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Rapid 3D Imaging of Contrast Flow: Demonstration of a Dual Beam Technique

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Abstract

Perfusion imaging in a 3D volume using ultrasound contrast agent may improve vascular characterization compared to 2D imaging. Conventional 3D acquisition requires excessive scan time. A dual transducer technique using conventional systems has been introduced that allows 3D imaging of contrast dynamics with drastically reduced scan times (LeCarpentier et al. 2003). Two transducers are translated across a volume where the leading transducer effects contrast clearance and the following transducer images at desired contrast refill times. With 2D arrays that allow simultaneous clearance and imaging pulses, scan times could be further reduced and the need for two transducers eliminated. The dual transducer technique was demonstrated on a tube phantom, with observed contrast profiles matching those expected. Measured center velocities of ($\pm$ std dev) 1.46 ± 0.21 and 2.25 ± 0.5 did not statistically differ from expected values of 1.75 and 2.50 (all mm/s), ($p > 0.05$). This technique is introduced for rapid acquisition of 3D contrast refill images.

Keywords

contrast refill; perfusion; blood flow; imaging; vasculature; angiogenesis

Introduction

Earlier studies have suggested that malignant masses have deviant vasculature including thin-walled blood vessels, increased microvessel density, disordered neovascularization penetrating the mass, arteriovenous shunting, and other histologic findings (Folkman and Beckner 2000; Vaupel et al. 1989; Weidner et al. 1991). Visualization, mapping, and quantification of the blood flow within and surrounding tumors may provide a means for differentiating between benign and malignant masses (Bell et al. 1995; Cosgrove et al. 1990, 1993; Delorme et al. 1995; Kedar et al. 1995, 1996; Lee et al. 1996; Peters-Engl et al. 1998; Vaupel et al. 1989). Extension into 3D may further improve the ability of discriminating between benign and malignant masses (Carson 1997). Additional Doppler volumetric scans with various quantitative blood-flow measures have been conducted in a variety of organs. Examples include breast (Bhatti et al. 2001; Carson et al. 1998, Hochmuth et al. 2002),

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prostate (Moskalik et al. 2001a, 2001b; Potdevin et al. 2001), uterus (Jokubkiene et al. 2006), placenta (Merce et al. 2005), and ovary (Chan et al. 2003). Mehta et al. (2004) have reviewed various studies which show the advantages of 3D ultrasound with and without contrast enhancement relative to 2D scans in the detection and staging of prostate cancer.

Extensive evaluation of ultrasound contrast agents for the measurement of blood flow has been previously performed (Porter and Xie 1995; Porter et al. 1997; Wei et al. 1998) and is related to the refill of contrast agent into the tissue after contrast clearance. In early studies, refill data were obtained using interval imaging (Kamiyama et al. 1996; Kamiyama et al. 1999; Ohmori et al. 1997; Wei et al. 1998), where a plane is cleared of contrast and allowed to refill for a given time. The process is repeated with different times to gather the images at various refill times. Signal intensities for regions of interest encompassing the image are plotted against their refill times. Fitting these data using a model for refill gives the mean transit time (MTT) of each region of interest. Combining the MTTs for regions throughout the image produces a refill map. Subsequent development of low-power, essentially non-destructive pulse sequences enables the measurement of refill curves in real-time after clearing the plane, in what is termed real-time refill imaging (Porter et al. 1999; Simpson et al. 1999).

Both of these techniques are capable of gathering refill data for a single imaging plane in a reasonable period. However, a tumor is a three-dimensional mass, and extending data collection to such volumes is impractical because of tremendous time requirements. Acquisitions that require a modest time t for a single plane may become unfeasible in 3D, since every single imaging plane constituting part of the volume would require t to acquire. The volume would also need to be perfused with contrast agent during this entire period. Ideally, the further development of two-dimensional arrays would allow the imaging of 3D volumes without the need for mechanical translation at frame rates comparable to those available with conventional 1D transducers (Hoskins 2002). However, their development has been problematic with large storage requirements and large number of required digital channels.

