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● *Original Contribution*

SPATIO-TEMPORAL FLOW AND WALL SHEAR STRESS MAPPING BASED ON INCOHERENT ENSEMBLE-CORRELATION OF ULTRAFAST CONTRAST ENHANCED ULTRASOUND IMAGES

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Abstract—In this study, a technique for high-frame-rate ultrasound imaging velocimetry (UIV) is extended first to provide more robust quantitative flow velocity mapping using ensemble correlation of images without coherent compounding, and second to generate spatio-temporal wall shear stress (WSS) distribution. A simulation model, which couples the ultrasound simulator with analytical flow solution, was implemented to evaluate its accuracy. It is shown that the proposed approach can reduce errors in velocity estimation by up to 10-fold in comparison with the coherent correlation approach. Mean errors (ME) of 3.2% and 8.6% were estimated under a steady flow condition, while 3.0% and 10.6% were found under a pulsatile condition for the velocity and wall shear rate (WSR) measurement, respectively. Appropriate filter parameters were selected to constrain the velocity profiles before WSR estimations and the effects of incorrect wall tracking were quantified under a controlled environment. Although accurate wall tracking is found to be critical in WSR measurement (as a 200 μm deviation from the wall may yield up to a 60% error), this can be mitigated by HFR imaging (of up to 10 kHz) with contrast agents, which allow for improved differentiation of the wall-fluid boundaries. *In vitro* investigations on two carotid bifurcation phantoms, normal and diseased, were conducted, and their relative differences in terms of the flow patterns and WSR distribution were demonstrated. It is shown that high-frame-rate UIV technique can be a non-invasive tool to measure quantitatively the spatio-temporal velocity and WSS distribution. (E-mail: mengxing.tang@imperial.ac.uk)

Key Words: **Flow measurement, Wall shear rate, Ultrafast ultrasound imaging, Motion effect, Microbubble contrast agents, Contrast enhanced ultrasound, Image tracking.**

INTRODUCTION

Studies have shown that hemodynamic shear stresses have a strong influence on the initiation and development of various vascular diseases. In response to imposed mechanical forces, endothelial cell layers not only endure the morphologic and functional changes (Chistiakov et al. 2017; Chiu and Chien 2011), but also trigger the biochemical event that results in the deposition and adherence of the platelet or the formation of atheroma (Caro 2009; Cecchi et al. 2011; Dhawan et al. 2010). Such observations are convincing evidence that local hemodynamic factors are associated with vascular diseases. It is therefore of clinical significance to quantitatively measure the flow patterns and wall shear stress (WSS), using the existing medical modalities.

Blood flow patterns, flow velocities or flow volume have been widely used to describe the spatio-temporal hemodynamic within a particular vessel or lesion. Although several techniques of measuring the flow velocities exist clinically, a standard technical basis for fluid shear estimation *in vivo* has not been established (Katritsis et al. 2007; Papaioannou and Stefanadis 2005). The most convenient and straightforward way to estimate WSS is based on the Hagen-Poiseuille formula, where the shear stress in a relatively straight vessel is computed in terms of either the average or maximum velocity and the radius of the vessel lumen (Mynard et al. 2013). However, the accuracy of such expression is dependent on the validity of the following assumptions: (i) The flow is steady and of a parabolic in nature; (ii) the blood behaves as a Newtonian fluid with constant viscosity; (iii) the vessel is axisymmetric;

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and (iv) the vessel wall is rigid. These conditions are met minimally in the physiologic environment where the flow is mainly pulsatile, the vessel is distensible and its diameter is inconsistent. These conditions therefore limit the application of such a technique to estimate the WSS. Another technique to estimate the WSS is based on the determination of the wall shear rate (WSR), which is the flow velocity gradient near the vessel wall (Cheng et al. 2002; Poelma et al. 2012). This produces a more reliable WSR measurement with no assumption of the geometry and flow required; however, the accuracy of such a technique is dependent on the temporal and spatial resolution of the modality used to obtain the flow velocity profile and track the wall position, and the interpolation or extrapolation algorithm. Because of such constraints, *in vivo* WSS measurement is limited and relies primarily on computational fluid dynamics (CFD). In this context, numerical simulation is employed to investigate the WSS distribution of a given geometry measured by means of imaging modalities. However, the accuracy of the simulation can be affected by the underlying assumptions on the geometry, wall properties, fluid properties and most importantly the initial and boundary conditions.

