

A Pattern Designable Hydrogel Vessel Phantom for Ultrasound Imaging

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Abstract—Medical ultrasound (US) imaging has been established as an essential diagnostic tool and US phantoms are fundamental tools to examine the performance of ultrasound imaging. We describe an inexpensive and reusable strategy to establish an ultrasound-imaging hydrogel phantom to satisfy researchers' requirement in this study. The result demonstrated that the transparent and durable ultrasound phantom contained two-vessel lumens, and its ultrasound imaging results were obtained with high-quality. Furthermore, we could observe a clear shape of the present word “PKU” on an ultrasound image by using phase change phantom, indicating that phantom with different internal shapes could be well designed using this strategy. In conclusion, the preparation strategy is feasible for pattern designable hydrogel phantom and can provide valuable prospects for ultrasound imaging.

Keywords—phantom, pattern designable hydrogel, ultrasound imaging

I. INTRODUCTION

Medical ultrasound (US) imaging has been established as an essential diagnostic tool due to its non-invasiveness, real-time capabilities and safety[1, 2]. Furthermore, the numerous US contrast agents have been approved and can be used in the ultrasound super-resolution imaging, which has an approximate 10-fold improvement on resolution in the tumor[3], brain[4] and kidney[5] for diagnosis. Ultrasound phantoms are essential tool to teach ultrasound-guided procedures to novice sonographers[6] and verify the ultrasound super-resolution result in study[7]. However, commercially available training phantoms are always expensive, ranging in cost from four hundred dollars to several thousand dollars[6]. The high cost of commercial phantoms has aroused the interest of researchers to explore alternatives, including agarose and gelatin hydrogel. The phantoms based on agarose at lower concentrations (1-3%) are firmer but have

a tendency to tear easily. More importantly, both the agarose and gelatin phantoms are the limited shelf life, which degrade and mold over short periods[8].

Actually, Acrylamide (AAm) is another common and available hydrogel material in many fields, particularly in biomedical, pharmaceutical and agricultural sector[9]. Compared with the traditional hydrogel materials, acrylamide hydrogel systems have been reported to possess remarkable fracture toughness and maximum compressive strain[10]. The strength, toughness, and stiffness of the hydrogels make them a good potential material for hydrogel phantom applications. The previous research demonstrated that N-isopropylacrylamide (NIPAM)-based hydrogel phantoms could be used under high-intensity focused ultrasound (HIFU) ablation due to their sonographic and thermal properties were closer to those of animal and human tissues[11, 12]. Additionally, our previous work proposed and designed an alternative antifungal hydrogel preparation strategy to obtain plasma-activated PAAm hydrogels with high antifungal abilities[13].

In light of those considerations, we described an inexpensive and reusable strategy to establish ultrasound-imaging hydrogel using available material acrylamide to satisfy researchers' requirement. A tunnel phantom and phase change (PC) phantom was designed in this study. And the tensile properties of phantoms were evaluated. Furthermore, the ultrasound imaging of the phantoms was also evaluated and analyzed in detail.

II. MATERIALS AND METHODS

A. phantom preparation

Two different phantoms were fabricated using available material polyacrylamide (PAAm), tunnel molds and phase-

change perfluorohexane nanodroplets. The tunnel phantom contained different size tunnels with 300 micrometers and 1 millimeter. Another phantom contained uniformly dispersed acoustic scatters in the background and with the word “PKU” shaped inclusion positioned in the center and this phantom was denoted as PC phantom.

For the tunnel phantom, 200 mL of degassed water was mixed with 30 g acrylamide monomer powders and 0.02 g N,N'-methylenebisacrylamide (MBAA). After stirring uniformly, 0.2 g ammonium persulfate (APS) was added. Next, 165 μ L of the polymerization inhibitor tetramethylethylenediamine (TEMED) was added. The entire solution was quickly poured into a rectangular container with 300 micrometers and 1 millimeter tunnel and allowed to polymerize for 30 min.

