound (US) devices are becoming very attractive in the clinical environment, particularly for medical diagnostics. This technology is used also in the cardiovascular field to quantify blood flows.^{1,2} The flow is calculated by multiplying blood velocity in a vessel, obtained with Doppler measurements, by its cross sectional area (CSA), measured on a B-mode video-clip.³⁻⁶

Differently from other methods used for the same purpose (for example phlebography or functional magnetic resonance imaging), such technology allows to do non-

invasive, cheap and safe examinations. Several studies published in the last decades highlighted a good reproducibility among US technicians trained in investigation of cerebral venous return.⁷⁻⁹

However, highly variable results still exist because Doppler measurements of blood velocity are strongly affected by two types of error, which are systematic and random.¹ A systematic error depends on the instrumentation: in order to overcome such problem, a calibration of the devices is necessary. This practice allows to know any device limits and to evaluate the correction factor to apply on each measurement.

Since the US technology is operator dependant, a random error is related to the operating mode of the specialist who is doing the US examination. In order to reduce this dependency, several investigators attempted to measure the cerebral venous outflow by means of quantitative US protocol. Nevertheless, such a protocol required very skilled personnel and a long period of time to collect measurements.^{2,10,11}

In particular, the technician has to pay attention when positioning the US probe along the vessels. He shall avoid pressing on the subject's skin, because the veins could collapse and change their CSA. Moreover, he has to manually adjust the orientation of the US cursor, which must be parallel to the blood flow.¹ Such operation allows the system to calculate the insonation angle between the US line and the blood flow. The choice of this parameter is fundamental, because the Doppler equation, required to determine blood velocity, depends on the inverse of the cosine of the angle.

Furthermore, it is known that veins tend to be tortuous, making measurements a challenge. In some cases, the presence of valves within the vessels also may lead to turbulences in blood flow. For example, the internal jugular vein region right before the subclavian junction is an anatomical point exposed to flow turbulence, both because of the vessel direction and since it is the most prevalent valvular location. In this venous segment, an error of about 30% in measuring the flow rate has been estimated, which is due to the uncertain velocity assessment.^{2,12}

Another source of variability during US examination is the intrinsic spectral broadening (ISB). ISB is a broadening of the Doppler spectrum due to the mechanism of delivering and receiving acoustic energy.¹³

To overcome some of these sources of errors a new experimental US platform was carried out.^{14,15} Such device uses a double US line, that allows to measure blood velocity by calculating the Doppler angle of

Correspondence: Valentina Tavoni, Department of Physics and Earth Sciences, University of Ferrara, via Mondaini 7, 42122 Reggio Emilia, Italy.
E-mail: valentina.tavoni@unife.it

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insonation in an instantaneous and automatic way. Therefore, this technology has a nominal better accuracy and precision than standard devices.

The aim of this paper is to compare the accuracy and precision of conventional echo color Doppler (ECD) equipment with those of the new one, in a model of venous flow.

Materials and Methods

The comparison of scanners flow estimations was performed through an *in vitro* study with a closed circuit, composed by a

homemade neck phantom and a gear pump that generates a static volume flow (Figure 1). The neck phantom was created with a plastic tube, with circular CSA equal to $(0.5 \pm 0.1) \text{ cm}^2$, inserted into a PMMA box $(20.0 \times 12.0 \times 20.5 \text{ cm})$ full of water. The tube was fixed to a goniometer indicating the insonation angle, *i.e.* the angle between the US line and the flow direction. The pump was used to drive blood mimicking fluid (BMF) (CIRS, Model 046, Norfolk, Virginia, USA) simulating venous blood flow. The BMF is a liquid with the same acoustic properties of the blood. The tank containing the BMF and a turbine flowmeter were also inserted in the circuit (Figure 1). The flowmeter, powered by a 9 V battery and connected to an oscilloscope, was used to calibrate the pump.

The test was done using two devices: equipment A (Conventional ECD device) and equipment B (ULA-OP platform, Florence, Italy) connected to a PC with ULA-OP starter software. The US probe used during the tests is a linear array probe (LA523, Esaote S.P.A., Florence, Italy). This was fastened over the circuit to a manual positioner, which allows moving the probe in very small steps and fixing it in the desired position.

During each test the flow set in the pump was varied between $(150 \pm 1) \text{ mL/min}$ and $(650 \pm 1) \text{ mL/min}$ in steps of $(100 \pm 1) \text{ mL/min}$.

The repeatability was tested by reiterating the same measurements during one experimental session, for five times with the equipment A and for twenty times with the equipment B. Moreover, the reproducibility was measured by repeating the entire procedure in different experimental sessions in order to have some statistics, for five times with the equipment A and for twenty times with the equipment B.

