Measuring blood velocity using 4D-DSA: A feasibility study

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Purpose: Four-dimensional (4D) DSA reconstruction provides three-dimensional (3D) time-resolved visualization of contrast bolus passage through arterial vasculature in the interventional setting. The purpose of this study was to evaluate the feasibility of using these data in measuring blood velocity and flow.

Methods: The pulsatile signals in the time concentration curves (TCCs) measured at different points along a vessel are markers of the movement of a contrast bolus and thus of blood flow. When combined with the spatial content, that is, geometry of the vasculature, this information then provides the data required to determine blood velocity. A Fourier-based algorithm was used to identify and follow the pulsatility signal. A Side Band Ratio (SBR) metric was used to reduce uncertainty in identifying the pulsatility in regions where the signal was weak. We tested this method using 4D-DSA reconstructions from vascular phantoms as well as from human studies.

Results: In five studies using 3D printed patient-specific cerebrovascular phantoms, velocities calculated from the 4D-DSAs were found to be within 10% of velocities measured with a flow meter. Calculated velocity and flow values from three human studies were within the range of those reported in the literature.

Conclusions: 4D-DSA provides temporal and spatial information about blood flow and vascular geometry. This information is obtained using conventional rotational angiographic systems. In this small feasibility study, these data allowed calculations of velocity values that correlated well with measured values. The availability of velocity and blood flow information in the interventional setting would support a more quantitative approach to diagnosis, treatment planning and post-treatment evaluations of a variety of cerebrovascular diseases. © 2018 American Association of Physicists in Medicine [<https://doi.org/10.1002/mp.13120>]

Key words: 4D-DSA, blood flow, blood velocimetry

1. INTRODUCTION

Measurement of blood flow using specialized catheters and guide wires is often done as a part of cardiac and peripheral vascular diagnostic and therapeutic procedures. These techniques are, for a variety of reasons, for example, small vessel size and tortuosity, seldom used in the diagnosis and endovascular treatments of cerebrovascular diseases. While blood flow measurements can also be done using MRA and Doppler techniques limitations in spatial resolution, long scan times, lack of acoustic windows, and unavailability at the time of endovascular treatment have also limited their utility in neurovascular diseases.

Shortly after the origin of x-ray angiography, investigators began efforts to use the modality to measure hemodynamic

variables and blood flow. In some instances these have been successful; however, they required the use of highly specialized methods which have not been adaptable to routine clinical practices. Today, except for the use of color-coded parametric, for example, time of arrival, maps from two-dimensional (2D) DSA, measurement of blood flow from x-ray angiographic images is, in clinical practice, limited to qualitative visual assessments.^{1,2} In a comprehensive review, Shpilfoygel and colleagues have summarized and compared the x-ray video-densitometric methods used from the 1950s to 2000.³ More recent reports have described efforts to use the combination of 2D and 3D DSA to quantify blood flow.^{4,5,6,7}

Described by Mistretta and colleagues in 2009, four-dimensional (4D) DSA provides three-dimensional (3D) time-resolved images which may be viewed at any angle at

any time during passage of a contrast bolus.^{8,9} Recent reports have demonstrated the usefulness of 4D-DSA both in analyzing the details of complex vascular lesions and in treatment planning.^{10,11} The high frame rate of the acquisitions (30 fps) combined with the high spatial resolution of the x-ray detector combine to provide images that allow visualization of minute changes in flow patterns and angio-architecture.^{10,11,12}

In preliminary studies, we have shown that, through use of a Fourier Phase technique, it is possible to obtain values of blood velocity using 4D-DSA data that are in agreement with data obtained using a doppler flow wire.¹³ In this report we describe and illustrate further development and testing of this approach. Our ultimate aim is to provide a robust automated algorithm that will use the spatial and temporal data from a 4D-DSA to provide clinicians with a color-coded display of blood flow and velocity in a vascular territory of interest. We believe that this will add value in diagnosis, treatment planning and postprocedural evaluations.

