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Simultaneous grayscale and subharmonic ultrasound imaging on a modified commercial scanner

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Abstract

Objective—To demonstrate the feasibility of simultaneous dual fundamental grayscale and subharmonic imaging on a modified commercial scanner.

Motivation—The ability to generate signals at half the insonation frequency is exclusive to ultrasound contrast agents (UCA). Thus, subharmonic imaging (SHI; transmitting at f_0 and receiving at $f_0/2$) provides improved visualization of UCA within the vasculature via suppression of the surrounding tissue echoes. While this capability has proven useful in a variety of clinical applications, the SHI suppression of surrounding tissue landmarks (which are needed for sonographic navigation) also limits its use as a primary imaging modality. In this paper we present results using a commercial ultrasound scanner modified to allow imaging in both grayscale ($f_0 = 4.0$ MHz) and SHI ($f_0 = 2.5$ MHz, $f_0/2 = 1.25$ MHz) modes in real time.

Methods—A Logiq 9 ultrasound scanner (GE Healthcare, Milwaukee, WI) with a 4C curvilinear probe was modified to provide this capability. Four commercially available UCA (Definity, Lantheus Medical Imaging, North Billerica, MA; Optison, GE Healthcare, Princeton, NJ; SonoVue Bracco Imaging, Milan, Italy; and Sonazoid GE Healthcare, Oslo, Norway) were all investigated *in vitro* over an acoustic output range of 3.34 MPa. *In vivo* the subharmonic response of Sonazoid (GE Healthcare, Oslo, Norway) was investigated in the portal veins of 4 canines (open abdominal cavity) and 4 patients with suspected portal hypertension.

Results—*In vitro*, the four UCA showed an average maximum subharmonic amplitude of 44.1 ± 5.4 dB above the noise floor with a maximum subharmonic amplitude of 48.6 ± 1.6 dB provided by Sonazoid. The average *in vivo* maximum signal above the noise floor from Sonazoid was 20.8 ± 2.3 dB in canines and 33.9 ± 5.2 dB in humans. Subharmonic amplitude as a function of acoustic

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output in both groups matched the S-curve behavior if the agent observed *in vitro*. The dual grayscale imaging provided easier sonographic navigation while the degree of tissue suppression in SHI mode varied greatly on a case by case basis.

Conclusions—These results demonstrate the feasibility of dual grayscale and SHI on a modified commercial scanner. The ability to simultaneously visualize both imaging modes in real time should improve the applicability of SHI as a future primary clinical imaging modality.

Keywords

Subharmonic imaging; ultrasound contrast agents; contrast-enhanced ultrasound

1. Introduction

The ability to exclusively image blood vessels and blood flow is clinically advantageous for a variety of diagnostic applications. For example, neovasculature within breast lesions has been shown to be an independent marker of cancer [1, 2]. Additionally, the ability to visualize tissue perfusion in real time using contrast-enhanced ultrasound imaging can be another useful indicator of malignancy or physiological malfunction [3, 4]. The use of diagnostic ultrasound imaging continues to expand, due to its safe, inexpensive, and portable nature [5]. The capability for real time ultrasound imaging is perhaps one of the biggest advantages of the ultrasound modality, and makes it an ideal imaging option for such many clinical applications.

Ultrasound contrast agents (UCA) are small (diameter of less than 8 μm) gas microbubbles, encapsulated by a shell for improved stability [6]. The difference in both impedance and compressibility of the gas core compared to the surrounding fluid provides efficient reflection and scattering (up to 30 dB) of the ultrasound wave [6]. The stabilizing shells of these agents also play a major role in the microbubble response through varying degrees of stiffness and dampening of the oscillations [6]. These agents are generally restricted to the vasculature due to their size (small enough to pass through the capillaries, but too large to extravasate) and used primarily for cardiac imaging. Additionally, when insonated at a transmit frequency (f_0) at sufficiently high acoustic pressures (> 200 kPa) the majority of UCAs behave nonlinearly, emitting signals at both higher harmonics ($2f_0$, $3f_0$, etc) and the subharmonic ($f_0/2$) [7]. Several contrast-specific imaging modes have been developed based on harmonic imaging (HI; transmitting at f_0 and receiving at $2f_0$) [7]. However, full tissue suppression cannot be achieved with HI, due to the non-linear acoustical properties of surrounding tissue resulting in unwanted echoes at the second harmonic. Other contrast-specific imaging modes rely on UCA destruction at higher pressure amplitudes (> 800 kPa), but these techniques either do not suppress tissue signals or cannot be implemented in real time [7, 8].