Calibration test

A preliminary calibration test was taken: this procedure consists in comparing the flow values set in the pump and the values measured by the flowmeter. The flowmeter gives a pulsed electric signal for each cycle, whose frequency was measured with an oscilloscope. The FFT mode of the oscilloscope provides us with the main frequency f , which is proportional to the measured flow $\Phi_{\text{flowmeter}}$, as described by the equation:

$$\Phi_{\text{flowmeter}} = f/k \quad (1)$$

with $k = 22,000 \text{ pulse/L}$.

The flow values measured with the flowmeter and those set in the pump were

verified to be not significantly different by a paired t-test. Therefore, the nominal values set was constructed with flow values set in the pump (Φ_{pump}). These were converted into velocity values through the CSA of the tube since $v = \Phi_{\text{pump}}/\text{CSA}$.

Test with equipment A

The measurements were performed by positioning the insonation angle at 30° , 45° and $60^\circ \pm 1^\circ$. The choice of these angles follows the guidelines to obtain reliable measurements.¹⁶

For each flow value set in the pump, the Doppler velocity was measured inside the vessel by choosing two different sizes of sample volume (SV): the smallest SV, *i.e.* 1 mm, and the biggest SV, which extends to include the whole diameter of the vessel, *i.e.* 8 mm.

Since the flow is assumed to be laminar, both the mean time average velocity (TAV) and half of the peak TAV were compared with the velocity set in the pump.

The other parameters set in the system are reported in Table 1.

Test with equipment B

The US mode used to do the experiment was the B-MSD-SpTR-Mode. This mode allows to automatically adjusting the angle of insonation using a double US line. Moreover, this mode enables to calculate the peak velocity in the point within the vessel, where a marker for the focus of the measurement is located.

The experiment was performed by positioning the tube at an insonation angle equal to $80^\circ \pm 1^\circ$. The choice of this angle is given by the best setting suggested by the manufacturer to obtain reliable measurements (personal communication).

The system automatically displays only the measurement of the peak velocity.

The other parameters set in the system are reported in Table 2.

Analysis of results

For every different experimental setup, a set of measurements was collected. A set

is composed by five or twenty velocity measurements corresponding to the single flow values set in the pump each time.

For every flow value of each set, mean values, standard deviations (SD) and coefficient of variation (COV) were calculated. Moreover, a simple linear regression was obtained for each set. Finally, paired t-test was used to state the null hypothesis that two set of velocity measurements were not significantly different from each other. All the tests done are reported in Table 3.

The tests with the equipment A were conducted with two different combination of insonation angle, SV and TAV: the suggested setup and the best setup. The first one is the setting suggested by the guidelines:¹⁶ insonation angle equal to 60° , SV 8 mm and mean TAV. The second one instead is the setting that reproduces the closest measurements to the nominal values. The insonation angle for this setting is equal to 30° , SV 8 mm and peak TAV.

Results

From the verification of reproducibility and repeatability of measurements, a different COV was obtained for every flow values. The range of variation of COV expressed in percentage is reported in Table 4. The results of the t-test between nominal values and measurements collected with equipment B and A for the two experimen-

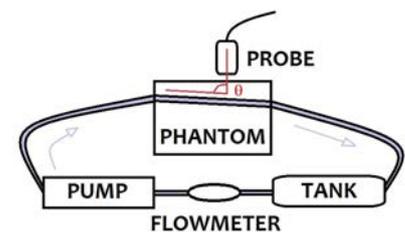


Figure 1. Scheme of the closed circuit composed by phantom, pump, tank and flowmeter. θ is the insonation angle.

Table 1. Parameter setting for equipment A.

Frequency of US beam	5.6 MHz
Maximum depth displayed	72 mm
Focus position	Set by the system
Gain	Set by the system
Sample distance	Central zone of the vessel to prevent the zone in which the flow is not fully developed
Pulse repetition frequency (PRF)	Between 3 kHz and 10 kHz with increasing flow, in order to avoid the aliasing without using excessively high values

tal setups are reported in Table 5. For the t-test the threshold of p-value for statistical significance is chosen equal to 0.05. The equations of the linear regressions applied to the curves of mean values are reported in Figure 2. Slope and intercept of each curve are reported in Table 6.

Discussion

The main result of this study is that the equipment B has a better performance than equipment A in estimating velocity, as shown in Table 5 and 6 and in Figure 2. As confirmation of this, it is worth noting that the equipment B registered values very closed to those measured with the flowmeter. Nonetheless, considering the results shown in Table 4, the equipment A has a better repeatability and reproducibility than the equipment B. In other words, the equipment B shows higher accuracy but lower precision. This apparently contradictory result is probably due to the fact that the equipment A displays the TAV value calculated in a certain time frame, while the equipment B shows a single velocity measurement that is continually refreshed.

