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2aBA6. Bubbles trapped on the surface of kidney stones as a cause of the twinkling artifact in ultrasound imaging

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A twinkling artifact (TA) associated with urinary calculi has been described as rapidly changing colors on Doppler ultrasound. The purpose of this study was to investigate the mechanism of the TA. Doppler processing was performed on raw per channel radio-frequency data collected when imaging human kidney stones in degassed water. Suppression of twinkling by an ensemble of computer generated replicas of a single received signal demonstrated that the TA arises from variability among the acoustic signals and not from electronic signal processing. This variability was found to be random in nature, and its suppression by elevated static pressure, and its return when the pressure was released, suggests that the presence of surface bubbles on the stone is the mechanism of the TA. Submicron size bubbles are often trapped in crevices on solid objects, but the presence of these bubbles in vivo is unexpected. To further check this mechanism under conditions identical to in vivo, stone-producing porcine kidneys were harvested en bloc with a ligated ureter and then placed into a pressure chamber and imaged at elevated atmospheric pressure. The result was similar to in vitro. Work supported by NIH DK43881, DK092197, RFBR 11-02-01189, 12-02-00114, and NSBRI through NASA NCC 9-58.

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INTRODUCTION

The twinkling artifact (TA) (Rahmouni *et al.* 1996, Vasiliev and Gromov 1997) appears as a dynamic color mosaic on the image of hard objects in a color-Doppler ultrasound display. Recent studies have reported that the TA, as a Doppler ultrasound artifact has a great potential to improve kidney stone detection. However, this artifact is inconsistent precisely because its origins are unknown: Its manifestation depends on the specific ultrasound imager, the sonographer skills, the machine parameter settings, and the type of stone. Our goal is to improve the understanding of the mechanism(s) that give rise to the TA as a step toward making the TA a reliable clinical tool.

Several studies have investigated the mechanism of the TA displayed by kidney stones. The sources of the artifact were attributed either “to the acoustics” or “to the machine”, *i.e.*, to peculiarities either of ultrasound scattering from the stone or in the system processing of the unique scattered signal. For most of the studies, the conclusions were drawn based on analyzing the Doppler images and Doppler spectrum that were generated by commercial ultrasound machines. Those images may vary between machines, depending on the imaging processing methods employed and different machine settings. The commercial ultrasound machines are “black boxes” in that it is very difficult to separate the acoustical effects (*i.e.*, scattering from a rough surface, stone reverberation, etc.) from the effects of the machine (*i.e.*, phase jitter, machine settings and signal processing, etc.). In addition, clinical ultrasound machines rarely provide users access to the raw radio-frequency (RF) data that are more fundamental than the images, since the raw per-channel RF signals originate directly from the ultrasound array elements, *i.e.*, are not distorted by any post-processing from the machine.

In this study, the raw per-channel RF data immediately following the analog-to-digital converter (ADC) were used. According to the conventional color Doppler imaging algorithm, the color pixels shown on the image are always encoded based on the variability within the Doppler ensemble that corresponds to strong Doppler power. Bearing that in mind, the Doppler power was used as the criterion of the TA. Based on the RF data analysis, the dominant reason for the occurrence of the TA was investigated by estimating whether the variability within the Doppler ensemble is introduced from the acoustic field or from the machine; in addition, a high static pressure study and other studies were performed to further investigate the mechanism(s) for the generation of the TA.

MATERIALS AND METHODS

A Verasonics Ultrasound Engine (VUE, Verasonics, Redmond, WA) and a 128-element linear ultrasound array with 5 MHz central frequency (a clinical probe ATL/Philips HDI L7-4, Bothell, WA, US) were used for all experiments. The raw per-channel RF data immediately following the analog-to-digital converter (ADC) were analyzed to study the TA. The Doppler power was used as the criterion of the TA.