Subharmonic imaging (SHI) provides improved suppression of tissue signal and real time visualization of contrast-enhanced blood flow compared to HI [9]. Unlike the much more linear responses of the fundamental and higher harmonics, the change in subharmonic amplitudes with increased acoustic pressures resembles an S-curve, with occurrence (roughly 100–200 kPa), growth (roughly 300–600 kPa), and saturation stages (roughly 600 kPa to UCA destruction) [9]. The subharmonic amplitude within the growth stage of the S-curve has been shown to be a good overall indicator of hydrostatic pressure, with variations of 10–13.3 dB over 180 mmHg pressure ranges [9, 10]. These findings lead to subharmonic aided pressure estimation (SHAPE) investigations by our group and others [11, 12] and may potentially provide an important diagnostic tool based on SHI.

SHI has been shown to be feasible by both our group [13–19] and others [20, 21]. Our group has successfully used SHI to estimate perfusion in canine kidneys, with results correlating well with radiolabeled microsphere findings ($r = 0.57$, $p < 0.001$) [17]. In a first in human pilot study, 14 women with 16 biopsy-proven breast lesions (4 malignant) were imaged with dynamic cumulative maximum intensity (CMI) SHI [16]. The area under the receiver operating characteristic curve (A_z) for the diagnosis of breast cancer was 0.64 for grayscale imaging, 0.76 for mammography, and 0.78 for SHI. For dynamic CMI-SHI, the A_z increased to 0.90 and this was significantly better than mammography ($p = 0.03$) [16, 18]. The diagnostic accuracy of SHI can be further improved through the use of parametric imaging, in which SHI based perfusion measurements have been shown to be a better automated tool for breast lesion characterization than CMI-SHI ($p = 0.002$ when comparing benign and malignant lesions with SHI perfusion alone, vs. $p = 0.80$ for CMI-SHI alone) [19].

While all these results are promising, imaging with SHI alone is difficult due to the suppression of surrounding tissue landmarks (anatomical structures or tissue heterogeneities, which allow sonographic navigation). Our previous in-human SHI study required prior imaging by either grayscale ultrasound or color flow imaging modes to identify lesion locations, which increased total scan time by 5–10 minutes and added uncertainty due to the possibility of motion occurring during the switch between imaging modes. Thus, a platform capable of dual imaging with both grayscale and SHI would allow identification of regions of interest (ROI) through imaging of surrounding tissue, while also simultaneously providing subharmonic information on vascular structures and blood flow as well as local intravascular pressures.

In this paper we demonstrate the feasibility of simultaneous grayscale and SHI imaging on a modified commercial scanner. The ability of the scanner to image subharmonic behavior of four commercially available UCA is first demonstrated *in vitro*. *In vivo* feasibility is then demonstrated through dual grayscale/SHI imaging using the UCA Sonazoid in the portal vein of four canines, followed by liver imaging in four patients with suspected portal hypertension. Both the variation in subharmonic amplitude as a function of acoustic output as well as overall image quality are compared for all three applications.

2. Materials and Methods

2.1 Modification of a Commercial Scanner

Ultrasound imaging was performed using a modified Logiq 9 ultrasound scanner (GE Healthcare, Milwaukee, Wisconsin) with a 4C curvilinear probe. SHI was implemented within the color flow processing chain to transmit variable acoustic output 4-cycle pulses at 2.5 MHz. A pulse inversion (PI) scheme was implemented to provide further suppression of linear tissue signals, although SHI is also possible without PI. An adjustable ROI with a subharmonic filter (i.e., a 1 MHz wide bandpass filter centered at 1.25 MHz) was implemented in order to detect received signals at 1.25 MHz. Intermittent 4.0 MHz B-mode pulses were used to generate a grayscale image in parallel to SHI. The acoustic output of the unit was measured using a 0.5 mm needle hydrophone (Precision Acoustics, UK; last calibrated on 3/30/2009) with a sensitivity of 337.2 mV/MPa at 2.5 MHz. The hydrophone was placed at the focus of the beam in a water bath. The focal point was determined by finding the point of maximum acoustic pressure using an electronic x-y-z positioning system (Newport Corporation, Irvine, CA). Measurements were performed for all acoustic pressures (from 0–100 % of maximum output power) in triplicate. The Logiq 9 was confirmed by hydrophone measurements to be operating at a transmit frequency of 2.5 MHz with acoustic pressure levels of 0 to 3.34 MPa (peak to peak, mechanical index = 0.8), which is well below the FDA's mechanical index limit of 1.9.

