

# Sonoluminescent tomography of strongly scattering media

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A novel optical imaging technique called sonoluminescent tomography was developed for cross-sectional imaging of strongly scattering media noninvasively. Sonoluminescence, which was generated internally in the medium by cw ultrasound, was used to produce a two-dimensional image of an object embedded in a scattering medium by means of raster scanning the medium. The image had a high contrast and good spatial resolution. The spatial resolution was limited by the focal-spot size of the ultrasound, and one could improve the resolution by tightening the focus. This inexpensive imaging technique has potential applications in medicine and other fields related to scattering media. © 1998 Optical Society of America

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Optical tomography of scattering media such as biological tissues is an increasingly active field because of its advantages in noninvasion, nonionization, and optical contrast when it is used for biomedical diagnosis.<sup>1</sup> Optical imaging techniques that are being investigated include time-resolved optical imaging, frequency-domain optical imaging, optical coherence tomography, photoacoustic tomography, and ultrasound-modulated optical tomography. The imaging contrast in these techniques is based on the difference in optical properties between abnormal and surrounding normal biological tissues. All these approaches use an external light source and overcome the light-scattering problem, allowing one to obtain optical images of scattering media.

We report, for the first time to our knowledge, a novel optical imaging technique, sonoluminescent tomography (SLT). SLT is based on light internally generated by ultrasound. The ultrasonic generation of light, known as sonoluminescence (SL), was first reported in 1934<sup>2</sup>; this was multiple-bubble sonoluminescence (MBSL). SL has attracted an extraordinary amount of attention since single-bubble sonoluminescence was reported in 1990.<sup>3-11</sup> Although the full explanation of SL is still in development, it is well known that light is emitted when tiny bubbles driven by ultrasound collapse. The bubbles start with a radius of several micrometers and expand to  $\sim 50 \mu\text{m}$  because of a decrease in acoustic pressure in the negative half of a sinusoidal period. After the sound wave reaches the positive half of the period, the situation rapidly changes. The resulting pressure difference leads to rapid collapse of the bubbles, accompanied by emission of light. The flash time of SL was measured to be tens of picoseconds.<sup>3</sup> Single-bubble SL is so bright that it can be seen by the naked eye even in the lighted room, whereas MBSL is visible only in a darkened room.<sup>8</sup> Researchers have envisaged possible applications of SL in sonofusion, sonochemistry, and building ultrafast lasers that use the ultrafast flash of light in SL.

SLT is a new application of SL. In SLT, minimally scattering ultrasound is used to image optically scattering media. SLT contains information that is not available in traditional ultrasonography. The major advantages of SLT include a high signal/noise ratio

owing to the internally generated SL signal; high imaging contrast; good spatial resolution, which is scalable with the ultrasonic focal size; and low cost (the cost of equipment to generate SL is as low as hundreds of U.S. dollars<sup>12</sup>).

We prepared a scattering medium, sample I, by mixing 1 ml of dominantly scattering Intralipid (20%) in 300 ml of distilled water. Since the spectrum of SL is broadband,<sup>13</sup> the optical scattering properties of the scattering medium were given at the 400-nm wavelength, which corresponds to the spectral peaks of the SL (Ref. 14) and the optical detector in our experiment. The reduced scattering coefficient was  $1.24 \text{ cm}^{-1}$  at 400 nm.<sup>15</sup> To enhance the SL signal,<sup>16</sup> we added the following chemicals to the scattering solution: 1.51 mM luminol (5-amino-2,3-dihydro-1,4-phthalazinedione; Sigma), 60 mmol of sodium iodide (Sigma), and 15 ml of 25-mM sodium hydroxide (EM Science). The sodium hydroxide increased the pH value of the medium to 9.

It is possible to generate SL without adding these facilitating chemicals. We prepared a scattering medium without these chemicals, sample II, by mixing 8.5 ml of Intralipid (20%) and  $3.5 \times 10^{-7}$  mol of dominantly absorbing Trypan Blue dye (Sigma T5526) in 370 ml of distilled water. The reduced scattering coefficient and the absorption coefficient of the sample were 8.5 and  $0.017 \text{ cm}^{-1}$  respectively, at 400 nm. The scattering property is comparable with those of biological tissues.<sup>17</sup>

The scattering solutions were sequentially contained in a 400-ml beaker and were held on an  $x$ - $y$  translation stage (Fig. 1). A pink rubber cube of  $11 \text{ mm} \times 11 \text{ mm} \times 11 \text{ mm}$  and another one of  $8 \text{ mm} \times 8 \text{ mm} \times 7 \text{ mm}$  were buried in the centers of sample I and sample II, respectively. The ultrasonic transducer was adjusted such that the focal spot of the ultrasonic wave was at the center of the buried cube. The distance between the bottom of the ultrasonic transducer and the center of the cube was 3.5 cm. The distance between the center of the cube and the bottom of the beaker was 4.5 cm for sample I and 4.0 cm for sample II. The motorized translation stage, which was controlled by a personal computer (PC), was able to scan along both the  $x$  and the  $y$  axes, which formed a plane perpendicular to the ultrasonic axis. An