Based on the RF data analysis, the dominant reason for the occurrence of the TA was investigated by estimating whether the variability within the Doppler ensemble is introduced from the acoustic field or from the machine. To test the response of the receiving electronic tract and signal processing of typical Doppler signals without using the ultrasound probe, a special break-out board was connected to the entrance of the electronic tract, which enabled sending, to any selected receiving channel, an electric signal from an external source. In particular, such a source could provide an electric signal similar to that appearing at the array element when receiving an ultrasound pulse scattered from a stone. Such a replacement of acoustically-originated signal by a controlled-source signal allowed us to determine if the TA originated in the machine (*i.e.*, in the electronic tract and signal-processing box) independently from whether the TA originated in the acoustics (*i.e.*, from fluctuations during acoustic scattering and propagation). As an external voltage source, a function generator (AFG 3022B, Tektronix, OR) was used. The generator signal was programmed to be identical to the acoustically originated signal.

In addition, a well-known technique – an overpressure test (Bailey *et al.* 2000; Sapozhnikov *et al.* 2002) was used to test for the possible role of bubbles. The overpressure system and

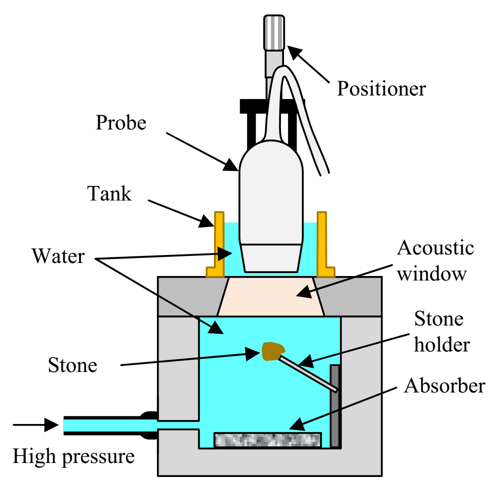

FIGURE 1. High-pressure chamber with the probe

experimental design are shown in Fig. 1. The chamber was of cylindrical shape with the inner diameter 11.2 cm and height 7 cm. Its walls, bottom, and upper lid were made of aluminum. A rubber acoustic absorber (1 cm thick) was placed on the bottom of the chamber to dampen the possible reverberations during the stone imaging. The stone under study was fixed on the tip of a brass needle of 1.6 mm in diameter that was rigidly attached to the chamber wall. A polystyrene puck was fixed in the middle of the lid to serve as an acoustic window for better ultrasound transmission. High static pressure was generated inside the chamber by a piston screw pump (model 37-6-30, High Pressure Equipment Company, Erie, PA). Three different pressure conditions were used: (a) Before applying excess pressure, (b) under high-pressure, and (c) after pressure was released back to the normal value.

RESULTS

Figure 2 shows typical signals that were analyzed to reveal the TA features. The left-hand side plots (A - C) describe data for imaging of a natural kidney stone from the stone laboratory, which was placed in gel. The plots A and B overlays 12 successive waveforms of the Doppler ensemble ultrasound pulses scattered from the stone recorded at the central element of the array. Here the imaging depth d corresponds to the time delay of the scattered signal t in accordance with the formula $d=ct/2$, where c=1540 m/s. The waveforms that are plotted on top of each other are barely distinguishable, because the corresponding changes are small. To reveal the difference between them in more detail, the Doppler power calculated from those waveforms is shown on the plot C. The Doppler power is shown in dB scale, relative to the background noise level. An obvious spike occurs about 2 – 3 μs after the arrival of the front of the stone-scattered pulse, which indicates that the corresponding part of the signal within the Doppler ensemble is fluctuating from pulse to pulse. Such a spike was observed for all studied stones and corresponded to the twinkling part of the color Doppler image. On the right-hand-side of Fig. 2 (D - F), results obtained for the simulated acoustic source experiment test are shown. The waveforms of the simulated Doppler ensemble pulses are shown in Figs. 2D and 2E, also 12 waveforms on top of each other. The waveforms of Figs. 2B and 2E are visually identical, which indicates the high quality of the mimicking procedure. As was described, the artificial Doppler ensemble was sent through the same signal path inside the machine as the original Doppler sequence. Figure 2F represents the result for the Doppler power calculated from the waveforms shown above. No obvious spike is seen in Fig. 2F. Therefore, the TA appearance must result from some effect of acoustic origin.