Theoretical Considerations

Laminar, viscous fluid flow through a straight, circular cylinder has a well-known parabolic velocity profile given by

$$u(r)=V_c \left[1 - \left(\frac{r}{R} \right)^2 \right] \quad (1)$$

where $u(r)$ is the flow velocity at radius r from the center, V_c is the center velocity, and R the tube radius. This velocity profile is independent of time.

Consider the case presented in Fig. 1. If at a given starting position along the cylinder one selects volume elements at uniform position $p=0$ at time $t=0$ for all r , then the position of the elements composing the front $p(r,t)$ is simply $tu(r)$. The front continually stretches with increasing t . Substitution provides

$$p(r,t)=tu(r)=tV_c \left[1 - \left(\frac{r}{R} \right)^2 \right] \quad (2)$$

Letting d represent the distance along the tube where the imaging transducer samples the contrast agent radii, with $d=0$ being the initial uniform position of the front at $t=0$, solving for the radius r as a function of d gives the following expression for $r(d,t)$

$$r(d,t)=R\sqrt{1-\frac{d}{tV_c}}. \quad (3)$$

Since the dual-transducer technique translates the imaging transducer along the tube after contrast clearance, contrast radii are measured as functions of d and t . Therefore, this model allows the testing of the dual-transducer technique in imaging three-dimensional flows via a comparison of observed and predicted radii. The actual profile predicted under these imaging conditions can be considered a “time-dilated” parabola as given by eqn 3 and shown in Fig. 1.

For a given transducer translation velocity v_T and transducer separation s (known from the dual-transducer configuration) and an observed time-dilated parabola, one could derive the center flow velocity V_c by substituting the expression $v_T t - s$ for d in eqn 3, reducing $r(d,t)$ to a function of only t

$$r(d,t)=R\sqrt{1-\frac{d}{tV_c}} \rightarrow r(t)=R\sqrt{1-\frac{v_T t - s}{tV_c}}. \quad (4)$$

One can fit all the measured radii at their known times t to the expression $r(t)$, and estimate the parameter V_c for any given experiment. Comparing the estimated and known V_c values (based on flow rates) provides a measure of the accuracy of the dual transducer technique.

Methods

A technique is described which makes three-dimensional contrast data collection more practical with 1D transducers. The technique is demonstrated by sweeping a transducer pair, composed of a clearance transducer and a low-power imaging transducer as a unit at velocity v over a contrast perfused tissue volume. The clearance transducer causes contrast to be cleared in the swept volume. Since contrast is continually perfusing, the emptied volume immediately begins to refill with contrast. The imaging transducer reaches the location previously occupied by the clearance transducer in time Δt for all positions. As Δt has elapsed regardless of the position along the volume, the imaging transducer images the state of contrast refill at all positions for time Δt after each sweep. Longer Δt values can be obtained by pausing the sweep immediately before the imaging transducer begins entering the volume of interest. A schematic of the method used to demonstrate the technique is shown in Fig. 2. Here, two transducers are used but the procedure could be applied for any approach in which separate clearance and imaging sequences can be combined with the logical extension to 3D imaging systems.

A series of sweeps with varying Δt allows collection of refill images for the volume. The dual-transducer technique requires only slightly more time than single slice interval imaging acquisition, thereby making the visualization and mapping of three-dimensional volumes practical in comparison to single-slice acquisition techniques (see Table 1 and the Appendix). Slice separation is determined by both acoustic frame rate and translation velocity. Under the normal operating limits of the translation system and scanner, the number of acquired image planes over the volume of interest does not affect the overall acquisition time.

In order to test the effectiveness of the dual-transducer technique for high-speed contrast imaging, flow through a tube phantom was imaged. A cylindrical tube was embedded within tissue mimicking foam, and contrast agent was pumped through at known rates. Since the flow profile through the cylinder is theoretically known, one can compare measured three-dimensional profiles with those expected from theory.

