Predicting Treatment Position of Thermal Responsive Droplet Vaporization by Ultrasound Thermal Imaging

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Background, Motivation and Objective

Acoustic droplet vaporization (ADV) by high-intensity focused ultrasound (HIFU) stimulation provides local bubble generation, physical damage, and drug release for tumor theranostics. Since the precision of HIFU treatment influences the therapeutic efficacy and side effects, the focal position of HIFU should be concerned. Ultrasound thermal imaging has been applied to monitor the *in vivo* temperature distribution and confirm the position of local heating. Therefore, our study predicted the treatment position of HIFU by thermal responsive droplets (TRDs) and ultrasound thermal imaging. The TRDs were designed to maintain stability under the hyperthermia temperature and can be vaporized by subsequent HIFU stimulation.

Statement of Contribution/Methods

Our homemade TRDs encapsulated the perfluorocarbon mixture of C_5F_{12} and C_6F_{14} to measure the ADV efficiency under the hyperthermia temperature (37-41 °C). The 7-MHz ultrasound imaging-guided 3.5-MHz HIFU system was used to collect ultrasound images, heat, and vaporize TRDs. After intravenous injection of 3×10^6 TRDs into TRAMP tumor bearing mice, the *in vivo* position of HIFU focus was predicted by thermal imaging during HIFU heating (5 MPa, duty 30%), and then transmitted a single-pulse (8 MPa, 4-cycle) to reveal the ultrasound contrast imaging after ADV. The overlapped position between heating and bubble formation were used to evaluate the accuracy of predicting HIFU treatment position by ultrasound thermal imaging. Finally, the intratumoral tissue damage and fluorescent dye distribution were demonstrated by histological images to simulate drug accumulation after HIFU treatment.

Results/Discussion

The optimal fabrication of TRDs (1.21±0.19 μm, volume ratio of C_5F_{12}: C_6F_{14}=7:3) increased 33±11% in ADV efficiency at 41 °C under the acoustic pressure of 8.6 MPa. The accuracy of ADV region prediction by ultrasound thermal imaging was 87.2±3.5% for the *in vitro* study and 83.2±8.6% for the *in vivo* study. The similar positions between the bubble enhancement on ultrasound images, 41 °C distribution areas on thermal images, and tissue damage on histological images showed the credibility of these estimations. Therefore, we considered this technique of predicting the position of HIFU treatment by using TRDs and US thermal imaging provided simplicity, portability, and accessibility to employ in the clinical tumor therapy.