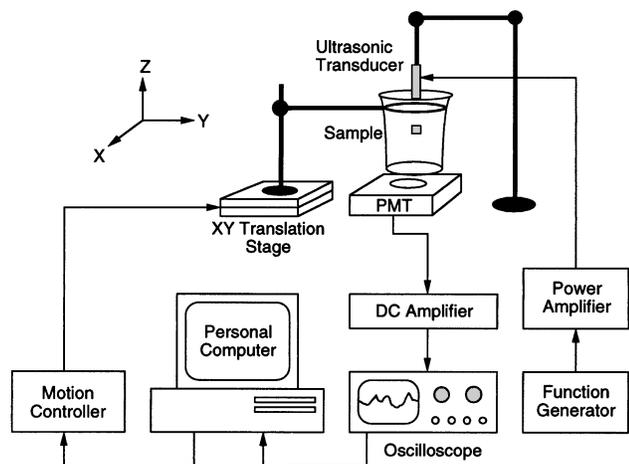


Fig. 1. Schematic diagram of the experimental setup for imaging scattering media with SL.

ultrasonic transducer (Panametrics V314-SU) with a focal length of 3.68 cm, a focal diameter of 0.3 cm, and a focal zone of 3.44 cm vertically transmitted an ultrasonic wave into the scattering medium. The ultrasonic transducer was driven by an amplified 1-MHz sinusoidal signal from a function generator (Stanford Research System DS345). Amplification was achieved with a power amplifier (Mini-Circuits TIA-1000-1R8) and a transformer. The SL signal was detected by a photomultiplier tube (PMT, Hamamatsu R928) beneath the beaker, differentially amplified by a low-noise preamplifier (Stanford Research System SR560), and recorded with a digital oscilloscope (Tektronix TDS 640A). Finally, the PC acquired the data from the oscilloscope through a GPIB interface.

First, we applied the ultrasound to a clear solution containing luminol, sodium iodide, and sodium hydroxide dissolved in distilled water. Using an 18-bit  $512 \times 512$  CCD camera cooled at  $-70^\circ\text{C}$  (EG&G Princeton Applied Research 1530-P), we obtained a picture of the MBSL in the clear solution (Fig. 2). It can be seen that the length of the SL column was  $\sim 3.5$  cm, which matched the focal zone of the ultrasonic field. The width of the SL column was  $\sim 0.3$  cm, which matched the focal diameter of the ultrasonic field. The SL intensity was obviously related to the intensity of the ultrasonic field. In fact, the SL column resembled the sound column depicted in the manufacturer's catalog for ultrasonic transducers (Panametrics).

The cubic object for sample I was mounted in the center of the clear solution and was imaged with the CCD camera [Fig. 3(A)]. The slight distortion in the image was caused by the deformation of the bottom of the beaker. When Intralipid was mixed into the clear solution to make sample I, the medium became turbid, and the object became invisible [Fig. 3(B)].

To measure the SL signal emanating from the scattering medium, we used a sensitive PMT. After background subtraction by differential amplification, the SL intensity was recorded as a dc voltage. The dc voltage represented the time-averaged SL intensity, and the time constant of the detection system was  $\sim 10$  ms. The maximum dc signal was 7.3 V for sample I and

4.6 V for sample II. The gain of the preamplifier was set to  $2 \times 10^4$  for sample I and  $5 \times 10^4$  for sample II. The dc voltage across the PMT was  $-899$  V for sample I and  $-986$  V for sample II. Based on the photocathode radiant sensitivity of 70 mA/W at the 400-nm wavelength, the total luminescence power received by the  $1.92\text{-cm}^2$  photocathode was estimated to be  $8.7 \times 10^{-15}$  W for sample I and  $1.3 \times 10^{-15}$  W for sample II.

While raster scanning the beaker in the  $x$ - $y$  plane with a step size of 1 mm, the PC recorded the dc

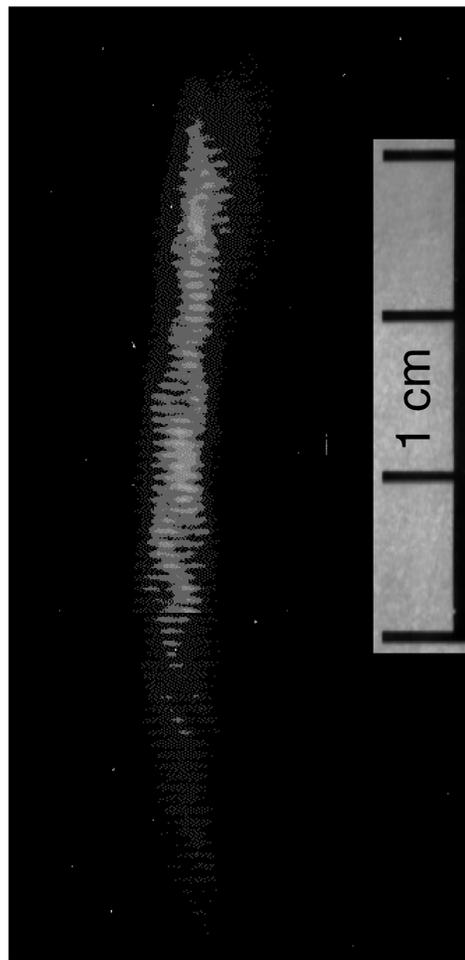


Fig. 2. Photograph of MBSL by a CCD camera (1 cm/division on the scale shown in the figure).