All scans were conducted within a water tank lined with sound absorbent rubber and filled with water that had been allowed to come to gas saturation. A schematic of the overall experimental setup is shown in Fig. 3. The phantom was mounted beneath the water on a stand and secured with two rubber bands. A dual transducer assembly is shown in Fig. 4 and was constructed using two stepper-motors and controls (Microkinetics Corporation, Kennesaw, GA, USA). The motors were controlled from a laptop computer through LabVIEW (National Instruments Corporation, Austin TX, USA) scripts and the DAQCard-700 (National Instruments). The scripts allowed control of both transducer separation and translation along the transducers' elevational direction. The transducer assembly was mounted upon a second stand that placed the transducers above the phantom being scanned.

To build the tube phantom, a block of tissue-mimicking foam (S80 - Crest Foam Industries, Inc., Moonachie, NJ, USA) was saturated with water and frozen in order to temporarily harden the block sufficiently for drilling. A circular hole with a diameter of 6.4 mm was drilled through the block and the foam was subsequently allowed to thaw. Next, a thin-walled (0.79 mm) latex rubber tube with a 6.35 mm inner diameter (Kent Elastomer, Kent, OH, USA) was threaded through the block, with sufficient additional tubing (~20 times diameter) on both ends of the block to dampen transitional flow effects due to connections. The foam block was degassed prior to use by submersion in boiling water and subsequently allowed to cool, after which the phantom was maintained under water at all times.

The tube phantom was connected to form a recirculating flow system using intravenous (IV) tubing. A variable rate IV pump (IVAC 560, IVAC Corporation, San Diego, CA, USA) drove the flow. All flow originated and terminated at a stirred flask containing a contrast suspension (Definity Bristol-Myers Squibb Medical Imaging at a 1:5000 dilution in water). The suspension was continuously circulated through the phantom.

A Toshiba Powervision 8000 scanner (Toshiba America Medical Systems, Tustin, CA, USA) with a 3.75 MHz (PVN-375AT) transducer in harmonic mode (power setting of P6 giving a MI=0.2 with a frame rate of 10 Hz) was used for contrast clearance. A GE Logiq 9 scanner (General Electric Healthcare, Milwaukee, WI, USA) with a 7L transducer in CPI (coded phase inversion) mode was used to image. Since the clearance transducer has a significant contrast disruption zone as indicated in Fig. 2, the effective clearance width in the elevational direction of the clearance transducer was measured by stopping the pump, applying a series of frames, and imaging laterally the contrast gap produced using the imaging transducer at low-power (1% acoustic output power setting giving a MI=0.06, focus at 10 mm). Calculations of Δt were based on the distance from the edge of contrast clearance to the center of the imaging transducer. The limit of the clearance width as the number of frames increased without bound was noted as 6 mm and used as the effective width as seen in Fig. 5. As such, the effective transducer separation for each scan was considered 3 mm less than the physical transducer separation.

The dual transducer system was used to image the tube phantom at two different flow rates (1.75 and 2.50 mm/s peak velocity) with effective transducer separations of 42, 57, 72, and 87 mm. The imaging transducer axial focus was changed to 20 mm in order to place it closer to the tube within the phantom. Cross-sectional images of the tube phantom were acquired

and assembled. Images through the tube center in the lateral-elevational plane were then extracted from the reconstructed 3D imaging volume and scaled appropriately for the transducer translation velocity v_T (6 mm/s) and frame acquisition rate (19 Hz). Imaged contrast was subsequently compared to expected “time-dilated” parabolae. Observed and expected profiles were compared visually and quantified by fitting the observed profiles to their corresponding measures of center velocity v_c provided by eqn 4. The lateral-elevational plane was selected for comparison to avoid asymmetric effects of overlying attenuation on the contrast profile. In addition, overlying attenuation due to contrast is eliminated at the profile edge, and a constant point-spread function is maintained throughout the plane.