We think that the user interface of equipment B has to be improved showing also the TAV value, in order to consider the system for the clinical environment.

In conclusion, the equipment B seems to produce more accurate results than the equipment A. This is an interesting outcome for all the fields where the velocity measurements play a critical role, such as diagnosis of carotid plaques and estimation of volume blood flow. For instance, our group has developed some lumped models based on volume blood flow estimation^{2,17,18} and one of the major limitation of such models was the low level of accuracy in flow quantification. For these reasons, we believe that more accurate velocity measurements can

give a great improvement to both diagnostic responsibility and open scientific disputes. The use of equipment B could be useful for the investigation of cerebral venous return both in physiological and in pathological condition, in particular avoiding as much as possible the errors linked to the blood flow quantification. Further studies will be required to analyse these issues in details.

Conclusions

In the present work it is shown that the new type of US device could be very attractive in future clinical environment, regarding diagnosis of cardiovascular diseases.

This system has the ability to measure the velocity with higher accuracy compared

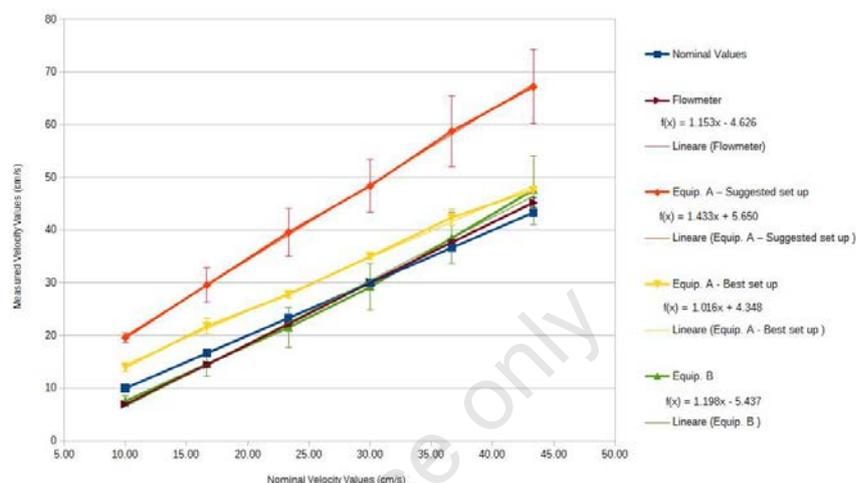


Figure 2. For each nominal velocity value, mean values of measurements collected with equipment A and B, together with nominal values and flowmeter measurements are plotted. Respective SD are marked over each mean value. Linear regressions are drawn over each curve: their equations are reported in legend.

Table 2. Parameter setting for equipment B.

Frequency of US beam	6.25 MHz
Maximum depth displayed	35 mm
Focus position	Set in the same position of the marker
Time Gain Compensation (TGC) A	30 dB
TGC B	0 dB/cm
Sample distance	Central zone of the vessel to prevent the zone in which the flow is not fully developed
PRF	11,996 Hz
Speed of sound	1480 m/s

Table 3. Tests done for the comparison between devices.

Verification of repeatability of measurements collected with equipment A during the same test
Verification of reproducibility of measurements collected with equipment A, using the same experimental setup in different sessions
Verification of repeatability of measurements collected with equipment B during the same test
Verification of reproducibility of measurements collected with equipment B, using the same experimental setup in different sessions
Paired t-test between the set of measurements collected with the equipment A (Suggested setup), and the set of nominal values
Paired t-test between the set of measurements collected with the equipment A (Best setup) and the set of nominal values
Paired t-test between the set of measurements collected with the equipment B and the set of nominal values
Paired t-test between the set of measurements collected with the equipment A (Suggested setup) and the set registered with the equipment B
Paired t-test between the set of measurements collected with the equipment A (Best setup) and the set collected with the equipment B
Calculation of intercept, slope and r ² for each curve obtained with both equipments

Table 4. Repeatability and reproducibility of measurements, tested on both equipments.

Test	Range of coefficient of variation (%)
Repeatability equipment A	1-2
Reproducibility equipment A (suggested setup)	7-12
Reproducibility equipment A (best setup)	0-5
Repeatability equipment B	7-15
Reproducibility equipment B	13-17

Table 5. Results of comparison between equipment A, B and nominal values.