The PC phantom was fabricated by three steps. 200 mL of degassed water was mixed with 30 g acrylamide monomer powders, 0.02 g N,N'-methylenebisacrylamide (MBAA) and 0.2 g ammonium persulfate (APS). Firstly, the 100mL resulting solution was added into a rectangular mold, and TEMED was added to crosslink the acrylamide, meanwhile, a PKU mold was positioned at the solution surface in order to form a cavity with “PKU” shape after the crosslink. Secondly, 100 μ L nanodroplets were added followed by 4.1 μ L TEMED into 5 ml solution, and then the nanodroplet solution was added into the cavity. Finally, the 78.4 μ L TEMED was added into the remain 95 mL solution and the entire solution was quickly poured into the mold for crosslink and form the phantom with a “PKU” inclusion.

B. Characterization of phantom tensile properties

The tensile properties of phantom were tested by a Universal Testing Systems (5969, Instron, USA) using a constant cross-head speed of 100 mm/min. The samples were prepared in dumbbell shapes with a concave width of 10 mm and a thickness of 5 mm.

C. Ultrasound imaging

Each phantom was imaged from the top a linear array probe L12-3 (Verasonics Inc., Kirkland, WA, USA). For the tunnel model, the home-made perfluoropropane MB suspension[14] was adjusted to have a concentration of $\sim 1.0 \times 10^7 \text{ mL}^{-1}$ in PBS and kept flowing at 1 mL min^{-1} in the tunnels. To image each phantom, the ultrasound transducer was driven at 7 MHz center frequency using a programmable ultrasound imaging system (Vantage 2561, Verasonics Inc., Kirkland, WA, USA) at B-mode and contrast mode.

III. RESULTS AND DISCUSSION

A. phantom preparation

The two different phantoms prepared by polyacrylamide hydrogel is shown in Figure 1. We can observe that the phantom has satisfactory light transmission properties. The two different size tunnels with 300 micrometers and 1 millimeter were clearly visualized in Fig 1a. Furthermore, we can design different shapes in polyacrylamide hydrogel. As shown in Fig 1b, we can clearly observe the shape of the letter “PKU” in the PC phantom, which is the bubbles formed by the nanodroplets vaporization during the polyacrylamide

polymerization process and those bubbles have strong echoes in ultrasound contrast imaging model[15]. Those results indicate that phantom with different size tunnels can be well fabricated using polyacrylamide hydrogel.

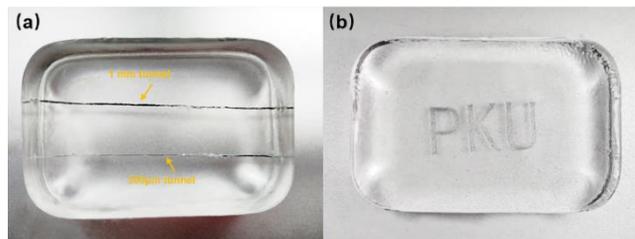


Figure 1 (a) The hydrogel phantom with different size tunnels. (b) The PC phantom.

B. Characterization of phantom tensile properties

The mechanical properties of polyacrylamide hydrogel were evaluated and the result showed that hydrogel exhibited excellent mechanical strength. It could be pressed without fragmentation (Fig 2a) and also exhibited outstanding stretchability (Fig 2b,c). A piece of hydrogel could be stretched into four times its original length without breaking and it was totally recovered after release. Furthermore, the tensile strength and deformation curves of hydrogel indicated excellent mechanical strength. Those results showed that the hydrogel has excellent strength and tensile properties with a long service life, which can meet the extrusion, friction and slip during ultrasonic experiments, and have long service life.