Results

For a given cross-sectional plane imaged over time, one would expect a series of enlarging discs of contrast as depicted in Fig. 6, which shows a single plane extracted from three-dimensional data sets acquired using the dual transducer technique, with circles outlining the expected discs. Representative composite images of time-dilated parabolas assembled from the cross-sectional images with their expected contrast outlines superimposed are shown in Fig. 7 for each sweep, with the flow rate and effective transducer separation noted. Since the transducer translation velocity v_T (6 mm/s throughout) was greater than the maximum flow velocity v_c , the imaging transducer reached and overtook the refilling front for each sweep. At all times, the radius of the observed contrast should be that found by eqn 3. As expected, for the reduced flow rate shown in Fig. 7B, the contrast profile does not progress as far as that for an identical Δt (14.5 s). Examination of the images in Fig. 7 reveals a generally good match between the observed profiles and those predicted with the clear exception being the axial center of each profile. The center of the profile does not progress as far as the prediction, and the discrepancy is greater for higher flow rates. Fitting the measured radii to eqn 4 to estimate v_c gives estimated values shown in Fig. 8 for all scans acquired. The mean measured center velocities were ($\pm$ std dev) 1.46 ± 0.21 and 2.25 ± 0.5 corresponding respectively to expected values of 1.75 and 2.50 (all in mm/s). In a statistical comparison to the expected values, a Student t-test yields $p=0.07$ and 0.39 ; as such the measured velocities cannot be said to statistically differ from those expected although there may be a trend toward an underestimation.

The slight discrepancy between the expected and observed contrast profiles within the cylindrical tube phantom may be due to some minimal amount of contrast clearance from repeated low-power ultrasound exposure during the imaging process. Contrast clearance is more pronounced near the center of the tube than at the edges, due to the reduction in relative velocities between the flow and transducer. The reduction in relative velocity causes contrast near the tube center to receive more exposure, and hence preferentially clearing it relative to other contrast as modeled in Fig. 9. In addition, the reduction in overlying attenuation at the axial center also contributes to increased contrast clearance. In spite of the effects of slight contrast clearance, peak flow velocity was measured on average to within 13.2% of that expected.

Conclusions and Discussion

We have demonstrated the efficacy of a new technique in contrast refill imaging. The dual transducer technique allows the imaging of contrast destruction/refill data in a three-dimensional volume in a drastically reduced time frame, compared to traditional techniques (real-time refill and interval imaging). The tube phantom provided a four-dimensional model that allowed the verification of the dual-transducer technique by comparing expected and observed contrast profiles. To our knowledge, this model has not been previously employed in four-dimensional imaging. Fitting observed profile radii to those predicted by eqn 4 gave

center velocity measurements v_c measurements that tended to be less than those expected except for one case ($\Delta t = 14.5$ s, 0.040 mL/s flow rate), although the difference in all cases was not statistically significant ($p > 0.05$). The v_c measurements may be low because of slight contrast clearance, which is exhibited in two ways. Looking closely at Fig. 7, one notes first that the observed profiles were truncated at their center. Second, the edge of the contrast profile tended to fall on or within ($r \leq r_{expected}$) the theoretical edge. Radii measurements less than those expected would depress the fitted v_c value.

The exception to the depressed v_c measurements is notable in that the observed contrast profile as illustrated in Fig. 7 exceeds the theoretical curve ($r > r_{expected}$) in places, and that the profile is notably brighter than the others. The increase in brightness could be due to higher contrast agent concentration for this scan. This scan was the first in the series and the contrast concentration could have been greater than in the other scans due to contrast depletion through the course of the experiment. Without adjusting for this brightness increase, the observed edge for a given threshold would be farther from the center due to partial volume effects. This increase in the observed radii would then raise the fitted v_c .