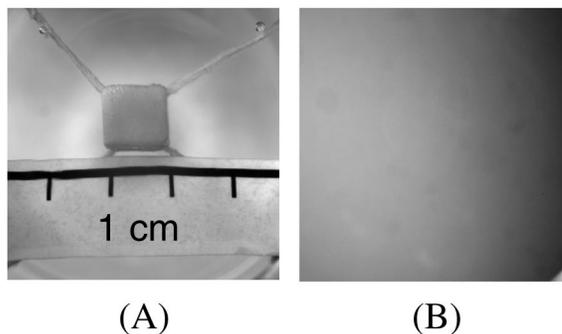


Fig. 3. Photographs of the cubic object with a scale of 1 cm/division (A) in a clear solution and (B) in a scattering solution.

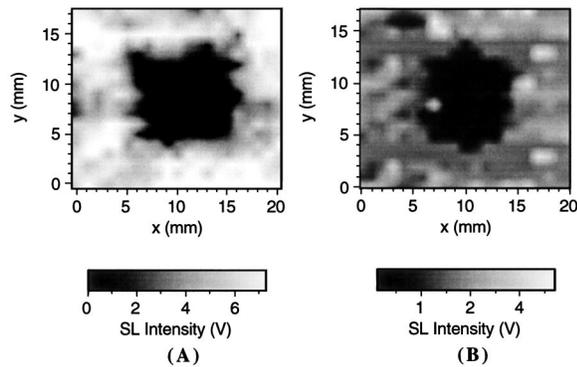


Fig. 4. (A) Two-dimensional SLT images of (A) a pink rubber cube in sample I and (B) a pink rubber cube in sample II.

signals of SL versus the values of  $x$  and  $y$ . The optical and the ultrasonic systems were fixed while the beaker was scanned. Two-dimensional pictures of the cubes buried in the scattering media, samples I and II, were plotted with the acquired data (Fig. 4). It can be clearly seen from the images that the contrast was excellent, and the spatial resolution was  $\sim 2$  to 3 mm. The contrast of the SL images was based on the difference between the optical and the ultrasonic properties of the objects and those of the surrounding medium. These objects were optically opaque and ultrasonically absorbing. When the object was moved toward the ultrasonic focus, the SL intensity dropped quickly for several reasons. First, the ultrasonic field was reduced at and below the focus. Second, the object yielded no SL signal. Third, the SL signal above the object was partially blocked by the object.

Although the object used in this experiment had both optical and ultrasonic contrast relative to the background medium, images of objects can be obtained with SLT based on several contrast mechanisms in general. When an object has contrast in SL generation, the SL signal originating from the object will differ from the signal originating from the background medium. SL generation can be affected by the local ultrasonic intensity or the local concentration of SL-enhancing chemicals if they are used. When an object has contrast in an optical absorption coefficient, a scattering coefficient, or scattering anisotropy, the SL signal from the object will be attenuated differently, because the SL light must propagate through the object.

Using the present ultrasonic system, we obtained a SL column of  $\sim 3.5$  cm in length and  $\sim 0.3$  cm in diameter. The length of the SL column limits the imaging resolution along the ultrasonic axis. Similarly, the diameter of the SL column determines the imaging resolution on the  $x$ - $y$  plane. A more tightly focused ultrasonic transducer could be used to reduce the size of the SL column significantly. When the SL column is reduced to a desired size, one can acquire three-dimensional images of scattering media by scanning in all three directions.

SL light propagates outward in the scattering medium in all directions. We can increase the signal/noise ratio of the detection system dramatically by integrating the SL light over a large detection area.

Although there are potentially harmful effects caused by cavitation, the threshold of ultrasound intensity leading to volume lesions is very high. The damage thresholds in spatial-peak-temporal-peak power were reported to be 400 and 900 W/cm<sup>2</sup> at 1 MHz for dog brain tissue and dog thigh muscle, respectively.<sup>18</sup> The peak pressure in our experiment was  $\sim 2.5$  bars at the ultrasonic focus, which corresponds to a spatial-peak-temporal-peak power of 2.1 W/cm<sup>2</sup>, which was 2 orders of magnitude less than the damage threshold. The peak pressure was also far less than the 23-bar safety limit set by the U.S. Food and Drug Administration, which is usually conservative.<sup>19</sup>

In conclusion, we have developed and demonstrated a novel optical tomography technique that uses sonoluminescence. Both the spatial resolution and the contrast of the images were very good and could be improved further. The SLT technique is expected to have applications in biomedicine and other fields involving highly scattering media.

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