2.2 Investigation of Subharmonic Amplitude as a Function of Acoustic Output

Subharmonic amplitude was determined for each of the 28 acoustic power levels (ranging from 0 to 3.34 MPa outputs) with an automation power control sequence implemented using Matlab R2009a (The MathWorks, Natick, MA). The subharmonic ROI was placed within a region containing contrast agent. The automatic power control algorithm then acquired 3 frames at each of the 28 acoustic outputs (frame rates ranged from 7–17 Hz). Radio frequency (RF) data from the filtered subharmonic spectrum was extracted from files stored within the color flow processing chain. A 50% thresholding mask was applied to remove portions of the vessel with lower subharmonic signal. The strength of the subharmonic signal in the masked area was then determined for each acoustic output and converted to dB relative to the noise floor.

2.3 Collection of unfiltered RF data

To verify the presence of subharmonic signals, unfiltered RF data was first obtained from the UCA Sonazoid (GE Healthcare, Oslo, Norway) using only the SHI mode without filtering (thus, providing the entire frequency response). A Sonazoid concentration of 0.2 ml/L saline was imaged within a tissue-mimicking flow phantom (Model 524; ATS Laboratories, Bridgeport, CT) with a 6 mm diameter vessel embedded at a depth of 2 cm. Homogeneity of the mixture was maintained by a magnetic stirrer prior to being pumped through the flow system by roller pump (S10K II; Sarns Inc., Ann Arbor, MI). The acoustic output of the ultrasound scanner was varied from 0 to 3.34 MPa and the frequency spectra of the unfiltered RF data acquired within the contrast-containing vessel was computed (using Matlab).

2.4 Investigation of Subharmonic Response in vitro

Four commercially available UCA were used for *in vitro* SHI. Definity (Lantheus Medical Imaging, North Billerica, MA), Optison (GE Healthcare, Princeton, NJ), SonoVue (Bracco Imaging, Milan, Italy), and Sonazoid were all reconstituted according to the manufacturers' instructions. A 2.2 L sealed water tank containing 0.2 ml/L of continually stirred UCA was submerged in a water bath and imaged with the transducer through a thin plastic acoustic window. The power control algorithm was then implemented on the scanner to collect RF data (with the total scan time less than 1 minute) at each available acoustic output. Images were also obtained with a 2.5 cm thick tissue phantom (thickness cut from rubber based tissue mimicking material, ATS Laboratories) placed in front of the acoustic window to demonstrate SHI's effectiveness at suppressing stationary tissue signals.

2.5 Investigation of Subharmonic Response in vivo

Ultrasound imaging of the portal vein and the inferior vena cava (IVC) was performed in four mongrel canines (22 to 25 kg in weight) following a midline abdominal incision as part of a larger ongoing SHAPE study. The study was approved by the Institutional Animal Care and Use Committee of Thomas Jefferson University. Dogs were initially sedated with an intravenous injection of Propofol (Abbott Laboratories, Chicago, IL; dose of 7 ml/kg) and anesthesia maintained with 2–4% Isoflurane (Iso-thesia; Abbott Laboratories, Chicago, IL). Body temperature was maintained with a warming blanket. Resuspended Sonazoid (1.5 μ L/kg/min) was co-infused with 0.9% saline (2 ml/min) through an 18-gauge catheter placed in a forelimb vein. Sonazoid was infused for roughly 5 minutes prior to data collection to ensure an adequate UCA concentration. Finally the power control algorithm was initiated, followed by image acquisition. Subharmonic amplitudes were determined as described in 2.2 above.