2. METHOD

2.A. Data acquisition

The injection protocol and acquisition protocol of a 4D-DSA is identical to those used for a 3D-DSA except that, in order to capture the inflow of a contrast bolus, a short x-ray delay (0.5–1 s) is used in the injection protocol. The two C-arm rotations (mask and fill) span 260° with the number of projections varying from 174 for a 6-s acquisition to 304 for a 12-s acquisition. A subtracted 3D-DSA volume is automatically reconstructed using standard cone-beam CT methods; the subtracted 3D-DSA volume is then used as the constraining volume for reconstruction of the time-resolved 4D-DSA. Each projection is back projected through the constraining volume with temporal information deposited only in those voxels recognized as containing vascular structures. Both reconstructions are performed on a $512 \times 512 \times 384$ voxel grid with a homogeneous voxel side length of 0.46 mm. This then creates a new time series of 3D volumes with temporal rate corresponding to the frame rate of 2D projection acquisition.¹⁴

2.B. Velocity measurement

The following conditions are required to determine the blood velocity within a vessel of interest.

1. A temporal oscillation in the concentration of iodinated contrast agent at points downstream of contrast injection. This signal, referred to as pulsatility, naturally arises when a fixed-rate injection of contrast agent mixes with variable-rate flow of nonopacified blood driven by the cardiac cycle.
2. The pulsatility must be identified and extracted from the time concentration curves (TCCs) measured at points along a vessel in the 4D-DSA reconstruction. Furthermore, the pulsatility must be measurable over a duration longer than double the cardiac period.

3. It must be possible to perform a 3D centerline determination in the vessel of interest.

Given contrast waveforms from two spatially separated points, the distance for passage of a contrast bolus between the two points, Δs , and the time for passage of a contrast bolus between the two points, Δt , allows a measure of the velocity

$$v \approx \frac{\Delta s}{\Delta t} \quad (1)$$

The average velocity over the length of the vessel can be measured by fitting the time vs position to a linear relation

$$t = a \cdot s + b \quad (2)$$

where $a = \frac{1}{v}$ is the slope, and is related to the velocity. Therefore, a shallower slope of t vs s yields a larger velocity. This holds true for waveforms of a contrast bolus regardless of the presence of pulsatility.

2.C. Flow measurement

Using a conventional 3D volume, centerlines are determined for each of the individual branches in which flow and velocity are to be measured. The centerline voxels mark the geometric center of the vessel and are parameterized for each branch. With a known centerline, the normal plane for each centerline voxel can be determined and the cross-sectional area at any plane can be calculated. Combining this with the velocity measurement allows calculation of flow.

2.D. Recognizing and characterizing pulsatility

In the following sections, reference to pulsatile waveforms refers to those along the centerline voxels. Pulsatile temporal waveforms can be decomposed into Fourier modes. A purely sinusoidal waveform would be described by a single Fourier mode. However, cardiac induced pulsatile waveforms are not purely sinusoidal, and thus contain higher harmonics. The Fourier transform in terms of the waveform, w_t , at timeframe, t , is given by

$$W_n = \sum_{t=1}^N w_t e^{-2\pi i \frac{nt}{T}}, \quad (3)$$

where $\frac{1}{T}$ is the sampling frequency, and N is the number of timeframes. Vascular segments where pulsatility is strong and consistent are locations where the derived velocity and flow information have been found to be most reliable. For a given frequency, f_n , with frequency index n , these regions can be determined by comparing the FFT power spectrum

$$PS_{f_n} = \frac{|W_n|^2}{N^2} \quad (4)$$

at this frequency with those of the neighboring frequencies.

Figure 1 shows an induced pulsatile waveform and its associated FFT power spectrum from the phantom experiments described below. In the power spectrum the fundamental

FIG. 1. Pulsatile waveform from a 4D-DSA TCC phantom study (left) and corresponding FFT power spectrum (right) showing areas of strong pulsatility at the first peak, corresponding to the fundamental frequency, and subsequent peaks indicating the presence of higher harmonics, in these nonsinusoidal waveforms. The waveform depressions at 3.5 and 6.5 s are due to vessel overlap. [Color figure can be viewed at wileyonlinelibrary.com]

