AN IN VITRO MODEL WITH PARTICLE TRACKING VELOCIMETRY THAT ENABLES VISUALIZATION OF LEFT ATRIAL HEMODYNAMICS POST LEFT ATRIAL APPENDAGE OCCLUSION

Manisha Singh,[1], Keegan Mendez,[1], Susan Su,[1], Aileen Liao,[1], Markus J Schmidt,[1], Lydia Bourouiba,[1], Ellen Roche,[1]

[1] Massachusetts Institute of Technology

Correspondence: Ellen Roche, etr@mit.edu

Background:

Atrial fibrillation is a cardiovascular disorder that results in a five-fold increase in the risk of stroke, with 90% of stroke-causing thrombi arising in the left atrial appendage (LAA)[1]. Existing devices for LAA closure, such as the WATCHMAN FLX™ (Boston Scientific) and the Amulet™ (Abbott) compare favorably to oral anticoagulants for reducing mortality and stroke risk[2], yet there is significant interpatient anatomical heterogeneity, which makes intraprocedural device sizing and placement challenging. Despite successful LAA occlusion— identified by the absence of peri device flow (≤5 mm jet) assessed on transesophageal echocardiology — appreciable post-procedural complications remain, likely due to patient-device mismatch, which can result in peri-device leakage (5-32% patients)[3], device-related thrombus (DRT) (3-4% patients)[4] or device embolization (~2% patients)[5] that all increase the risk of mortality and stroke. To enhance understanding of the impact of device positioning on post-procedural complications we can use experimental methods such as particle tracking velocimetry to study the effect of device positioning on atrial flow hemodynamics including velocity fields, flow patterns, and vortices.

Objectives:

This work aims to develop a patient-specific benchtop setup to improve understanding of postprocedural outcomes of LAA closure using particle tracking velocimetry (PTV). By combining a hemodynamic model of the LA with PTV, detailed velocity fields and regional flow stasis can be identified in vitro which are often challenging to assess in vivo using transesophageal echocardiography. Due to the difficulties in characterizing flow patterns around the irregular geometry of the LAA using a benchtop PTV setup, our preliminary in-vitro setup utilizes simplified rectangular chambers to approximate the size of the left atrium, with varying chamber wall geometries to simulate three device placement conditions: (1) completely occluded, device at ostium; (2) completely occluded, device proximal to ostium, protruding into

the LA; and (3) completely occluded, device at ostium with small protrusion into the LA (Figure 1A). These three conditions will enable us to assess the possible risks associated with device geometry and device positioning in the context of LAA occlusion.

Methods:

Computer-aided designs of the test chambers were created using Fusion 360 and 2D drawings were exported into Adobe Illustrator for laser cutting the walls. Each chamber was designed to be 40mm x 40mm in width and depth and 50mm in height, with ½" inlet and outlets on either side to simulate the approximate positions of the pulmonary vein and mitral valve (Figure 1A)[6]. The chambers had an internal volume of 46.8 mL, corresponding to a volume index of 24.63 mL/m2, which is within the range of the average left atrial volume index of an adult male (20±6 mL/m2)[7]. Chambers were then connected to a flow loop and a suspension of red fluorescent particles (Cospheric UVPMS-BR-1.050, diameter 106-125um) in water was pumped through the chamber at rate of 45 bpm and stroke volume of 40 ml with a pulsatile pump (HEARTROID Inc.). Particles were visualized with a CW laser (532 nm). A Powell lens was used to create a 2D light sheet. Images were captured via a high-speed camera (Photron Fastcam Mini UX 100) with a macro-objective (NIKKOR 105MM F/2.8 D) at 2000 frames per second.

Results:

We demonstrate the fabrication of a simplified, modular left atrial (LA) geometry that is compatible with particle tracking velocimetry-based investigation of hemodynamics. For visualization of the seeded particles, the fabricated chambers are connected to a mock circulatory loop mimicking the left atrial circulation. Our custom-made PTV setup houses a fluid reservoir, a pulsatile pump to displace the fluid at physiologically relevant heart rates and stroke volumes, an optically clear LA-mimicking chamber, a laser positioned perpendicular to the chamber, and a high-speed camera to capture the movement of the particles along the plane of laser illumination (Figure 1B). Light from the laser is absorbed by the particles, which then emit another wavelength of the absorbed energy. The light emitted is captured by high-speed camera imaging. Sequential images are shown for case 1—completely occluded, device at ostium (Figure 1B, sample data). The sample data demonstrates that the setup allows for the visualization of the seeded red fluorescent particles and enables flow and velocity vector tracking when frames are processed in the Jupyter Notebook using OpenCV and OpenPIV Python packages. A signal-to-noise threshold that filters out the vectors of high noise and replaces outliers by averaging neighboring vectors is determined, which in turn yields velocity fields in mm/s. As previously described by our group[8], we have developed a workflow whereby patient-specific MRI data is used to generate soft, LAA geometries using silicone casting of

3D-printed molds, that can be made dynamic with the addition of soft robotic actuators. As the next step, our goal is to develop a model with compliant, contractile, patient-specific, interchangeable LAA geometries to study hemodynamics using PTV (Figure 2). This will enable high-resolution quantification of peri-LAA flow dynamics pre-and post-LAA occlusion and is part of ongoing work with quantitative flow field data expected in the near term.