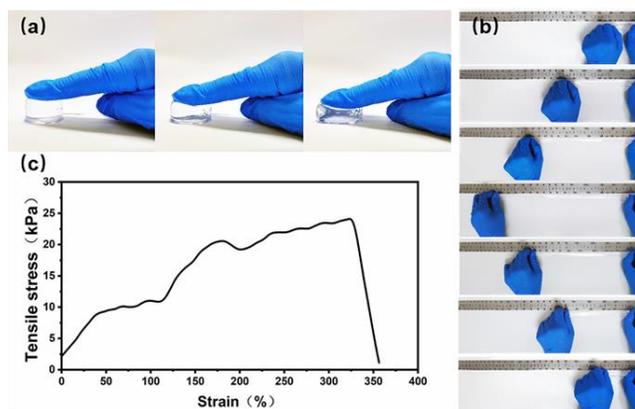


Figure 2. Mechanical properties of polyacrylamide hydrogel. (a) A free standing hydrogel can be pressed without fragmentation; (b) The photographs of the stretchable hydrogel; (c) Typical tensile strength and deformation curves of different hydrogels.

C. Ultrasound imaging

We used the verasonics system to image the two different phantoms. As shown in Fig 3a. Since the saline was injected into the tunnel lumen, we cannot see the shape of tunnels in ultrasound contrast mode. However, we can clearly see the contour and size of the tunnel with the injection of microbubbles. The size of the 1mm tunnel under sonography

is also approximately 1mm, which is consistent with the optical image; the size of the 300 μm tunnel under sonography is greater than 300 μm , which is caused by the limitation of the ultrasonic resolution. The ultrasound image can present a vessel size that is consistent with the actual by ultrasonic super-resolution algorithm[16], indicating that the phantom we prepared can be used to validate the ultrasound super-resolution algorithm. In addition, the PC phantom is produced by the vaporization of phase-change nanodroplets to form microbubbles, as such strong echoes are presented in B-mode and contrast mode, and we can clearly see the shape of the internal letters in PC phantom. It is reasonable to believe that the proposed phantoms with different patterns will have potentials to offer promising tools in clinical training for ultrasound imaging.

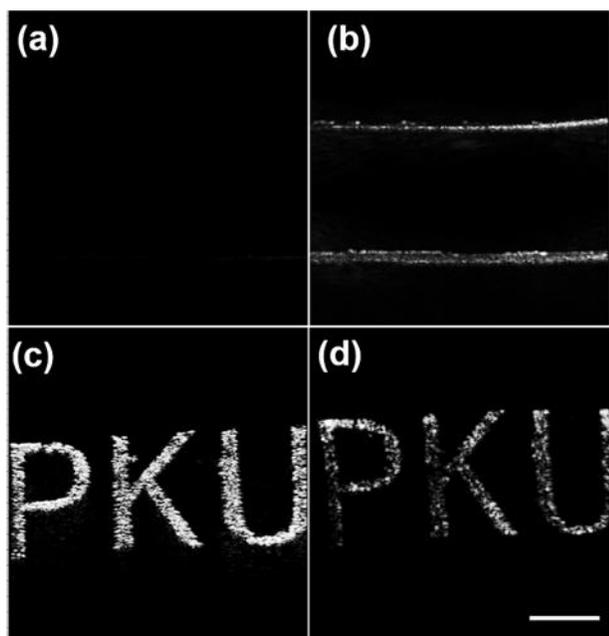


Figure 3 ultrasound images of different phantoms. Tunnel phantom with injection of saline (a) or microbubbles (b) in ultrasound contrast mode; PC phantom in B-mode (c) or ultrasound contrast mode (d). Scale bar: 10 mm

IV. RESULTS AND DISCUSSION

In conclusion, the hydrogel based preparation strategy is feasible for pattern designable phantom and can provide valuable tools for ultrasound imaging.

ACKNOWLEDGMENT

This project was supported by Peking University Biomed-X Foundation

REFERENCES

[1] X. H. Zhang, and C. Xiao, "Ultrasonic diagnosis combined with targeted ultrasound contrast agent improves diagnostic sensitivity of ultrasonic for non-small cell lung cancer patients," *Experimental and Therapeutic Medicine*, vol. 16, no. 2, pp. 908-916, Aug, 2018.