Theoretically, radiation force effects could distort the flow of contrast agent through the flow phantom by pushing the contrast away from the tube center. However, radiation force effects were not evident in the observed profiles since the circular cross-sectional images of the contrast tended to remain centered in the tube throughout, as seen in Fig. 6.

We have shown that the technique gives expected results in the laminar tube flow phantom. The laminar tube flow phantom provided a four-dimensional flow with well-known characteristics, albeit one that is directional. In perfused tissues, the vasculature is much less directional, often having no clear direction of flow visible in the capillary bed. A perfused vascular bed, nevertheless, should be imageable in 3D with this method using alternative measures of agent flow such as contrast mean transit time previously mentioned. Further studies will be needed to test this method under *in vivo* conditions.

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Appendix

The required scan times for imaging a three-dimensional volume using interval imaging, real-time refill, and the dual-beam technique (demonstrated here with two transducers) are calculated as follows:

ρ : slice density (slices/unit length)

T : volume thickness (length units)

N_s : number of slices, $N_s = \rho T$

N_t : number of time points

t_{clear} : contrast clearance time needed for one slice

t_{max} : maximum time point acquired on refill curve

v_T : transducer translation speed (distance/unit time), $v_T = N_t t_{trans}$ (see below)

t_{trans} : time to translate one slice thickness, $t_{trans} = 1/(\rho v_T)$, $t_{trans} \rightarrow 0$ for two dimensional arrays where translation is unnecessary to image the volume and imaging rates are controlled by propagation and other processing considerations.

t_M : time to reach time point M , $t_M \leq t_{max}$

t_r : time to return transducers to starting position

For real-time imaging with a one-dimensional array, the time required is

$$N_s [t_{clear} + t_{max} + t_{trans}] \quad (5)$$

which is the number of slices N_s multiplied by the time required to acquire one slice (time to clear the plane plus the maximum time point in the refill curve), plus the time needed to translate the transducer one slice thickness. The number of time points acquired is limited only by the transducer frame rate and does not affect the acquisition time.

For interval imaging, the time required is

$$N_s \left[\sum_{M=1}^{N_t} (t_{clear} + t_M) + t_{trans} \right] \quad (6)$$

where $t_M \leq t_{max}$ and the sum is the total time required to obtain the image for all time points t_M . The required time can vary significantly depending on the selection of points t_M .

The time required for the scans using two transducers to demonstrate the dual beam technique is given by

$$\sum_{M=1}^{N_r} [N_s t_{trans} + t_M + t_r] - t_r \quad (7)$$

where the clearance transducer has traversed the volume in $N_s t_{trans}$ and the imaging transducer arrives at the volume boundary after time t_M . As N_s is moved into the summation, one can understand how a dramatic reduction in required scan time generally takes place compared to conventional real-time and interval acquisition. If imaging and clearance could be alternated between the two transducers, there is no need to return the transducers to their starting position after each sweep. Under such circumstances, t_r would be 0.

Note that the time required with the dual transducer technique does not depend on the number of slices acquired for a given v_T . That is, for a given v_T , an increase in the number of slices N_s would result in a corresponding decreases in the translation time between slices t_{trans} , and overall acquisition time would remain constant. The velocity v_T is generally constrained by the acoustic frame rate (AFR) and desired slice density ρ , i.e. $v_T \leq AFR/\rho$ rather than by the capabilities of the translation system. The minimum t_M that can be acquired is limited by translation velocity v_T and the minimum transducer separation. Clearance time t_{clear} is not present because the clearance transducer clears the volume as it is swept.

For a 2D array imaging a volume completely contained within its field of view, the scan time required is given by eqns 5 and 6 for real-time and interval imaging, respectively (with $N = 1$). The term $t_{trans} \rightarrow 0$ and the imaging rate is limited by the volumetric frame rate and beam propagation considerations. The minimum acquirable t_M is based on the time required to electronically sweep through and read the volume.

Fig. 1.

