Viscoelastic property and stability of lipid-based microbubble with indocyanine green derivative

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Background, Motivation and Objective

We developed the lipid-based microbubbles (MBs) with indocyanine green (ICG) derivative for dual imaging of near infrared (NIR) fluorescence and ultrasound. The dual imaging will complement disadvantages such as poor penetration depth in NIR fluorescence and small-field view of ultrasound and will be an effective technique in clinical situation, e.g. leading to surgery navigation for sentinel lymph-node biopsy. To understand the performance as acoustic scatterer and fluorescence probe of the MBs, we characterized NIR-fluorescence intensity, viscoelastic property and stability of lipid shell.

Statement of Contribution/Methods

Lipid shell was composed of DSPC, DSPE-PEG2000, lecithin and ICG-derivative and represented as (ICG (+), lecithin (+)). We aimed to enhance the fluorescence intensity by adding the lecithin. For understanding how the lecithin and ICG derivative affect the performance as acoustic scatterer and as fluorescence probe, we prepared other three controls; (ICG (+), lecithin (-)), (ICG (-), lecithin (+)) and (ICG (-), lecithin (-)).

Fluorescence intensity was evaluated by NIR fluorescence microscope. The attenuation of MB suspension was evaluated by transmitting 5-MHz ultrasound in a chamber filled with MB suspension and receiving the echo from a reflector. The attenuation was calculated from the signal intensity ratio between in the presence and absence of MBs in frequency domain. By fitting the numerically-calculated attenuation to the measured one, the dilatational elasticity E^S and viscosity κ^S of lipid shell were estimated. The stability of MBs was evaluated in the circulating system. The MBs suspension flowed in a channel inside a gel phantom. The ultrasound was transmitted from a linear array probe equipped with a commercial scanner above the phantom. By analyzing the change of video-intensity of the channel in B-mode image, the time constant was quantified as the acoustic lifetime of MBs.

Results/Discussion

Figure 1(a)-(c) show the bright-field and NIR fluorescent image of four types of MBs, viscoelastic parameters (E^S and κ^S), and time constant, respectively. In Fig. 1(a), the lecithin enhanced the fluorescent intensity. In contrast, E^S and κ^S and time constant for lecithin (+) was significantly small than those for lecithin (-) in Fig. 1(b) and (c). There seems to be trade-off between characteristic as fluorescence probe and that as acoustic scatterer.

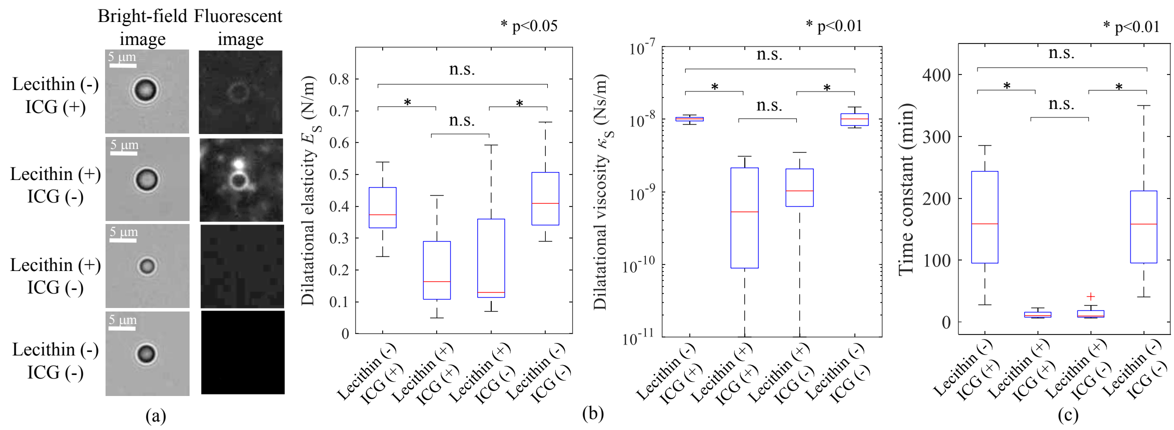

Fig. 1 Characteristic of four types of microbubbles; (Lecithin(-), ICG(+)), (Lecithin(+), ICG(+)), (Lecithin(+), ICG(-)), (Lecithin(-), ICG(-)). (a) microscopic bright-field image and NIR fluorescence image. (b) Viscoelastic property of lipid shell, dilatational elasticity E^S and dilatational viscosity κ^S based on frequency-dependent attenuation analysis. (c) Time constant of intensity-time curve in B-mode image.