Paired t-test	Results of comparison	P-value
Equipment A (suggested setup) - Nominal values	Significantly different	$<1 \times 10^{-3}$
Equipment A (suggested setup) - Equipment B	Significantly different	$<1 \times 10^{-4}$
Equipment A (best setup) - Nominal values	Significantly different	$<1 \times 10^{-5}$
Equipment A (best setup) - Equipment B	Significantly different	$<1 \times 10^{-2}$
Equipment B - Nominal values	Not significantly different	>0.8

Table 6. Slope and intercept of flowmeter, equipment A and equipment B.

	Slope	Intercept	R ²
Flowmeter	1.153	4.626	1.000
Equipment A (suggested)	1.433	5.650	0.999
Equipment A (best)	1.016	4.348	0.998
Equipment B	1.198	5.437	0.995

to the standard devices.

Further improvements could enhance the precision of Doppler measurements.

Moreover, future developments should take into account the B-mode, in order to complete the US quality control test on the device.

References

- Gill RW. Measurement of blood flow by ultrasound: accuracy and sources of error. *Ultrasound Med Bio* 1985;11: 625-41.
- Zamboni P, Sisini F, Menegatti E, et al. An ultrasonographic model to calculate the brain blood outflow through collateral vessels: a pilot study. *BMC Neurology* 2013;13-81.
- Hoskins PR, Fish PJ, McDicken WN, Moran C. Developments in cardiovascular ultrasound: Part 2. Arterial applications. *Med Biol Eng Comput* 1998;36:259-69.
- Sisini F, Tessari M, Gadda G, et al. An ultrasonographic technique to assess the jugular venous pulse: a proof concept. *Ultrasound Med Bio* 2015;41:1334-41.
- Nakamura K, Qian K, Ando T, et al. Cardiac variation of internal jugular vein for the evaluation of hemodynamics. *Ultrasound Med Bio* 2016;42:1764-70.
- Sisini F, Tessari M, Menegatti E, et al. Clinical applicability of assessment of jugular flow over the individual cardiac cycle compared with current ultrasound methodology. *Ultrasound Med Bio* 2016;1-14.
- Menegatti E, Genova V, Tessari M, et al. The reproducibility of colour Doppler in chronic cerebrospinal venous insufficiency associated with multiple sclerosis. *Int Angiol* 2010;29: 121-6.
- Dolic K, Marr K, Valnarov V, et al. Sensitivity and specificity for screening of chronic cerebrospinal venous insufficiency using a multimodal non-invasive imaging approach in patients with multiple sclerosis. *Funct Neurol* 2011;26:205-14.
- Ciccione MM, Galeandro AI, Scicchitano P, et al. Multigate quality Doppler profiles and morphological/hemodynamic alterations in multiple sclerosis patients. *Curr Neurovasc Res* 2012;9:120-7.
- Monti L, Menci E, Piu P, et al. A sonographic quantitative cutoff value of cerebral venous outflow in neurologic diseases: a blinded study of 115 subjects. *Am J Neuroradiol* 2014 [Epub ahead of print].
- Thibault P, Lewis W, Niblett S. Objective duplex ultrasound evaluation of the extracranial circulation in multiple sclerosis patients undergoing venoplasty of internal jugular vein stenoses: a pilot study. *Phlebology* 2015;30:98-104.
- Zamboni P. Why current Doppler ultrasound methodology is inaccurate in assessing cerebral venous return: the alternative of the ultrasonic jugular venous pulse. *Behav Neurol* 2016;2016:1-7.
- Evans DH, McDicken WN, Skidmore R, Woodcock JP. *Doppler ultrasound: physics, instrumentation, and clinical applications*. New York, NY: John Wiley & Sons; 1989.
- Tortoli P, Bassi L, Boni E, et al. ULA-OP: an advanced open platform for ultrasound research. *IEEE Trans Ultrason Ferroelectr Freq Control* 2009;56:2207-16.
- Tortoli P, Dallai A, Boni E, et al. An automatic angle tracking procedure for feasible vector Doppler blood velocity measurements. *Ultrasound Med Bio* 2010;36:488-96.
- Gerhard-Herman M, Gardin JM, Jaff M, et al. Guidelines for noninvasive vascular laboratory testing: a report from the American society of echocardiography and society of vascular medicine and biology. *J Am Soc Echocardiogr* 2006;19:955-72.
- Gadda G, Taibi A, Sisini F, et al. A new hemodynamic model for the study of cerebral venous outflow. *Am J Physiol* 2015;308:217-31.
- Gadda G, Taibi A, Sisini F, et al. Validation of a hemodynamic model for the study of the cerebral venous outflow system using MR imaging and echocolor Doppler data. *Am J Neuroradiol* 2016;37:2100-9.