To calculate the WSS *in vivo*, flow velocity information can be assessed using existing non-invasive imaging modalities such as phase contrast magnetic resonance (Masaryk et al. 1999; Stalder et al. 2008) and ultrasound (Poelma et al. 2012; Zhang et al. 2011). However, it has been a challenge clinically to provide a reliable WSS distribution with the existing medical imaging technique.

A high-frame-rate (HFR) plane wave ultrasound imaging velocimetry (UIV) system has been developed and evaluated recently for the generation of flow velocity mapping with high spatial and temporal resolution (Leow et al. 2015a). This technique benefits from the combination of the HFR ultrasound imaging, contrast imaging and UIV algorithm. HFR ultrasound imaging provides high temporal resolution, of up to tens of thousands of frames per second, to track high spatio-temporal variation flow within the field of view. The use of microbubbles—together with a pulse-inversion contrast-imaging sequence—enhances the signal-to-noise ratio (SNR) and helps differentiate between the wall–fluid boundaries. The high temporal resolution and SNR imaging technique therefore allows the UIV algorithm to estimate the flow velocities and subsequently the WSS unambiguously.

Here, a previous study has been extended to provide both robust quantitative velocity flow field measurement and spatio-temporal WSS, using a modified UIV technique based on ensemble-correlation of images without coherent compounding. An incoherent ensemble-correlation approach such as this avoids the effects of motion on the coherently compounded images. The accuracy of the system in estimating flow velocity vectors and WSR mapping is evaluated. Ultrasound flow simulation, which consists of a straight tube phantom driven by steady and pulsatile flow with known reference values, fully evaluates this technique. *In vitro* studies on two anthropomorphic carotid bifurcation phantoms are also conducted to further highlight the performance of the technique.

METHODS AND MATERIALS

Ultrasound flow simulation

Flow model generation. Synthetic ultrasound images were generated from ultrasound flow simulation that coupled the analytical flow solution with the ultrasound simulator. Such realistic models are necessary to compare the developed technique with the known reference value computed from the analytical solution. Under such circumstances, a rigid model, consisting of a straight cylindrical vessel phantom filled with Newtonian fluids driven by an analytical solution, was created.

Poiseuille flow

Straight vessel phantoms with inner diameters of 3 mm and 6 mm were created. Established steady laminar flow with a parabolic flow profile was generated by moving the flow scatterers at radius r from the center of the vessel with the velocity as follows:

$$v(r) = v_0\left(1 - \frac{r^2}{R^2}\right) \tag{1}$$

where v_0 is the centreline velocity and R is the radius of the vessel. The WSS, given a fluid with dynamic viscosity μ, is defined as:

$$\tau_{wall} = \mu\frac{2v_0}{R} \tag{2}$$

In this study, flow simulations under three flow rates ($v_0 = 20$, 50, 80 cm/s) were generated in a 3- mm diameter vessel to investigate the accuracy of flow estimation. The vessel was positioned with a beam-to-flow angle of 60° and the radial velocity errors were calculated. In a 6-mm diameter vessel, steady flow with the centerline velocity of 50 cm/s, Reynolds number (Re) of 1500 and resulting WSR of 333 s^{-1} was also simulated. The vessel was oriented with a beam-to-flow angle of 90° for the simplicity of the WSS analysis.

Womersley flow

While arterial flow is pulsatile, Womersley flow was generated as described previously (Evans and McDicken 2000). In brief, pulsatile flow is considered as the sum of both steady flow component and a series of oscillatory components. Poiseulle's equation can be reformulated to