Conclusions:

We present a PTV setup that will enable us to observe the field flow and velocity changes after LAA occlusion with compliant, dynamic, and anatomically accurate LAA models. This experimental setup will allow us to collect patient-specific data with a variety of device sizes and positions and will validate and complement computer simulations of these flow profiles. Flow analysis of this nature could be helpful in the context of occluder design, device positioning, and cardiovascular flow characterization post-LAA occlusion, where thrombogenesis is determined by blood flow patterns. Limitations of our set-up include the simplified and rigid LA geometry, but insights gained from this experimental endeavor will inform future workflows toward more realistic models.

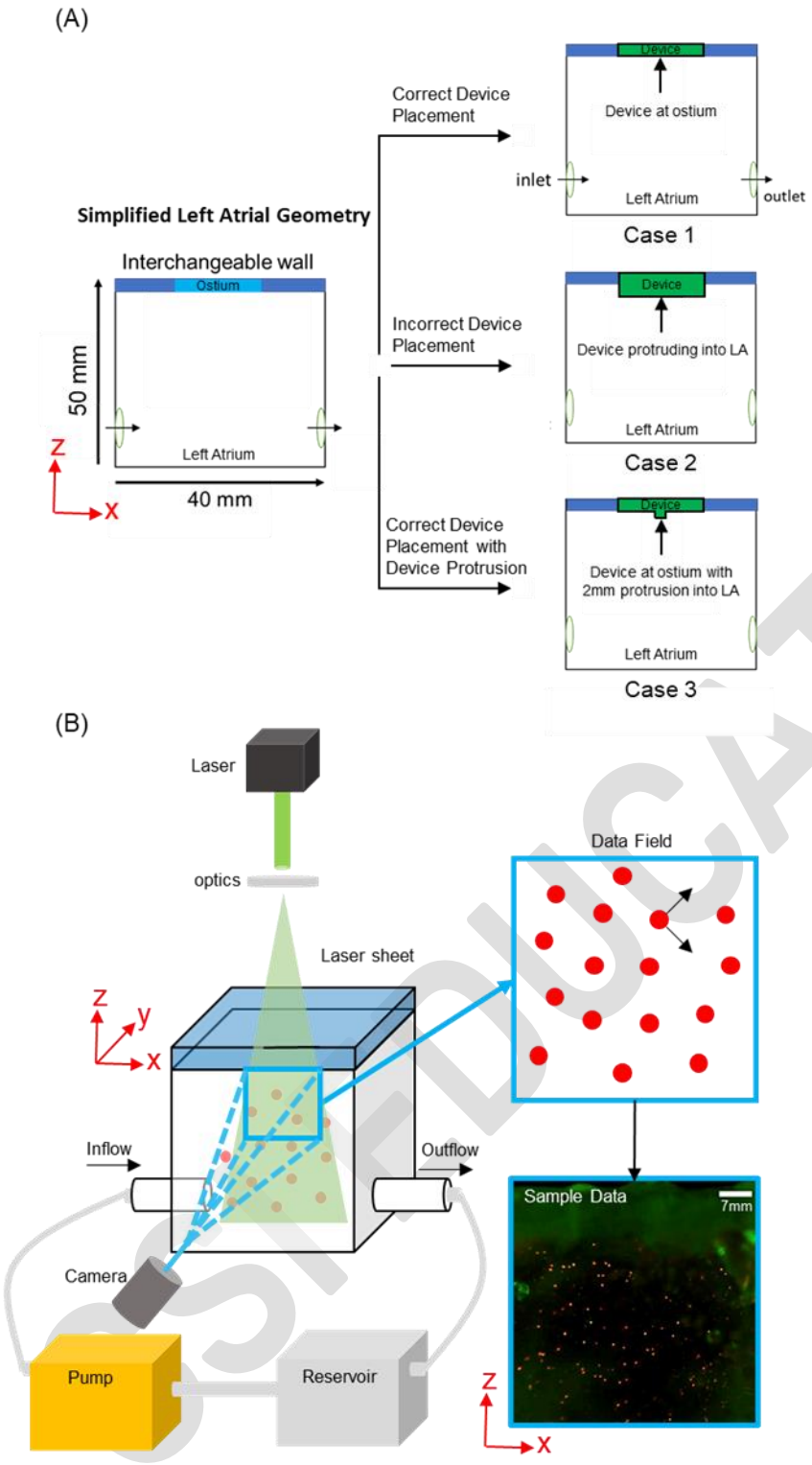

Figure 1. (A) Schematic of the simplified test chamber with three different conditions (cases 1-3). The inlet and outlet mimic the pulmonary inflow and mitral outflow, respectively. (B) A schematic of the experimental setup for particle tracking velocimetry (PTV) indicating relative positions of the laser, flow loop components, and the camera. The dimensions of the fabricated chambers in the x, y, and z directions are 40, 40, and 50 mm, respectively.