frequency located at $f = f_0$ and harmonic peaks of the pulsatility located at integer multiples of f_0 can be easily seen. Identifying these peaks is straightforward for regions where there is clearly defined pulsatility, but can become problematic in regions where the pulsatility is, for a variety of reasons, weakened. To further reduce noise and increase confidence in recognizing the Fourier frequency in such regions a sideband ratio (SBR) metric was derived. We define the SBR as a ratio between the local FFT Power Spectrum (PS) and the average of neighboring background frequencies, where this average serves as an estimate of the background noise level at the frequency in question. This ratio of the power spectrum and sideband value is, therefore, a proxy for a signal to noise ratio and makes it possible to pick out strong pulsatile frequencies above the noise and artifacts caused by scatter, motion, and/or vessel overlap in the raw projection data. This sideband value is explicitly given by

$$SB = \frac{1}{M} \sum PS_{f_i}, \quad (5)$$

where the sum contains the M closest neighboring frequency points, excluding f_0 . The Sideband Ratio (SBR) at f_0 is therefore defined as

$$SBR = \frac{PS_{f_0}}{\frac{1}{M} \sum PS_{f_i}}. \quad (6)$$

Values larger than unity indicate a pulsatility that is stronger than background noise or other signals. Based on the data analyzed thus far, $SBR \gtrsim 3$ correspond to waveforms that appear acceptable for flow and velocity measurements. The progression of power spectrum to sideband ratio for a typical waveform is illustrated in Fig. 2.

2.E. Extracting velocity from pulsatile waveforms

For a defined timeshift, Δt , the Fourier transform is altered up to an overall phase given by

$$W'_n = w_t e^{-2\pi i \frac{f}{T}(t+\Delta t)} = w_t e^{-2\pi i \frac{f}{T}t} e^{-2\pi i \frac{f}{T}\Delta t} = W_n e^{-2\pi i \frac{f}{T}\Delta t} \quad (7)$$

This illustrates that for a given shift in time, an overall phase shift, $e^{-i\Delta\phi}$, is imparted on the FFT, with the relation

$$\Delta t = \frac{\Delta\phi}{2\pi \frac{f}{T}} = \frac{\Delta\phi}{2\pi f}, \quad (8)$$

where f is the pulsatile frequency, for which the period is $T_0 = \frac{1}{f}$. Using this FFT shift property, the time delay of a pulsatile wave is determined by inspecting the phase of the characteristic frequency of the pulsatility.

Note that, due to aliasing, the phase can jump by 2π along the vessel length. Therefore, at any point where wrapping causes such a change, a phase shift is required for correction. This makes the phase monotonically increasing for positive velocity, and a fit can then easily be obtained. With the unwrapped phase, the velocity becomes

$$v = 2\pi \frac{f}{m}, \quad (9)$$

and can be determined from the linear slope, m , of the fit to the unwrapped FFT phase vs the distance along the vessel centerline.

2.F. Determining velocity and flow in vessels that are not straight or are diseased

While determining velocity and flow according to the above sections is straightforward it can become problematic for more complicated vessel configurations where the cross-sectional area changes at a short radius curvature or stenosis. For an incompressible fluid and rigid vessel walls, volumetric flow, $\mathcal{F}$, is a conserved quantity and can readily be computed (within measurement errors caused by motion, noise, overlap or discretization of the 4D-DSA reconstruction) from a

FIG. 2. Power spectrum (top), sideband of neighboring frequencies, taken as Eq. 5 with $M = 4$ (middle), and Sideband Ratio (bottom) showing the characteristic frequencies of strong pulsatility. From the SBR, the fundamental frequency contains the strongest pulsatility. [Color figure can be viewed at wileyonlinelibrary.com]

product of the velocity at the center of the vessel and cross-sectional area using

$$\mathcal{F} = \alpha v \cdot A, \quad (10)$$

where α is a scaling parameter which takes into account the velocity profile across the vessel, $\alpha = 1$ for plug-flow and $\alpha = \frac{1}{2}$ for purely parabolic flow. As we measure the velocity from the waveforms at the centerline, the value of total flow derived must make an assumption of the velocity profile. Here, we simply note that this scaling factor can be used as a way of parameterizing that profile. While rigid vessel walls cannot be guaranteed, as a first approximation, the vessel walls are assumed to be rigid in the estimation of flow.

