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System for real-time forward-viewing intravascular imaging of 3D velocity fields

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***Abstract*—Direct estimation of 3D blood flow velocity components in vivo could provide important diagnostic information, as demonstrated by computational fluid dynamics. Several approaches have been proposed, however, direct intravascular estimation has not been demonstrated despite the value of fluid dynamics for predicting major adverse cardiac events in stable coronary artery disease. Given that minimally-invasive diagnostic procedures are routinely performed in these patients (e.g. side-viewing IVUS, FFR), a forward-viewing intravascular system could allow direct estimation of velocity components in 3D, with reduced effects of tissue motion and increased resolution relative to non-invasive approaches. Initial data acquisitions using a forward-viewing 4 mm, 118-element ring array transducer in a tissue-mimicking flow phantom and in a pig are described.**

Keywords— intravascular ultrasound, matrix array, ring array, forward viewing transducer, transverse oscillation, vector velocity, 3D ultrasound

I. Introduction

Risk stratification in stable coronary artery disease is a frequent problem in developed nations [1, 2]. Currently, the decision to place stent in a stenotic artery is guided by fractional flow reserve (FFR), a guidewire-based technique measuring decrease in pressure across a coronary artery stenosis. 12% of patients who are not initially stented based on FFR require a stent within 2 years [3], thus improved diagnostic technology is needed. Flow-derived parameters (e.g. wall shear stress, WSS) based on anatomical imaging of vessel geometry and computational fluid dynamics (CFD) are emerging as strong predictors of the likelihood of plaque rupture, with CFD recently demonstrating incremental prognostic value over FFR alone and the ability to predict myocardial infarction in patients with stable coronary artery disease [1]. However, CFD can be limited in its ability to guide intervention because substantial post-procedural time (on the order of weeks) is required for computation and analysis of data sets acquired via minimally-invasive procedures. Though these times are reducing and utilization of CFD to guide clinical decisions is increasing, if technology could be developed to quantify blood flow velocity fields via direct imaging during the procedure, it might be possible to quantify relevant parameters such as elevated wall shear stress in the proximal section of the stenosis and thus determine which lesions require stenting during the interventional procedure [1]. Specifically, patients at increased risk for rupture and myocardial infarction based on 3D blood flow velocity analysis could have a stent placed even if FFR is in the normal range.

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In this work, we present initial proof-of-concept of intravascular 3D velocity quantification using a forward-viewing catheter-based device. In the future with a smaller catheter transducer, such technology could be used for risk stratification in stable CAD and other vascular diseases driven by aberrant blood flow dynamics (e.g. thrombosis, restenosis). Initial steps towards development of an intravascular 3D imaging system for real-time 3D quantification of intravascular blood flow velocity fields and derived parameters (e.g. wall shear stress, WSS) are reported. While our current array is too large for coronary imaging (4 mm), we demonstrate proof-of-concept for 3D velocity estimation with a forward-viewing interventional array transducer for the first time in phantom studies and in a porcine femoral artery.

II. Methods

A. Imaging system, transducer, and processing

As an initial proof of concept, a custom printed circuit board was used to connect a 4 mm-diameter, 118 element double ring array transducer (Fig. 1) described previously [4] to a research imaging system (Verasonics Vantage 256, Kirkland, WA, USA). 7 steered plane wave transmit events at 5 MHz are used in this work to provide imaging at a user-selected rate.

One approach for estimating 3D velocity components is transverse oscillation, which can be implemented in the frequency domain by bandpass filtering acquired data in the lateral direction (and also in the elevation direction for a 2D array) [5-7]. A bandpass filter centered at 1.6 cycles/mm with -6 dB bandwidth of 93% was applied in both directions. The result is complex, allowing flow direction to be determined in lateral and elevation directions. Fourth-order autocorrelation estimation was used to determine the lateral and elevation velocity components v_x and v_y [8]. The axial velocity component v_z was determined using a standard cross-correlation estimator. Stationary echoes were filtered with a cutoff of 250 Hz and an ensemble size of 50 in phantom studies.

B. Phantom studies

Seven steered plane wave transmit events were acquired at a rate of 3.5 kHz (i.e. 500 Hz for 7 transmit events) in a custom flow phantom with continuous flow of 10 g/L corn starch in water. The direction of flow was away from the transducer at either 35 mm/s or 3 mm/s. For 35 mm/s flow, retrograde flow was introduced manually retrograde flow for a 0.5 s duration.

C. In vivo imaging study

The use of animals for this procedure were reviewed and approved by the Institutional Animal Care and Use Committee at Emory University, and the procedures were performed in an AALAC accredited facility following the NIH guidelines for animal research. One Yorkshire swine was sedated, intubated, mechanically ventilated and maintained on anesthesia per previously reported protocols [9]. Under general anesthesia, an arterial cutdown was performed in the right groin to expose the femoral artery, and ~5 cm length was dissected carefully from surrounding tissues with ligation of side branches. The distal and proximal ends of the exposed vessel were temporarily clamped, and a transverse incision was performed in the vessel to insert the tip of the forward viewing IVUS catheter. The distal clamp was removed to allow blood flow through the femoral artery towards the catheter, and imaging was performed. 3D imaging volumes were acquired with 7 compounding events at a rate of 700 Hz (100 Hz post-compounding). The heart rate of the animal under anesthesia was approximately 40 beats per minute according to a heart monitor. Stationary echoes were filtered with a cutoff of 20 Hz and an ensemble size of 50.

