Acoustic microbubble generation from nano droplet for diagnostic and therapeutic application

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Stabilized microbubbles show high echogenicity and characteristic non-linear acoustic responses and widely used as contrast agent for diagnostic ultrasound. Recently it has been revealed that they also work as ‘sensitizers’ for HIFU (high intensity focused ultrasound) therapy. If microbubbles were selectively placed in targeted tissues, targeted diagnosis and therapy would be possible. However, microbubbles are too large to be delivered into tissues from blood vessels. For tumor detection and therapy, we propose the use of nano-sized liquid precursor of microbubbles (nano droplet) that are small enough to be delivered into tumor tissues yet acts as microbubbles once stimulated by ultrasound pulses.

We have developed nano droplets containing perfluoropentane [1] and found that microbubbles can be generated with ultrasound pulses from a medical ultrasound scanner (modified for this study) at negative peak pressure at about several MPa in water [2]. Figure 1 shows microscopic images of nano droplets in polyacrylamide gel in water before and after ultrasound pulse exposure. We also confirmed that such microbubbles generation induces brightness changes in ultrasound echography. Further, such echographic changes were observed in living biological tissues such as tumors and livers [2].

Such ‘in situ’ generation of microbubbles would contribute to site specific contrast imaging with proper targeting mechanism. Furthermore, since bubbles amplify thermal effect of ultrasound at present region, it would also contribute to site specific minimally invasive therapy with the aid of therapeutic ultrasound.

Keywords: contrast agent, microbubble, phase change, nano droplet