A collection of measurements, Q , can be partitioned into a mean measurement value, $\langle Q \rangle$, and a residual value, δQ , whose mean is zero. With these definitions, the average flow rate becomes

$$\begin{aligned} \langle \mathcal{F} \rangle &= \alpha \langle (\langle v \rangle + \delta v) \cdot (\langle A \rangle + \delta A) \rangle \\ &= \alpha \langle v \rangle \cdot \langle A \rangle + \alpha \langle \delta v \cdot \delta A \rangle. \end{aligned} \quad (11)$$

where the cross terms $\langle \delta v \cdot A \rangle$ and $\langle \delta A \cdot v \rangle$ vanish because the mean of the residuals δv and δA vanish. Therefore, the average flow rate can be estimated by a product of the average velocity and cross-sectional area if the residuals in v and A are uncorrelated.

Along the length of the ICA, which is the focus of this work, there is little change in the cross-sectional area. We recognize that in the more distal segments, for example, MCA over a few cm there is a significant decrease in diameter. For instances where the cross-sectional area changes considerably, the residual area may decrease below the mean and the residual velocity, therefore, increases. In these occasions, the covariant terms must be retained to account for the variation.

The calculation of velocity in Eq. 9 assumes there is no change in cross-sectional area while traversing the vessel. In instances of large changes in cross-sectional area, the phase must be modified to take into account this area change due to mass conservation. The equivalent flow phase is identified with the following assignment

$$\Phi_N^{\mathcal{F}} = \phi_0 + 2 \sum_{i=1}^{N-1} \frac{\phi_{i+1} - \phi_i}{A_{i+1} + A_i}, \quad (12)$$

where ϕ_i and A_i are the FFT phase and cross-sectional area, respectively, for centerline voxel with index, i . The offset phase, ϕ_0 , can readily be set to zero as it does not affect the velocity calculation. The quantity $\Phi_N^{\mathcal{F}}$ is the effective flow phase at centerline point N that is used to calculate the volumetric flow rate. Again, after fitting $\Phi_N^{\mathcal{F}}$ vs vessel baseline distance to obtain the slope $a_{\mathcal{F}}$

$$\mathcal{F} = 2\pi \frac{f}{a_{\mathcal{F}}}. \quad (13)$$

Typically, due to the voxel size of the 3D reconstruction, the cross-sectional area calculation can be determined to no better than 12% for vessel diameters of 5mm, as is typical in the ICA¹. If the fractional area change along the course of a vessel is larger than the statistical uncertainty afforded by discrete voxels, it is more advantageous to use the flow phase as discussed above. Otherwise, for relatively little variance in the cross-sectional area, the average velocity and area can be used to reliably compute the flow. This is applicable to the ICA and phantom of this study, therefore, Eq. 9 was used for computing the velocity.

The general outline of our method for determining flow from pulsatile angiographic data is illustrated in Fig. 3.

¹This assumes the area error is due to the discrete nature of the periphery. If one assumes the radial error is δr , the area error will be $\delta A = 2\pi r \delta r$. Here, a radial error of 1/4 voxel with a voxel scale of 0.46 mm/voxel is assumed.

2.G. Optimizing waveform selection

Regions of strong and consistent pulsatility are most likely to be locations from which it will be possible to obtain the strongest quality of fit. We have optimized the selection of such regions from that described earlier by using an adapted map with the SBR as a metric. For each point (s, t) in the time vs centerline index waveform maps, the local power spectrum and SBR over a window region defined within the region $(s, t \pm \Delta t)$ are calculated. The extent of Δt is taken to be multiples of the fundamental period. Good results are found with $\Delta t = 2T$, although $\Delta t = T$ may also offer acceptable regions, albeit with lower confidence. From this SBR map, a low-pass filter is applied and a threshold of one-fourth the median SBR is enforced. This resulting threshold cuts low pulsatile signals from consideration in the fit. The remaining region defines a mask map over which the phases will be included in a linear regression.