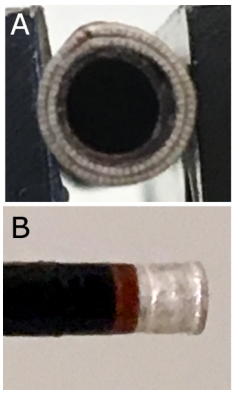

Fig. 1. (A) Forward view, and (B) side-viewing 118-element array transducer.

III. Results

A. Flow phantom experiments

Results of imaging in the flow phantom are shown in Fig. 2 as velocity vs. time (A) and flow patterns at individual time points (B-D). In Fig. 2A, the velocity at the center of the lumen for both flow rates is presented over the duration of a 1 s acquisition. For the higher flow velocity case, the transient retrograde flow (0.25 s) can be seen in this plot. Selected 2D representations (i.e. C-scan slices) of 3D vector velocity data acquired in real-time in flow phantom studies are shown in Fig. 2B-D to show sensitivity to slow flow (B) and to variation in primary flow direction (B-D).

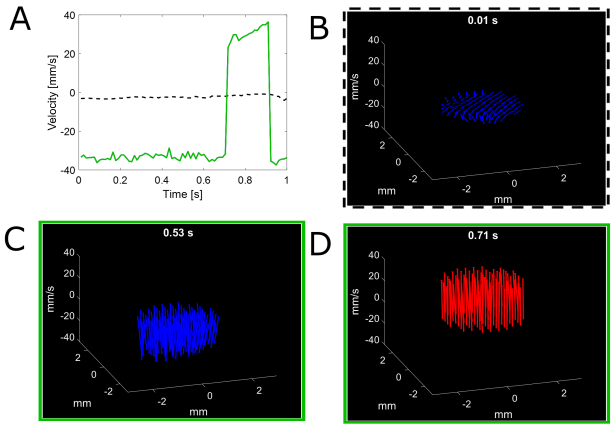

Fig. 2. Velocity in flow phantom experiments. (A) Velocity in the primary flow direction at the center of the lumen as a function of time during a one-second acquisition for constant flow away from the transducer at 3 mm/s (dashed black line) and at -35 mm/s (solid blue line). At 0.7 s, the flow direction is reversed for 0.25 s. (B) A single 2D representation of vector velocity for the constant slow flow case (dashed line in A). Single 2D representations are shown at times before (C), and during (D) flow reversal.

B. In vivo porcine studies

A single representation of velocity fields is shown in Fig. 3 for both 3D and 2D views. The 2D view allows visualization of these velocity components (i.e. orthogonal to the direction of primary flow along the long axis of the vessel), which is difficult to appreciate in the 3D visualization of Fig. 3A.

Finally, in Fig. 4, the spatially-averaged velocity is shown in the primary flow direction over the entire lumen at a distance from the transducer of z=12 mm, illustrating the cyclical flow pattern over 4 cardiac cycles. While a spatially-averaged measurement can encapsulate the primary flow velocity with respect to the cardiac cycle, additional spatial information across the diameter of the vessel is lost in this display, which is similar to what a Doppler wire might measure. Within the single measurement of mean velocity at each time point, there are many complex underlying flow dynamics (Fig. 4B-F). These results show that spatial averaging of positive and negative flow in the longitudinal direction can result in a single mean value that obscures the underlying dynamics.

Different phases of blood flow in time are also visible in this data. In considering only the time-averaged blood flow (Fig. 4A), this data is consistent with spatially discrete measurements of femoral artery blood flow dynamics in previous studies in humans and in animals [10, 11]. The acceleration phase [11] can be seen (Fig. 4B), followed by the maximum flow phase (Fig. 4C), then the deceleration phase and period of reversed volumetric flow [11], as in Fig. 4D. Positive flow then resumes for the following cycle (Fig. 4E-F).