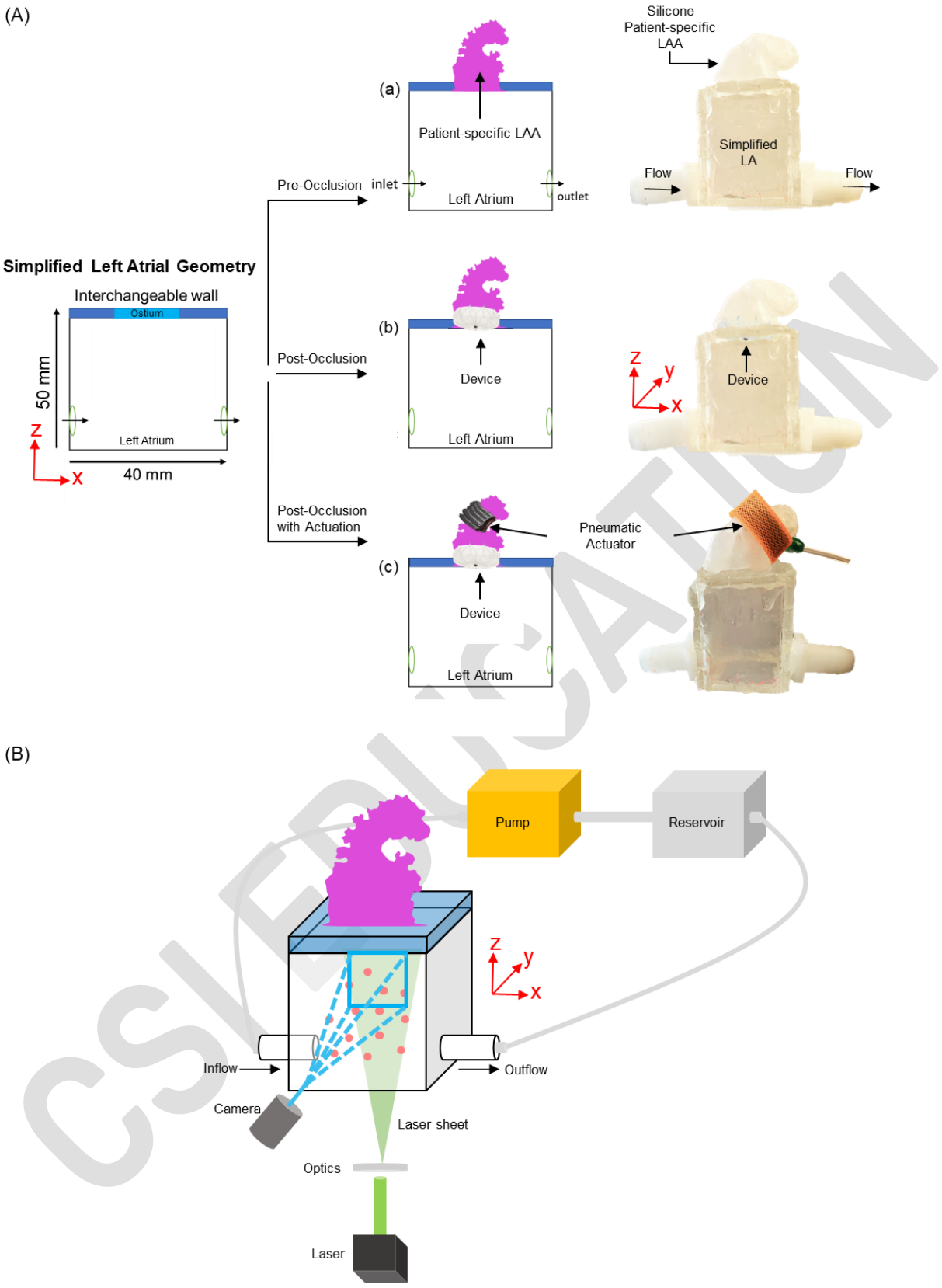

Figure 2. Future designs of the setup with interchangeable, patient-specific, and dynamic LAA geometries pre-and post-occlusion for enhanced particle tracking velocimetry studies.

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