Noninvasive ultrasound liver imaging was performed in four patients (weights of 64 to 107 kg, BMI range of 22 to 45) with suspected portal hypertension as part of an ongoing human SHAPE study. The study was approved by Thomas Jefferson University's Institutional Review Board and was compliant with the Health Insurance Portability and Accountability Act. The use of Sonazoid and the modified scanner was approved by The United States Food and Drug Administration. All patients provided written informed consent prior to taking part in the study. As above, resuspended Sonazoid ($1.5 \mu\text{L/kg/min}$) was co-infused with 0.9% saline (2 ml/min) through an 18-gauge catheter in the antecubital vein. Sonazoid was infused for approximately 5 minutes prior to collection of RF data and images. Subharmonic amplitudes were determined as described in 2.2. Patients were monitored for any adverse events during and one hour after the end of the contrast infusion.

2.6 Statistical Analysis

Significant variation while comparing multiple UCA's subharmonic amplitudes *in vitro* was determined using a one-way ANOVA with α equal to 0.05. Significance of *in vivo* results comparing the level of subharmonic signal was determined using a Student's t-test. While the sample size in this study is quite limited ($n = 4$), this pilot study is intended to show feasibility of fundamental/SHI dual imaging, not diagnostic efficacy. All statistics were analyzed using Prism version 5.0 (Graphpad Software, San Diego California, USA).

3. Results and Discussion

Spectra of unfiltered RF data from Sonazoid at varying acoustic outputs after pulse inversion are shown in Figure 1. The fundamental peak of the frequency spectra can be seen at roughly 2.5 MHz despite the pulse inversion, although some variation is present from pulse to pulse. A distinct subharmonic peak at 1.25 MHz is seen in Figures 1b and 1c. A secondary subharmonic peak is also seen at 1 MHz in Figure 1c due to a secondary spurious fundamental peak at 2 MHz which is not cancelled out during pulse inversion. Consistent with work obtained with single element transducers [9, 10], the subharmonic amplitude shows a period of initial occurrence (Fig 1a), growth (Fig 1b–1c), and saturation (Fig 1d), at which point signal from microbubble destruction fills the entire spectra. While a great deal of variability exists between individually acquired pulses (for example the frequency of the fundamental ranges from 2.5 to 2.8 MHz in figure 1), these results demonstrate that the ultrasound system's output is capable of both eliciting and detecting a subharmonic response from the microbubbles.

In vitro subharmonic behavior of four commercially available UCA was investigated as a function of acoustic output pressure as shown in Figure 2. No significant difference ($p = 0.7$) was detected in peak subharmonic signal between Definity (48.1 ± 1.3 dB) or Sonazoid (48.6 ± 1.6 dB), while a significant ($p < 0.0001$) decrease in subharmonic enhancement was seen in the subharmonic signal generated by both SonoVue (42.5 ± 1.3 dB) and Optison (37.1 ± 1.6 dB). These values result in an average amplitude variation of 44.1 ± 5.4 dB over an acoustic output range of 3.34 MPa with a maximum subharmonic amplitude of 48.6 ± 1.6 dB provided by Sonazoid. The subharmonic S-curve behavior discussed previously was seen for all agents. Shi et al. showed that subharmonic amplitude enters a growth stage at roughly 300–600 kPa [9]. While that work utilized Levovist (Schering AG, Berlin, Germany), an earlier generation UCA, results are somewhat consistent with those shown in Figure 2, demonstrating a subharmonic growth stage from roughly 200 kPa to 1 MPa before reaching saturation. This nonlinear behavior shows that subharmonic signals from the UCA are being detected by the system.

Figure 3 presents images from the dual imaging software during *in vitro* imaging of Sonazoid. Dual grayscale images of the setup are shown with and without the subharmonic

filter overlaid and displayed in a yellow ROI. Figure 3b shows a similar setup, but with a 2.5 cm tissue phantom (green circle) held in front of half the acoustic window. Signals from within the tissue are markedly suppressed in SHI (in yellow ROI) relative to the grayscale ultrasound image, although the boundaries are still visible, presumably due to the surface creating wider broadband reflections. SHI has less attenuation (proportional to frequency) than conventional B-mode imaging and the benefit of this is seen in the variation of signal levels detected behind the tissue phantom. In the grayscale (at 4.0 MHz) image contrast is undetected behind the phantom, due to higher signal attenuation within the phantom. However some subharmonic signal (transmitting at 2.5 MHz, receiving at 1.25 MHz) is still detected in this area, although the total detectable depth of contrast media is reduced by approximately 6 cm.