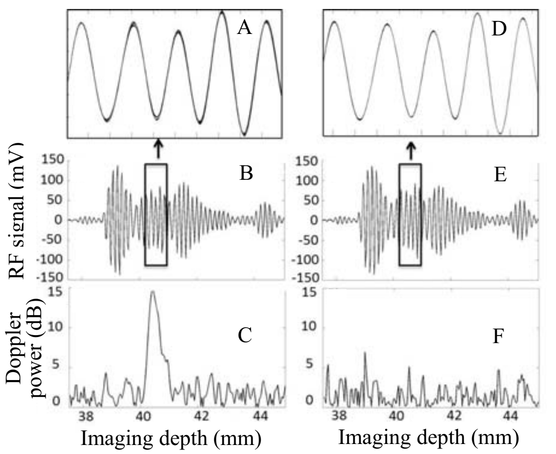

FIGURE 2. Results of kidney stone imaging and simulated acoustic source experiments. Figures A and B show the unbeamformed Doppler pulses (12 pulses on top of each other) recorded from the stone imaging, and figure C shows the corresponding Doppler power. Figures D and E show the unbeamformed Doppler pulses (12 pulses on top of each other) acquired from simulated acoustic source experiment, and F shows the corresponding Doppler power.

FIGURE 3. Results of the overpressure experiment on natural kidney stones. From the left to the right: twinkling is seen before increasing pressure (left), no twinkling is present during the high-pressure of 8.5 MPa (middle), and twinkling returns after the pressure is released (right).

Common candidates for random ultrasound scatterers are bubbles. Indeed, the gas bubbles may interact stochastically with ultrasound. The bubbles may be present in the bulk of propagation medium, or they may also rest on the stone surface, especially if there are microscopic cracks and crevices. The possible presence of bubbles was studied using overpressure test using set-up shown in Fig. 1. Figure 3 shows Color Doppler image of a stone positioned in the overpressure chamber under varied static pressure. The images were recorded by a camcorder directly from the VUE display. There is an obvious TA in the left and right images that correspond to ambient pressure conditions. The image in the middle shows the stone image when high-pressure was applied. The TA has completely disappeared.

DISCUSSION AND CONCLUSIONS

The current study provides several important experimental facts concerning the twinkling artifact: 1) The TA is caused by acoustic effects, not by an abnormal response of the machine electronic circuits or improper signal processing; 2) The acoustic scatterers that cause the artifact respond to the imaging Doppler pulses randomly; 3) The TA is suppressed by overpressure and by more efficient wetting of the stone surface. Those results provide strong evidence that the twinkling artifact is caused by small bubbles that are trapped and stabilized in cracks and crevices on the stone surface. Such bubble stabilization mechanisms have long been known as the principal nucleation sites for cavitation (Apfel 1970; Crum 1979, 1982). It is likely that there will be some rectified diffusion (Crum 1980), but perhaps just enough to change the scattering coefficient, and possibly the phase of the reflected signal. Other possible sources of the TA (e.g., radiation force, phase jitter of the machine, scattering from the rough surface) would not be sensitive to overpressure or the type of liquid in which the stone is immersed. The bubble hypothesis does not contradict many of the existing observations reported in previous publications on this subject. For example, the evidence that roughness of the stone surface enhanced the TA agrees well with the fact that a rough surface could harbor more bubbles (Rahmouni *et al.* 1996; Kamaya *et al.* 2003; Louvet 2006). Observations that the biochemical content of the stones correlates with the TA efficiency also can be explained by the bubble hypothesis, because surface wetting is sensitive to the composition of the stone (Chelfouh *et al.* 1998). A recent study on the effect of ultrasound frequency on the TA indicating that the artifact is pronounced at low frequencies (Gao *et al.* 2012), is a typical feature of acoustic cavitation. An adequate depiction of how the bubbles are formed on the stone surface is not a simple task. A typical stone consists of proteins and crystals. Some hydrophobic regions on the stone surface (*e.g.*, proteins) may trap gas and form crevice bubbles. The crevice bubbles are probably extremely small (submicron or even nanometer size) and thus may not be seen even with μCT and other imaging technologies. Nevertheless, considerable evidence has been presented here that the twinkling artifact is caused by bubbles on the surface of stones, even those taken freshly from the body of patients.

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