## ACOUSTICS2008/2540 Sub-harmonic response from polymer-shelled contrast agents with a 40-MHz excitation

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There is a growing interest in using acoustic contrast agents with high-frequency ultrasound (> 15 MHz) in order to better visualize microcirculation. Experiments were performed with polycaprolactone-shelled agents (POINT Biomedical, San Carlos, CA) having mean diameters of 0.56, 1.1, and 3.4  $\mu$ m. The agents were heavily diluted in filtered water and injected through a 200  $\mu$ m channel into the focal zone of a 40-MHz transducer that had a focal length of 12 mm and an outer diameter of 6 mm. Backscatter signals from single agents were digitized using tone bursts of 5 to 20 cycles at peak-negative pressures of 0.6 to 6.3 MPa. 1000 valid single-bubble backscatter events at each exposure condition were digitized and then analyzed for 20-MHz subharmonic content. The data showed that the subharmonic response was initiated between 5 and 10 cycles and the likelihood of a subharmonic event increased as the number of cycles increased. A subharmonic backscatter response was most likely at 3.9 MPa for the 3.4 \$ $\mu$ m agent and 1.7 MPa for the 0.56 and 1.1  $\mu$ m agents. The increased pressure for subharmonic activity for larger agent was consistent with its larger size.