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The Real Time Effect of a Radiotherapeutic Photon Beam in the Acoustic Response of Phospholipid-Shelled Monodisperse Microbubbles

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Background, Motivation and Objective

In vivo dosimetry is a key step to detect deviations from the treatment plan in photon radiotherapy. Nevertheless, no technique has emerged as a gold standard. In *Verboven et al.* 2014 IEEE IUS, lipid-shelled microbubbles (MBs) were proposed as dosimeters since they showed a linear decrease in the acoustic attenuation with the delivered dose after radiation. Here we want to measure in real time the change in the acoustic response of the MBs due to radiation to detect possible transient effects, and to study the influence of the acoustic pressure on the measured change. As the attenuation spectra of polydisperse MB populations have a complex dependency on the bubble size and shell properties, changes in these parameters can be easily misinterpreted. Thus, we decided to use monodisperse MBs.

Statement of Contribution/Methods

Monodisperse MBs with a lipid shell (DSPC + DPPE-PEG5k) and a C_4F_{10} gas core, of 4.7 μm diameter, were produced in a microfluidic device. *In vitro* diluted samples of MBs were irradiated with a clinical 6 MV photon beam. A total dose of 15 Gy was delivered during 180 s. The acoustic attenuation was measured during radiation using 5 kPa (peak negative pressure) pulses. It was also measured before and after using 5, 25, and 50 kPa. Pulses were narrowband, with center frequencies from 1 to 4.9 MHz. Control measurements were performed on fresh samples of MBs, using equal handling and acoustic sampling, yet without radiation.

Results/Discussion

The attenuation, before and after radiation, is shown in Fig. 1A. The changes observed are due to both delivered dose and time related processes, such as diffusion. To compensate for the latter, the change in attenuation of the control samples is subtracted from the change in attenuation of the irradiated samples in further analysis. Thus, Fig. 1B shows a 0.4 dB/cm decrease for 15 Gy in the maximum attenuation, similar to those shown in *Verboven et al*. for lipid-shelled MBs. The vertical dashed lines represent the start and end of the radiation. No remarkable transient effect is found in either of the events. The decrease at 5 kPa represents a 6% of the initial peak attenuation, whereas for 25 and 50 kPa the decrease is 4% and 1.5% respectively. The larger influence of the radiation on the lower pressures suggests a modification of the shell parameters, but also a lower relevancy for dosimetry as *in vivo* the used pressure typically is the larger.

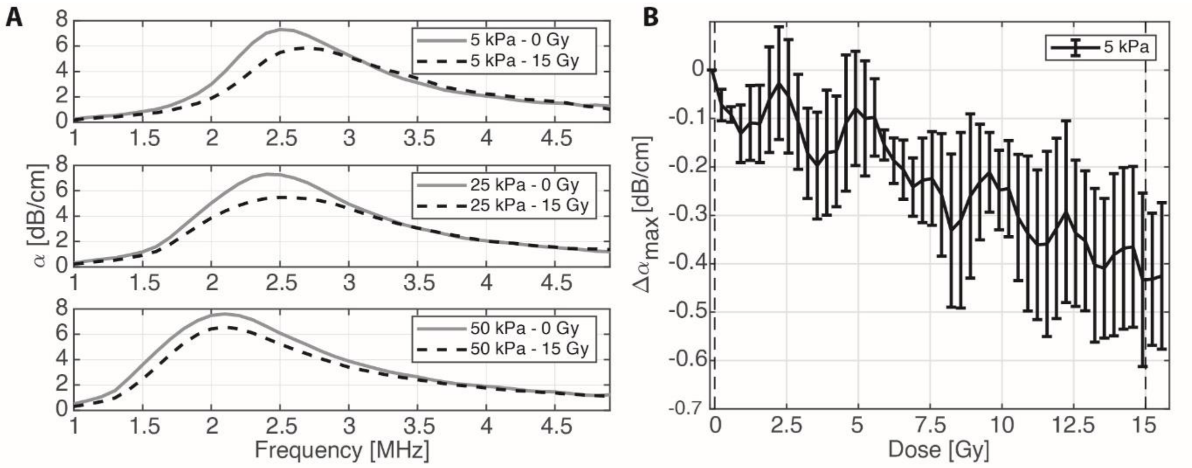

Fig. 1 A, Acoustic attenuation spectra, before and after radiation, for 5, 25, and 50 kPa. B, Change in the maximum attenuation as a function of delivered dose, with time effects corrected using the control measurements.