Subharmonic signals from Sonazoid were investigated in the portal vein of four canines as part of a larger ongoing study investigating portal hypertension. Subharmonic amplitudes increased with acoustic output an average of 20.8 ± 2.3 dB (relative to the noise floor) within portal veins at depths ranging from 1–2 cm. Overall the curves show a similar S-curve behavior although the total amplitude variation was substantially reduced (48.6 dB *in vitro* vs. 20.8 dB *in vivo* for Sonazoid, $p < 0.001$).

Figure 5 shows two dual images of the portal vein and IVC in two open abdomen canines. Both cases show improved contrast to tissue visualization when imaged with SHI. Also in both cases, some bubble destruction is present, as evidenced by the stronger subharmonic signal upstream in the vessels. While some tissue suppression is taking place in SHI, the reflections from the highly heterogeneous tissues are not fully suppressed. However, it is important to note that despite the very slow infusion (1.5 $\mu\text{L/kg/min}$), the contrast-enhanced blood flow is more visible with SHI.

No adverse events were reported in any of the four patients during or one hour after Sonazoid infusion. Figure 6 shows the subharmonic S-curve response from Sonazoid in the portal veins of four patients with suspected portal hypertension. The greater level of variability between data sets compared to Figures 2 and 4 is attributed to the varying location of the patients' portal veins (depths of 5 to 11 cm). The overall range of subharmonic amplitudes as a function of acoustic power was 33.9 ± 5.2 dB relative to the noise floor, with a range of 39.5 to 28.7 dB. The maximum average subharmonic signal was significantly ($p = 0.0037$) higher relative to the canine data, despite imaging at a greater depth, and significantly lower than the *in vitro* range of Sonazoid ($p = 0.0057$). These differences between the canine levels are partially attributed to imaging in the near-field during canine scanning, which may have altered incident acoustic pressures and subharmonic acquisition. While this problem can often be avoided using a common gel pad stand-off, in this case this was not feasible due to the transducer being inserted through the midline incision and held up inside the upper abdominal cavity. The reduction in subharmonic amplitude relative to *in vitro* data is believed to be a result of higher attenuation within the tissue (approximately 0.5 dB/cm/MHz) compared to the water bath measurements (attenuation less than 0.005 dB/cm/MHz).

Figure 7 shows the liver of two patients with suspected portal hypertension. Figure 7a shows an ideal case with high tissue suppression and strong signal within both the portal and hepatic veins. Figure 7b depicts a poorer quality case with less tissue suppression, making it difficult to clearly identify contrast enhancement within the vasculature. Variations in liver function were briefly investigated as a potential difference in suppression levels. However the two patients showed similar levels of fibrosis (Model for End-Stage Liver disease scores of 8 and 9; Fibrosis grades of 1 and 2 for a and b respectively), identical bilirubin levels (1

mg/dL), and identically graded ascites (graded as mild). These findings indicate the variation in tissue suppression is not due to variations in cirrhosis.

Previous results in our lab using SHI alone for breast imaging have shown superior tissue suppression after implementation on a commercial scanner [16]. In this work a SHI transmit frequency was selected as part of an ongoing SHAPE study to provide optimal sensitivity to hydrostatic pressure ($f_0 = 2.5$ MHz and $f_0/2 = 1.25$ MHz determined *in vitro* [10]). As can be seen in the frequency spectra (cf., Figure 1), a great deal of variability exists between pulses, as well as overlap from the fundamental. However, transmission at a higher frequency with a wider bandwidth probe (for example $f_0 = 4.4$ MHz and $f_0/2 = 2.2$ MHz as used in our previous in human SHI work [13]) is certainly feasible and would further separate the fundamental and subharmonic spectra, thus reducing the amount of overlap of the fundamental into the subharmonic filter. Additionally this study used a relatively low, continuous infusion (1.5 μ L/kg/min) in order to maintain a constant level of contrast throughout the 15 mins of imaging (as a requirement of our ongoing SHAPE study). However, previous human SHI studies, which focused primarily on imaging, used a significantly higher concentration with a bolus contrast injection (1.4–4.0 ml) [16]. Future SHI studies may use higher UCA concentrations to better elevate subharmonic signals and improve the contrast to tissue signal levels relative to those seen in this study. Finally, after its initial vascular enhancement, Sonazoid has been shown to be phagocytosed by Kupffer cells within the liver as quickly as 5 minutes after injection [22, 23]. As a result of this uptake, the lack of tissue suppression in some cases may be due more to Sonazoid accumulation within the stationary liver tissue rather than an inability to suppress non UCA-containing regions. Despite these limitations, this study shows the feasibility of grayscale/SHI imaging, its implementation on a modified commercial ultrasound scanner, and its potential clinical application in contrast-enhanced liver imaging.