Dual transducer tube flow dynamics. a) At a given time t_1 , contrast refilling the tube cleared previously by the clearance transducer forms a parabolic profile. The imaging transducer images a slice of the profile in cross-section at position d_1 . Within that cross-section, the refilled contrast has a radius r_1 . b and c) The contrast profile remains parabolic as the tube refills. At times t_2 and t_3 , the cross-sections are imaged at positions d_2 and d_3 respectively. Even though the contrast profile at any instant in time t is parabolic, the measured radii r are taken of contrast profiles at *different* times. d) If the transducer translation velocity v_T were much larger than the flow velocity, the contrast profiles at each time would not substantially evolve, and r would solely be a function of the position d and the initial delay time between contrast clearance and profile imaging. However, there is a simple relationship for $r(d, t)$ (derived in the text) when the contrast profiles evolve significantly, given by $r(d, t) = R\sqrt{1 - d/tV_c}$, where R and V_c are respectively the tube radius and center flow velocity. Assembling the measured radii from an evolving contrast profile produces a predictable “time-dilated” parabola (shown by the dashed line).

Fig. 2.

Dual transducer method schematic. Each transducer is assigned a separate task, with the clearance transducer translated over the tissue ahead of the imaging one. The clearance transducer is operated at sufficient power and pulse repetition frequency (PRF) to clear the volume of interest of contrast agent during each sweep. The imaging transducer is operated in a minimally destructive mode, and it reads the amount of contrast agent that has refilled since contrast clearance. Both transducers are swept through the volume of interest at constant velocity v . Based on the separation distance s , the refill associated with a specific interval Δt can be measured. Due to significant clearance zone thickness, s' is less than s the transducer center-to-center distance. Additional delay can be added by pausing the sweep after clearance and before imaging.

Fig. 3.

Schematic of dual-transducer apparatus and experimental setup. The dual-transducer apparatus consists of a dual-transducer positioning stage, which consists of translation (M_T) and separation (M_S) motors. Each motor turns a threaded rod, which translates a platform that contains a transducer holder. The platforms translate within the tracked slide. Motors are connected to a powered control module, which contain the electronics driving the motors. The control module is linked to a laptop computer through the DAQCard-700. Using LabVIEW scripts, transducers are translated as required. The transducers are positioned above the phantom being scanned, with the clearance transducer (T_C) positioned at the edge of the volume of interest. The phantom is continuously perfused with dilute (1:5000 concentration) contrast pumped from a stirred flask.

Fig. 4.

Photograph of the constructed dual-transducer apparatus. Two stepper motors turn two threaded rods parallel to each other to move the ultrasound transducers, which are held by the transducer holders shown. Transducer holders translate on a guided slide (400L - THK Corporation Japan). The separation motor, mounted upon a stand, adjusts transducer separation. The stand in turn is translated by the larger translation motor, which controls the sweeps over the volume of interest. Imaging and clearance transducers are mounted as shown. The complete apparatus was placed above a rubber-lined water tank upon a stand, and cables connect the motors to a control box (not shown), which provided drive power and was in turn controlled by a laptop computer using the DAQCard-700 and LabVIEW scripts.

Fig. 5.

Image of contrast clearance zone thickness. This image, obtained from the imaging transducer at low power shows the 6 mm gap in stationary contrast generated by the clearance transducer after a series of 10 pulses (settings described in the text). The size of the gap asymptotically approaches this value with clearance transducer pulses. As such, the effective transducer separation was considered half of the gap (3 mm) less than the physical transducer separation.

Fig. 6.

Sample planar images of tube flow. For the 0.040 mL/s flow rate, these images are a sample of those directly obtained in the transducer axial-lateral plane of the flow at a distance d of 16 mm for differing values of Δt . The circles of contrast have observed diameters respectively of 3.36, 4.47, 5.53, and 5.97 mm corresponding to theoretical values (outlined) of 3.67, 4.36, 4.76, and 5.02 mm with increases in Δt .