[2] M. A. Borden, and K. H. Song, "Reverse engineering the ultrasound contrast agent," *Advances in Colloid and Interface Science*, vol. 262, pp. 39-49, Dec, 2018.

[3] S. K. Kasoji, J. N. Rivera, R. C. Gessner *et al.*, "Early assessment of tumor response to radiation therapy using high-resolution quantitative microvascular ultrasound imaging," *Theranostics*, vol. 8, no. 1, pp. 156, 2018.

[4] E. Claudia, P. Juliette, P. Sophie *et al.*, "Ultrafast ultrasound localization microscopy for deep super-resolution vascular imaging," *Nature*, vol. 527, no. 7579, pp. 499-502, 2015.

[5] D. Ghosh, F. Xiong, S. R. Sirsi *et al.*, "Toward optimization of in vivo super-resolution ultrasound imaging using size-selected microbubble contrast agents," *Medical physics*, vol. 44, no. 12, pp. 6304-6313, 2017.

[6] D. S. Morrow, J. A. Cupp, and J. S. Broder, "Versatile, Reusable, and Inexpensive Ultrasound Phantom Procedural Trainers," *Journal of Ultrasound in Medicine*, vol. 35, no. 4, pp. 831-841, Apr 1, 2016.

[7] G. Zhang, S. Harput, S. T. Lin *et al.*, "Acoustic wave sparsely activated localization microscopy (AWSALM): Super-resolution ultrasound imaging using acoustic activation and deactivation of nanodroplets," *Applied Physics Letters*, vol. 113, no. 1, Jul 2, 2018.

[8] A. Richard, J. Z. Kartchner, L. A. Stolz *et al.*, "A novel and inexpensive ballistic gel phantom for ultrasound training," *World Journal of Emergency Medicine*, vol. 6, no. 3, pp. 225-8, 2015.

[9] Y. Meng, J. Lu, Y. Cheng *et al.*, "Lignin-based hydrogels: A review of preparation, properties, and application," *International Journal of Biological Macromolecules*, vol. 135, pp. 1006-1019, Aug 15, 2019.

[10] M. M. Fitzgerald, K. Bootsma, J. A. Berberich *et al.*, "Tunable Stress Relaxation Behavior of an Alginate-Polyacrylamide Hydrogel: Comparison with Muscle Tissue," *Biomacromolecules*, vol. 16, no. 5, pp. 1497-1505, May, 2015.

[11] J. Shieh, S. R. Chen, G. S. Chen *et al.*, "Acrylic acid controlled reusable temperature-sensitive hydrogel phantoms for thermal ablation therapy," *Applied Thermal Engineering*, vol. 62, no. 2, pp. 322-329, Jan 25, 2014.

[12] M. K. Sun, J. Shieh, C. W. Lo *et al.*, "Reusable tissue-mimicking hydrogel phantoms for focused ultrasound ablation," *Ultrasonics Sonochemistry*, vol. 23, pp. 399-405, Mar, 2015.

[13] Z. X. Liu, Y. P. Zheng, J. Dang *et al.*, "A Novel Antifungal Plasma-Activated Hydrogel," *Acs Applied Materials & Interfaces*, vol. 11, no. 26, pp. 22941-22949, Jul 3, 2019.

- [14] F. H. Dong, J. B. Zhang, K. L. Wang *et al.*, “Cold plasma gas loaded microbubbles as a novel ultrasound contrast agent,” *Nanoscale*, vol. 11, no. 3, pp. 1123-1130, Jan 21, 2019.
- [15] D. Cosgrove, “Ultrasound contrast agents: An overview,” *European Journal of Radiology*, vol. 60, no. 3, pp. 324-330, Dec, 2006.
- [16] O. M. Viessmann, R. J. Eckersley, K. Christensen-Jeffries *et al.*, “Acoustic super-resolution with ultrasound and microbubbles,” *Physics in Medicine and Biology*, vol. 58, no. 18, pp. 6447-6458, Sep 21, 2013.