

The use of gas filled microbubbles as contrast agents for ultrasound imaging (US) is well established by now. Such contrast agents are used world-wide to improve the diagnostic capabilities of US especially when employed in combination with novel nonlinear contrast imaging modes such pulse inversion second harmonic and subharmonic imaging (SHI).

Our group has investigated the use of SHI in breast imaging and has produced the first ever human SHI images as well as developed a new contrast imaging mode: dynamic cumulative maximum intensity (CMI) SHI. Fourteen patients with 16 breast lesions, who underwent breast biopsies with histopathological assessment, participated in a pilot study of mammography and contrast US. A Logiq 9 scanner (GE Healthcare, Milwaukee, WI) was modified to perform grayscale SHI (transmitting/receiving at 4.4/2.2 MHz). Of the 16 lesions, 4 were malignant. Mammography had a sensitivity of 100 % and a specificity of 20 %. Baseline grayscale US and PDI both achieved a sensitivity of 50 % and a specificity of 92 %, while contrast-enhanced PDI produced 75 % and 75 %, respectively. SHI had a sensitivity of 75 % and specificity of 83 %. All the ultrasound modes produced higher specificities than mammography ($p < 0.04$). The area under the ROC curve (A_z) for the diagnosis of breast cancer was 0.64 for grayscale and PDI, 0.67 with contrast enhanced PDI, 0.76 for mammography and 0.78 for SHI. For dynamic CMI-SHI mode the A_z increased to 0.90 and this was significantly better ($p = 0.03$) than mammography.

More recently, the utility of contrast microbubbles for quantitative measurements of hydrostatic pressure (in mmHg) have been explored. Changes in ambient pressure affect the reflectivity of ultrasound contrast microbubbles leading to an excellent correlation between subharmonic signals and hydrostatic pressure ($r^2 > 0.90$). We have proposed subharmonic aided pressure estimation (SHAPE; U.S. patent 6,302,845) and provided proof of concept of the feasibility of in vivo SHAPE. The heart and aorta of four dogs were scanned with a Sonix RP scanner (Ultrasonic Medical Corporation, Richmond, BC, Canada) modified to perform SHAPE. Simultaneously, the instantaneous pressures within the aorta were measured using a manometer-tipped catheter. The instantaneous in vivo pressure measurements and those based on SHAPE were in good accordance over a pressure range of 0 to 70 mmHg (r^2 from 0.65-0.85).

In conclusion, a new contrast specific imaging technique, SHI, has been investigated for in vivo breast imaging and for quantitative measurements. SHI appear to improve the diagnosis of breast cancer relative to conventional ultrasound and mammography; albeit based on a very limited patient population. Some encouraging results in pressure estimation have been achieved.

Learning Objectives:

1. Understand the origin of subharmonic bubble signals
2. Understand the pro's and con's of SHI
3. Understand the principle of SHAPE