The phases calculated from the window region are computed and displayed as a phase map. Note, it is advantageous to consider this phase before unwrapping since each phase region defines a cardiac cycle, which are shown in Fig. 4 as discrete strips. These regions are defined as a continuous 2D region in the time index vs centerline index plane where neighboring points have a difference in phase of no more than π . A linear regression of the phase vs vessel position is performed within each cardiac cycle (e.g., top left panel of Fig. 4), offering what is then a largely independent measure of the velocity from one cardiac cycle to the next. In reality, the 2D subregion encompasses several cardiac cycles, so there is some cross-cardiac cycle correlation in the velocity estimate. With a number of cardiac cycles included, however,

a measure of the dispersion of velocity measurements and therefore a measure of the uncertainty of the velocity and flow measurements can be determined.

Within each cardiac cycle phase region, the regression and the associated Pearson's r -correlation are calculated. The final velocity or flow is determined after rejecting cycles with low r -correlation by computing the slope of the data points in the centerline vs timeframe plane. Only measurements above a correlation value are included in the combination. The trial correlation cut is raised until the relative uncertainty of the measurement is minimized, but retaining at least five cardiac cycles. Figure 4 shows a summary of selecting regions of strong pulsatility and using these regions for the velocity/flow fit. Most of the cardiac strips have very high Pearson's r -correlation, with the exception of the last strip, where the measurement is less certain, and provides an anomalously high velocity. The final trial correlation cut removes this and other similarly poorly measured strips from the final velocity estimate.

Due to the limited number of cardiac regions in a waveform, the statistical uncertainty in the measurement may be underestimated. To address this, the method is extended to consider pairs of points in the waveform as being independent measurements, thereby increasing the number of velocity samples. The pairs of points selected can be refined by selecting points with large SBRs and a minimum threshold of time-shift and spatial displacement. An optimization step is performed wherein these thresholds are independently varied to provide a smallest total uncertainty, and includes the uncertainty due to a limited sample size. A histogram of velocities from the ensemble of pairs then reflects the velocity distribution and can be taken as a proxy for the probability distribution of velocities. This is illustrated in Fig. 5 for one of the phantom experiments where the distribution of velocities from the ensemble of centerline pairs are shown. Confidence intervals are defined by the regions encapsulating 68% and 95% of the velocity measurements.

2.H. Phantom experiment

The developed approach was evaluated in phantom and patient data. The phantom (Vascular Simulations, Stony Brook, NY, USA) consists of a pulsatile pumping mechanism simulating blood dynamics, as well as a silicone-based cranial vascular tree derived from clinical data [Fig. 6(a)]. The main component of the arterial tree represented is a left ICA up to the MCA junction with two stylized MCA arteries. The stylized MCA vessels are joined prior to the outlet of the phantom (Fig. 6). The diameter of the ICA is 5 mm and the diameters of the stylized MCAs are 4 mm (Right) and 3.5 mm (Left). The model included a large aneurysm with a 21 mm diameter. The 4D-DSA acquisition sequence consisted of a mask and a fill run covering 260° with 304 projection images in a duration of 11.6 s for each run. Tube output was set to 70 kVp with a detector target dose of 0.36 μ Gy/Frame.

FIG. 3. Flowchart showing workflow for extraction of flow using the Fourier phase technique. The FFT of the waveform, A , gives the power spectrum PS_A . Using the sideband analysis, characteristic frequencies, k_{peak} , of the pulsatility are found. The corresponding phases, $\tilde{\phi}$, are then unwrapped to arrive at the native phase, ϕ . A linear fit of the phase and displacement along the vessel yields the velocity and flow.

FIG. 4. Overview of selecting strong pulsatility regions for velocity measurement determination in a phantom experiment. Top row: The full 2D acquisition waveform (left), cardiac strips showing local phases determined after strong pulsatility isolating SBR mask applied are shown as discrete vertical strips. Bottom row: Pearson's r^2 -correlation of the fit of each cardiac cycle region after cycle selection (left), and velocity measurements for each cardiac cycle region (right). The centerline index refers to the consecutive voxel number from the beginning of the vessel, measured along the centerline, and the time index refers to the time-frame number in the 4D-DSA data. The centerline voxel size is 0.46 mm/voxel and each time index is 1/30 s. [Color figure can be viewed at wileyonlinelibrary.com]

Selective artery injections were performed aimed at deriving a contrast agent injection and imaging protocol that would yield information on contrast flow and dynamics, as well as capture enough consistently filled data to provide a high-quality 3D image of the vasculature [Fig. 6(b)]. Experiments were performed on a Biplane Angiographic imaging system (Artis Zee, Siemens AG, Forchheim, Germany). The final derived injection protocol used 3 mL/s for 7 s with no x-ray delay.

