DOI 10.5162/SMSI2025/P40

Branching Wall-less Vessel System in Tissue-Mimicking Materials for Magnetomotive Ultrasound Imaging

Christian Heim[1], *Christian Huber*[2,3], *Ingrid Ullmann*[3], *Helmut Ermert*[2],
Stefan Lyer[2], *and Stefan J. Rupitsch*[1]
[1] Department of Microsystems Engineering (IMTEK), Laboratory for Electrical Instrumentation and Embedded Systems, University of Freiburg, Georges-Köhler-Allee 106, Germany
[2] Department of Otorhinolaryngology, Head and Neck Surgery, Section of Experimental Oncology and Nanomedicine (SEON), Professorship for AI-Controlled Nanomaterials (KINAM), Universitätsklinikum Erlangen, Glücksstraße 10a, Germany
[3] Institute of Microwaves and Photonics (LHFT), Friedrich-Alexander-Universität Erlangen-Nürnberg, Cauerstraße 9, Germany
Christian.Heim@imtek.uni-freiburg.de

Summary:

In this contribution, we present an extended manufacturing process and evaluation method of a branching wall-less vessel system in tissue-mimicking materials for the development of Magnetomotive Ultrasound (MMUS) imaging algorithms. Blood flow in vessels around a tumor can interfere with MMUS imaging and has to be considered for algorithm development. A water-soluble filament can be used to integrate a branching wall-less vessel system into phantom manufacturing. Branches can be evaluated exploiting 3D ultrasound imaging and vector-flow imaging in combination with a highly echogenic fluid.

Keywords: Magnetic Drug Targeting (MDT), superparamagnetic nanoparticles (SPIONs), Magnetomotive Ultrasound (MMUS), local cancer treatment, ultrasound imaging.

Motivation

Magnetic Drug Targeting (MDT) with superparamagnetic iron oxid nanoparticles (SPIONs) is an emerging cancer therapy with localized treatment. In combination with Magnetomotive Ultrasound (MMUS), the spatial distribution of the SPIONs can be monitored during enrichment [1]. A review of MMUS imaging can be found in [2]. MMUS is based on the time-tracking of magnetically induced small tissue displacements in the SPION-laden areas by applying time-varying magnetic fields. For the development of MMUS algorithms, ultrasound phantoms made of tissue mimicking materials (TMMs) are commonly used for baseline studies. However, real tumors have a branching vessel system as shown in Fig. 3 (left), which can interfere with MMUS imaging [1]. In order to extend phantoms by adding wall-less vessels, manufacturing methods for complex flow phantoms have been developed using different combinations of soluble 3D printing filaments [3, 4]. In this contribution, we present a manufacturing process using water-soluble polyvinyl alcohol (PVA) filament to manufacture a wall-less vessel system to improve phantom models for MMUS algorithm development. Branches have been evaluated exploiting 3D ultrasound (3DUS) and speckle tracking based vector-flow (STVF) imaging according to [5, 6].

Manufacturing Process

Phantom manufacturing involves many different methods and materials. A recent overview of ultrasound phantom manufacturing can be found in [7]. In this contribution, PVA (10 wt%, DuPont Elvanol 71-30) was chosen for the hydrogel due to its ability to harden phantoms with varying stiffness and to mechanically couple different phantoms. PVA can also be used as a water-soluble filament (Formfutura Atlas Support Natural) for vessels and as a scattering material (DuPont Elvanol 71-30) to mimic tissue echogenicity. To demonstrate the manufacturing process, we manufactured a wall-less vessel system around a SPION-laden phantom, as illustrated in Fig. 1.

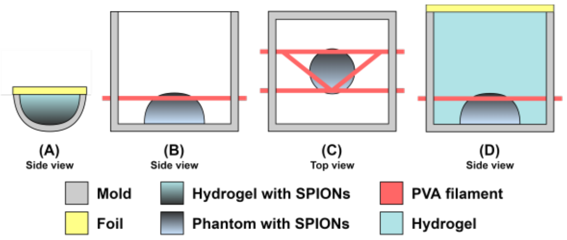

Fig. 1. Phantom manufacturing steps: (A) Pre-hardening with two freeze/thaw cycles of a SPION-laden tumor phantom with an iron content of 17.2 mg/ml, (B) Placement of tumor phantom and PVA filament, (C) Connect PVA filament parts using a heat gun, (D) Fill (4x4x4) cm mold with hydrogel and cover with foil.