Contrast-enhanced ultrasound of the liver continues to emerge as an important diagnostic tool. The modality is currently used in many countries for the detection and characterization of liver lesions [24–26]. While several imaging modes have been employed, HI has been shown to have the highest diagnostic accuracy (97% in one study), [25] due to its improved ability to suppress tissue and visualize lesion vascularity relative to fundamental imaging. Recently, Zhang et al. looked at contrast-enhanced ultrasound for determination of portal hypertension by correlating pressure values in 31 patients with hepatitis B virus-related liver disease with the hepatic artery to hepatic vein transit time of SonoVue [27], an approach employed by other groups as well [28–29]. The group used HI to determine contrast transit time through the liver and found a statistically significant correlation ($p = 0.009$) between the two parameters in patients with portal hypertension [27]. As SHI offers improved contrast to tissue ratios over HI, implementation of a dual grayscale/SHI imaging approach has the potential to improve results in both of these applications.

4. Conclusions

A modified scanner has been developed that provides simultaneous display of conventional grayscale and SHI ultrasound modes. *In vitro* results demonstrated the capability to capture nonlinear subharmonic behavior of four commercially available UCA while also suppressing tissue echoes. These capabilities were also demonstrated *in vivo*, although the technique was subject to patient variability and the sample size was quite limited. This implementation is expected to improve the clinical feasibility of SHI for future applications.

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Research Highlights

- A commercial ultrasound scanner has been modified to allow simultaneous imaging in grayscale and subharmonic imaging (SHI) modes in real time
- *In vitro* ultrasound contrast agents showed a subharmonic amplitude variation of 44.1 ± 5.4 dB relative to the noise floor over an acoustic output range of 3.34 MPa.
- *In vivo* the subharmonic response of Sonazoid (GE Healthcare, Oslo, Norway) was investigated in the portal veins of 4 canines (open abdominal cavity) and 4 patients with suspected portal hypertension (a first-in-humans application).
- Subharmonic amplitude as a function of acoustic output matched the results observed *in vitro* with average signal variations of 20.8 ± 2.3 dB in canines and 33.9 ± 5.2 dB in humans.

Figure 1. Examples of frequency spectra obtained from Sonazoid *in vitro* without filtering (a: 0.7 MPa; b: 1.1 MPa; c: 1.7 MPa; d: 2.5 MPa). The subharmonic components of the spectra are shown within the red border.

Figure 2.

In vitro subharmonic response measured using the dual-imaging setup from four commercially available ultrasound contrast agents.

Figure 3.

In vitro images from the dual imaging software showing grayscale ultrasound on the left and subharmonic on the right. The area of subharmonic filtering is shown within the yellow ROI, overlaid on an identical grayscale image. The UCA (Sonazoid; circled in red) is observed (a) within a chamber viewed through an acoustically transparent window (4 to 5 cm from the transducer), while similar setup, with a 2.5 cm tissue phantom covering half the window (shown in green circle) is presented in (b).

Figure 4. In vivo subharmonic response measured using the dual-imaging setup from infused Sonazoid within the portal vein of four open chest canines.

Figure 5.

Examples of dual images showing Sonazoid response within the portal vein (red arrow) and IVC (blue arrow) of two open-chest canines. Flow is occurring from right to left. Figure 5a shows a case with sufficient signal from Sonazoid to make out the IVC and portal vein within the subharmonic ROI. Figure 5b shows a poorer case with less contrast-enhanced subharmonic signal in the vessels, making differentiation difficult.

Figure 6.

In vitro subharmonic response measured using the dual-imaging setup from infused Sonazoid within the portal vein of four patients with suspected portal hypertension. Portal veins were located at depths of 8 cm (red), 5 cm (blue), 7 cm (black), and 11 cm (green).

Figure 7. Examples showing Sonazoid response within the liver of two different patients with suspected portal hypertension. The hepatic veins are shown by the green arrows, the portal veins by red, and the IVCs by blue. Figure 7a represents a good example with higher overall levels of tissue suppression compared to figure 7b, which shows a poorer case with little tissue suppression, making differentiation of the vessels difficult.