Rotational projection images were acquired using techniques identical to those previously described. The detector frame rate was 30 Hz for all but one of the experiments, where the rate was 60 Hz. A total of five studies were performed. The 4D-DSA volume data were reconstructed using prototype software developed jointly with the vendor of the Angiographic system (Siemens Healthineers, Forchheim, Germany).

Flow measurements were performed using a volumetric flow rate meter (Transonic 400-Series Multi-channel Flowmeter, Ithaca, NY, USA). The flow meter has an error of $\pm 10\%$ and was positioned near to the ICA inlet, just downstream from the site for injection of contrast medium.

2.1. Clinical case evaluation

The proposed technique was also tested on 4D-DSA volumes selected from an existing institutional database. Patient datasets from a given date range were reviewed and three consecutive cases with no patient motion or extreme vascular anomalies (large arterial-venous malformation (AVM)) were selected. Two of these had no vascular anomalies; one had an ICA aneurysm. The aneurysm was well downstream from the

ICA segments from which 4D-DSA values were calculated. Velocity and flow values were determined in the ICA of the vascular volume. The ICA diameters and cross-sectional areas were 4.3, 4.4, and 4.8 mm and 14, 15, and 18 mm², respectively. While no ground truth data are available for these measurements, the determined values were compared to available literature values.

3. RESULTS

The phantom studies showed good correlation between the velocity measurements made using the flow meter and those from the 4D-DSA as calculated using the FFT phase method. As shown in Table I, the estimated root mean square error between the flow meter velocity measurements and the velocity computed using 4D-DSA was 10.0%, which is comparable to the measurement error of the meter. This is comparable to the velocity measurement uncertainty, which has RMS uncertainty of 13.5%.

The 4D-DSA-based velocities and blood flow values in the three human ICAs were found to be in the range of those reported in literature using phase contrast MRA and an optical 2D–3D-DSA method (4 mL/s).^{15,16} Assuming a parabolic radial velocity profile, a flow value of 4 mL/s corresponds to a center line velocity of around 36 cm/s which is within the range of calculated 4D-DSA velocities found in the human studies as seen in Table II.

4. DISCUSSION

In the current endovascular environment, information for treatment decision is mainly derived from static images. With

FIG. 5. Centerline velocity (CV) estimate in cm/s from position pairs in cardiac strip after threshold optimization for a phantom study. Shown is the shift in the timeframe between pairs of centerline points (top left panel) and the distribution of this timeframe shift and the positional gap (bottom left panel), which is the number of voxels along the centerline separating the voxel pairs. A minimum shift of three timeframes is observed for optimizing the uncertainty for this case. The slope of each point in this plane populates the histogram of velocities (top right panel) where a cumulative distribution (bottom right) can be interpreted as a quantile range for velocity measurements. [Color figure can be viewed at wileyonlinelibrary.com]

FIG. 6. (a) Vascular simulation phantom with pulsatile flow through pneumatic cardiac heart and patient derived cerebral vasculature. (b) 3D DSA from rotational angiographic images using artery-specific injection. (c–e) Projection images of contrast progression through phantom during rotational projection image acquisition. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE I. Velocity values comparing flow meter values with Fourier Phase-based 4D-DSA calculations. Overall RMSE and flow uncertainty are 10.0% and 13.5%, respectively

Case	Meter velocity (cm/s)	4D-DSA velocity (cm/s)	Relative uncertainty	Meter vs DSA error (relative error)	Average SBR
1	47.6	40.0 ± 8.6	22%	7.6 (16%)	3.4
2	47.6	45.4 ± 4.8	11%	2.2 (4.5%)	6.9
3	71.3	64.8 ± 5.7	8.8%	6.5 (9.1%)	18.7
4	95.1	85.0 ± 11.2	13%	10.1 (10.6%)	16.2
5	71.3	75.0 ± 6.9	9.2%	3.7 (5.2%)	13.7

TABLE II. Velocity measurements in three human clinical ICA cases. The velocities fall within expected physiological ranges of Ref. [9,15].