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After step (D), the final phantom was hardened in a climate chamber using two freeze-thaw cycles (FTCs). Fig. 2 shows the utilized temperature profile of one FTC. Finally, the PVA can be removed by placing the phantom in a water bath.

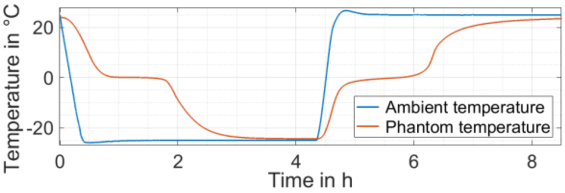

Fig. 2. Temperature profile of one FTC. The Phantom temperature was measured using a PT100 sensor placed in the center of a reference phantom.

Experiment and Results

To evaluate the braches, a highly echogenic fluid composed of the same hydrogel used to manufacture the phantom with 5 mg/ml PVA powder was utilized in combination with a Whadda WPM447 peristaltic pump to generate a fluid flow. Ultrasound data was collected by means of an Ultrasonix SonixTouch ultrasound scanner in combination with a L9-4/38 ultrasonic transducer exploiting STVF imaging and a 4DL14-5/38 ultrasonic transducer exploiting 3DUS imaging. The results are depicted in Fig. 3 and Fig. 4.

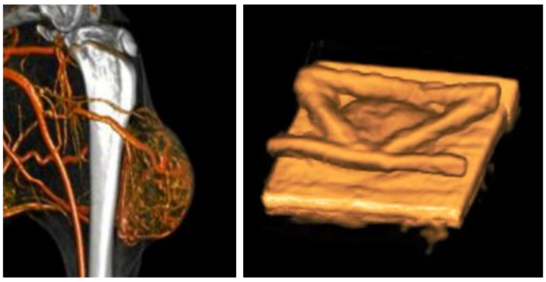

Fig. 3. Angiographic image of a VX2-tumor below the knee of a rabbit (left, SEON). 3DUS image of the phantom with a center frequency of 10 MHz, mechanical index of 0.28, and thermal index of 0.27 (right).

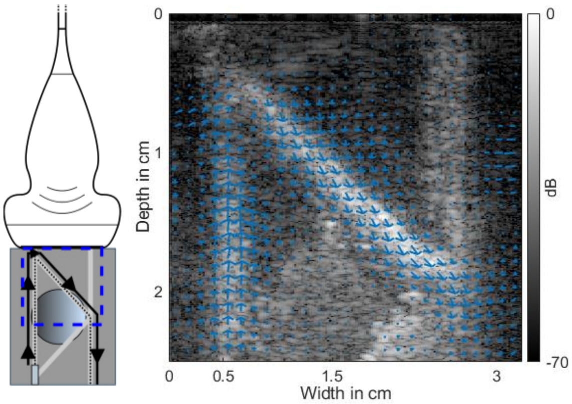

Fig. 4. STVF image with a center frequency of 6.6 MHz, 88 frames per second, mechanical index of 0.53, and thermal index of 0.37. Peristaltic pump is connected to inlet at (depth/width) of (4/0.5) cm. The blue box indicates the area used for the STVF image.

Conclusion and Outlook

This contribution demonstrates an extended manufacturing process for MMUS phantoms with a branching wall-less vessel system using water-soluble PVA filament. It could be shown that local heating using a heat gun can be used to connect PVA parts to build a branching wall-less vessel system around a tumor phantom. Furthermore, it could be shown that highly echogenic fluid enables evaluation of braches exploiting 3DUS imaging and STVF imaging. In addition, unlike Doppler imaging, STVF allows the characterization of speckle pattern movements independent of the orientation of the ultrasonic transducer. Future research will focus on disturbances caused by SPIONs in vessels and their impact on MMUS imaging.

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