Fig. 7.

Reconstructed images along the length of the flow tube showing the contrast agent flow. These are corrected for the time-dilation effect described in the text and Fig. 1. The white line shows the theoretical position of the contrast front. The flow passed through a tube of radius 3.175 mm at a rate of a) 0.040 mL/s and b) 0.028 mL/s. Transducer translation velocity v_T was 6 mm/s. Expected profiles closely match those observed, except at the center of the leading edge. It is believed that the discrepancy is due to slight contrast destruction due to both increased beam exposure and decreased overlying attenuation from overlying contrast (see text).

Fig. 8.

Fitted v_c results for cylindrical tube phantom. Dual transducer scans were acquired for the cylindrical tube phantom with two center flow velocities (1.75 and 2.50 mm/s - corresponding to the flow rates of 0.028 and 0.040 mL/s respectively from Fig. 7) using four different refill times. Shown are the measured values of v_c (1.46 and 2.25 mm/s) obtained by fitting measured contrast radii to the eqn given in eqn 4 for all measurements along with the mean and standard deviation for the measurements grouped by flow rate. Dashed lines denote theoretically known values of v_c . The measurements tended to be less than those expected except for one case ($\Delta t = 14.5$ s, 0.040 mL/s flow rate), although the difference in all cases was not statistically significant ($p > 0.05$).

Fig. 9.

Simplified model of time spent in the ultrasound beam for various flow speeds. Flow speeds are represented in “beam-widths” per second (bw/s) for normalization. Flow velocity V is considered parabolic, with a profile given by $V(r) = V_{max}[1 - (r/R)^2]$, where r is the tube radius and V_{max} the maximum velocity. With a stationary transducer, the fluid closest to the tube wall is exposed to the beam for the longest period of time, and these exposure durations decrease with increased flow velocity as shown by the three curves representing V_{max} at 1 and 10 bw/s. The thicker shaded curve represents what happens as the transducer is translated along the axis of the tube at a speed higher than the maximum flow velocity. In this case, where V_{max} was set to 10 bw/s and the transducer speed V_T was set to 1.5 times

V_{max} , the maximum exposure to the beam occurs at the center of the tube. This may help explain the center peak cut-off of the flow profiles shown in Fig. 7. That is, the contrast may be exposed to sufficient pulses in the center to break the bubbles at higher flow velocities. This effect is compounded by the fact that there is also less overlying attenuation due to the profile shape.

Table 1

Comparison of required total time for interval imaging, real-time refill, and the dual transducer technique. Constant parameters used to compute the times are a transducer translational velocity v_T of 6 mm/s, a transducer separation of 60 mm, and a volume of interest thickness of 40 mm. Chosen timepoints for interval imaging and the dual-transducer technique are (in s) 10, 20, 30 for 3 time points, with the additional points 15 and 25 for 5 time points. Real-time refill imaging acquires all time points continuously up to the maximum time point. Transducer translation time is negligible for real-time refill and interval imaging (~6.5 s) and is covered in the rounded times. For the dual-transducer case, the transducer pair is moved back to the starting position after the acquisition of each timepoint, except for the final one. Time required to clear contrast is negligible (< 2 s) for both interval imaging and real-time refill acquisition. Note that using the dual-transducer method causes a dramatic reduction in the time required to image a three-dimensional volume. Since the dual-transducer technique's time requirement is independent of the slice thickness, image slices could be acquired as closely together as necessary without requiring additional time, subject only to the imaging transducer frame rate, unlike traditional techniques.

Slice Separation (mm)	Number of Time Points (Interval and Dual Transducer Imaging)	Interval Imaging	Dual-Transducer Technique	Real-Time Refill
0.5	3	80 min	1 min 53 s	40 min
1	3	40 min	1 min 53 s	20 min
2	3	20 min	1 min 53 s	10 min
1	5	67 min	3 min 20 s	20 min