Case	4D-DSA velocity (cm/s)	Relative uncertainty	Average SBR
1	50.6 ± 7.3	14%	3.7
2	31.3 ± 4.9	16%	4.4
3	28.1 ± 6.1	22%	4.0

the ever increasing complexity of disease treated in the interventional suite, the evaluation of blood velocity and flow through vessels may yield additional information and quantitative endpoints. Applications may entail evaluation of blood velocity and flow before and after implantation of a flow diverting stent to evaluate the likelihood of capillary bleeding due to increased flow/velocity, delineation of flow in arterial-venous malformation feeding arteries to assess which of the arteries to embolize first, as well as the evaluation of blood flow following mechanical thrombectomy in neurologic stroke, potentially developing a metric to gauge the risk for post-thrombectomy hemorrhage.

In this feasibility study we have shown the capability of measuring velocity and blood flow using 4D-DSA data obtained in phantoms and human subjects using a novel FTT-based method. The calculated 4D-DSA values correlate well with those measured in phantoms using a flow meter. The success of our efforts was dependent upon development of methods which: (a) allowed use of the spatial information in a 4D-DSA reconstruction to determine the cross-sectional area of a vascular segment and, (b) used the temporal information to determine the velocity of blood flow. This work provides the background for additional studies which will be aimed at extending the measurements into smaller intracranial and peripheral vessels using techniques that will allow validation of the accuracy of our method, for example, flow wires.

Development of a method that is based on an analysis of a FFT power spectrum of the waveforms in the TCCs used for a 4D-DSA reconstruction allowed us to recognize and characterize the strength and reliability of the pulsatility that propels a contrast-blood bolus through the vasculature. These data

can be used to determine the time required for the bolus to pass from an upstream to a downstream location; this allows determination of velocity. The spatial information from a volumetric reconstruction allows determination of the cross-sectional area of a vascular segment. Taken together, these data allow a measure of blood flow.

Obtaining an accurate measure of blood flow relies on accurate tracking of the contrast bolus waveform as it traverses the vessel. Since the features that are tracked in the waveform are inherently pulsatile, detecting high levels of pulsatility using the SBR map is required for good velocity measurements. This accomplishes both HR identification and optimized waveform region selection. To our knowledge, using these data to determine velocity and blood flow has not been previously reported using a single acquisition with x-ray angiography.

While the calculated values from the three human studies are consistent with ones from the literature and demonstrate the feasibility of calculating velocity and flow with a precision that would be acceptable in clinical studies, this does not allow a statement regarding the generalization of this method to human studies. In ongoing studies, we are exploring the degree to which patient motion, scatter, and vascular overlap may introduce errors into calculated 4D-DSA values. Validation against a clinical gold standard is necessary. Validation studies should investigate both healthy and diseased vessels.

The present method focuses on flow in cerebral arteries, which are relatively stationary over the course of C-arm rotational acquisitions. Motion-compensated 4D-DSA techniques¹⁷ may enable its application to other organ systems, although this remains to be demonstrated. Other potential shortcomings of this method include the requirement for the presence of consistent pulsatility waveforms for reliable measurement. Loss of pulsatility can occur in vessels in the intracranial circulation and more distal vessels. Because accurate determination of the cross-sectional area of a vessel is dependent upon accurate geometry of a 3D reconstruction, it is necessary to use an injection protocol which results in even distribution of the contrast medium during the acquisition. Because a contrast bolus obtained using an IV injection is fully mixed with blood and, thus will be seen by the detector as being homogenous (there will be not be a combination of un-opacified blood and contrast-blood mixture during each cardiac cycle) our method will not be applicable in such studies, or in intravenous injections where the pulsatility is markedly low. Injection protocols are, therefore, required to be designed to give high pulsatility strength. Finally, this technique is not applicable to vessels which are close to or beyond the spatial resolution limit of the reconstructed 4D-DSA.

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CONFLICTS OF INTEREST

Dr. Shaughnessy, Dr. Strother and Dr. Mistretta have patents pending on techniques related to this work.

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