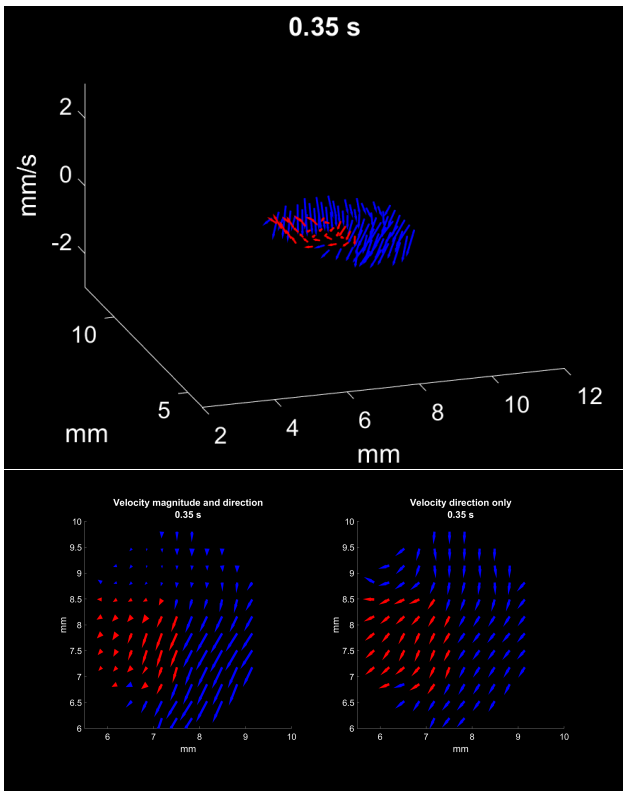

Fig. 3. (A) 2D and (B) 3D views acquired in a porcine femoral cross-section at a given point in time (0.35 s) for z=12 mm from the transducer.

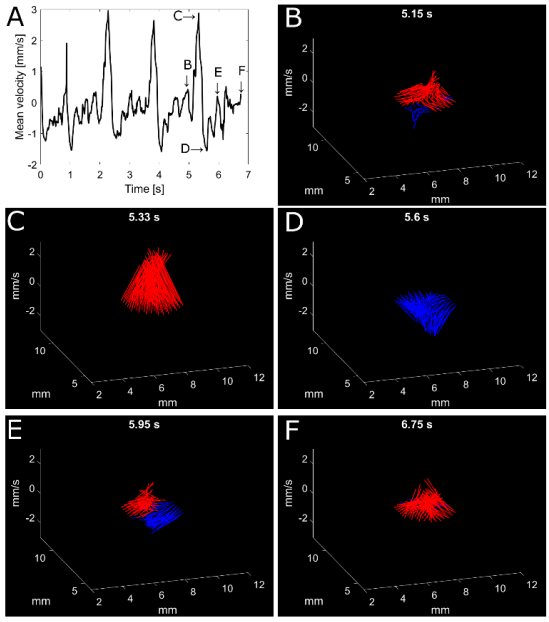

Fig. 4. (A) Time course of mean velocity across the vessel and (B-F) corresponding 2D slices at z=10 mm at time points indicated in A.

IV. Discussion

3D blood flow dynamics were measured using a forward-viewing intravascular 2D array for the first time. Initial testing was performed in phantom studies (Fig. 2), followed by in vivo imaging in a porcine femoral artery. The estimated mean velocity in the primary blood flow direction (Fig. 4) shows the expected cyclical behavior and agrees well with the period of the heart monitor, i.e. 1/(40 bpm) corresponding to a period of 1.5 seconds, as seen in Fig. 4A. The ability to estimate 3D velocity could be useful for assessing blood flow dynamics at the vessel wall surrounding lesions, where high wall shear stress proximal to the lesion indicates increased likelihood of plaque rupture [12]. For this task, the component along the vessel wall would need to be estimated rather than the cross-sectional components shown; these data are contained within the acquired sequence of volumes and can be interpolated to account for the angle of the vessel wall as needed.

In order to translate the benefits of a forward-viewing 2D array-based system to clinical diagnosis or risk stratification, validation with computational fluid dynamics is needed to assess accuracy of this technique relative to the more extensive studies that have been previously performed with CFD in the clinical context. Additional animal studies would also increase the confidence in blood flow estimation accuracy using the 2D array-based system.

Several technical improvements could increase the accuracy of 3D blood flow velocity estimates made by this system, including directional beamforming, which would yield increased velocity estimation accuracy [13]. Additionally, in this work, processing was performed offline, however, implementation of online or rapidly reconstructed velocity

maps would be needed to stratify risk in the cardiac catheterization lab. Improvements in filtering such as automatic selection of the clutter filter threshold or singular value decomposition (SVD) filtering may also improve the quality of the velocity estimates. Most importantly, in order to translate to carotid imaging, a smaller, higher resolution forward-viewing matrix array transducer needs to be developed.

V. Summary

This article presents the first demonstration of a 2D array for intravascular imaging of 3D blood flow velocity fields. Proof-of-concept for spatiotemporal analysis was demonstrated using a 118-element forward-viewing array operating at 5 MHz. Development of an intravascular 3D system for real-time 3D quantification of intravascular blood flow velocity fields and derived parameters (e.g. wall shear stress) could be used to assess likelihood of plaque rupture in interventional procedures, for example in stable coronary artery disease, where studies with computational fluids dynamic have shown the ability to predict likelihood of major adverse cardiac events. By developing an imaging system capable of direct 3D estimation of blood flow velocity fields in the cardiac catheterization lab, this assessment could be performed directly in situ without the need for computation based on vessel geometry.

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