ACOUSTICS2008/3141
Use of radiation force for enhancing efficacy of molecular targeted ultrasound contrast agents - in vitro and in vivo

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Intravenously injected modified ultrasound microbubbles possessing molecule specific targeting ligands hold significant promise as a method for "molecular imaging". Unfortunately, although microbubbles can achieve specific adhesion in regions of vascular pathology, the method breaks down in high blood flow regions where the bond formation process is more problematic. I present results indicating that acoustic radiation does increase the specific targeted adhesion of microbubbles by pushing the bubbles towards the periphery of a vessel. During in vitro studies, radiation force enhanced microbubble adhesion up to 60-fold. Microbubble adhesion is observed to increase approximately with the square of acoustic pressure between 25 and 122 kPa, but decreases at higher pressures as the bubbles rupture. Our in vivo studies involved using intravital microscopy to assess the adherence of P-selectin targeted microbubbles in the mouse cremaster microcirculation and femoral vessels. Acoustic radiation force enhanced microbubble retention four-fold in cremaster venules and in the femoral vein. A 20-fold enhancement was observed in the femoral artery. I discuss the potential for derivatives of the technique to provide molecular targeted therapeutic contribution.