

# Effects of Sub-Atmospheric Pressure and Dissolved Oxygen Concentration on Lesions Generated in Ex Vivo Tissues by High Intensity Focused Ultrasound

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## Research

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# **Effects of sub-atmospheric pressure and dissolved oxygen concentration on lesions generated in *ex vivo* tissues by high intensity focused ultrasound**

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## Abstract

**Background:** Acoustic cavitation plays an important role in the medical treatment using high intensity focused ultrasound (HIFU), but unnecessarily strong cavitation also could deform the morphology and enlarge the size of lesions. It is known that the increase of ambient hydrostatic pressure ( $P_{\text{stat}}$ ) can control the acoustic cavitation but the question how decrease of  $P_{\text{stat}}$  and dissolved oxygen concentration (DOC) influences the strength of cavitation has not been thoroughly answered.

**Methods:** *Ex vivo* bovine liver tissues were immersed in degassed water with different DOC of 1.0 mg/L, 1.5 mg/L and 2.0 mg/L. Ultrasound (US) of 1 MHz and the spatial and temporal average intensity ( $I_{\text{sata}}$ ) of 6500 W/cm<sup>2</sup> was used to expose two groups of *in vitro* bovine livers for two seconds; one group was under atmospheric pressure ( $P_{\text{stat}} = 1$  bar) and the other was under sub-atmospheric pressure ( $P_{\text{stat}} = 0.1$  bar). Acoustic cavitation was detected by a passive cavitation detector (PCD) during the exposure process. Echo signals at the focal zone of HIFU were monitored by B-mode ultrasound imaging before and after exposure.

**Results:** The results demonstrated a significant difference of broadband acoustic emissions from the cavitation bubbles, echo signals on B mode image, morphology of lesions under various condition of ambient pressure and DOC. The lesion volume in tissue was increased with the increase of ambient pressure and DOC.

**Conclusion:** Cavitation could be suppressed through sub-atmospheric pressure and low DOC level in liver tissue, which could provide a method of controlling cavitation in HIFU treatment to avoid unpredictable lesions.

**Keywords:** HIFU; Cavitation; Lesion; Sub-atmospheric pressure; Dissolved oxygen concentration

## Background

As a noninvasive therapy for cancer treatment, high intensity focused ultrasound (HIFU) has recently been received more and more attentions [1]. The absorption of highly localized ultrasound energy by the targeted tissue in the focal region allows the temperature *in situ* rapidly rise over 60°C, consequently the irreversible coagulation necrosis takes place instantaneously [2], while the surrounding tissues are spared from the significant damage [3]. During HIFU treatment, acoustic cavitation plays an important role through the collapse of oscillating microbubbles in tissues [4, 5]. Cavitation enhances lesion formation mainly by local high intensity acoustic wave, thermal deposition of acoustic radiation from the compressed bubbles and the viscous loss of bubble oscillation through tissue organization and the body liquid [6-8]. Coussios *et al.* [9] indicated that the appearance of cavitation bubbles would change the acoustic impedance and attenuation coefficient, resulting in more severe lesion. Chen *et al.* [10] and Watkin *et al.* [11] found that the morphology and size of targeted tissue were out of control due to severe cavitation. Sokka *et al.* [12] observed that lesions with cavitation in the region closer to the transducer of thigh tissue of rabbit were about 2 ~ 3 times larger by volume than the lesions under the same exposure conditions without cavitation. He *et al.* [13] proved that cavitation contributed more to lesion formation when high intensity HIFU exposed to *ex vivo* bovine liver tissue, and the morphology of lesion was distorted seriously by cavitation. Hynnen[14] showed that an enhanced heating effect in dog's thigh tissue during sonications, and concluded that such effect should be avoided in clinical therapy because they might lead to unpredictable thermal and mechanical damage. Chapelon *et al.* [15-17] observed irregular lesion outside the focal zone when uncontrolled cavitation occurred during HIFU treatment, which affected the therapeutic effects of targeted tissue. They strongly recommended that acoustic

cavitation during the treatment should be avoided.

Several researchers elevated the ambient hydrostatic pressure ( $P_{\text{stat}}$ ) to suppress cavitation[18-20] in HIFU treatment. Caupin and Herbert[21] demonstrated that cavitation threshold would increase with the increase of hydrostatic pressure, but sub-atmospheric pressure would strengthen the process of expansion motion of microbubbles and promote the activities of cavitation bubbles. After systematic experiment and molecular dynamics simulation, Kinjo and Matsumoto [22] manifested that cavitation nuclei would appear immediately under the condition of a sub-atmospheric pressure of 0.2 bar, and the appearance time would delay when under sub-atmospheric pressure with  $P_{\text{stat}}$  equal to 0.4 bar. As sub-atmospheric pressure was used to accelerate the processing for extraction from compound [23-26], lower acoustic energy was needed for generation of cavitation under sub-atmospheric pressure. Thus, cavitation was easier to take place, which made the substances extraction efficiency higher. However, all these studies were all performed in water. It is still unknown whether the sub-atmospheric pressure would influence cavitation activities in biological tissues such as the liver during the process of HIFU exposure.

Dissolved oxygen concentration (DOC) also plays a significant role to ensure the efficiency and safety of HIFU treatment. A change in the gas content of a medium can affect the propagation of focused ultrasound beam, leading to an unpredictable lesion. Saito and Soetanto [27] showed that the quantity of microbubbles would increase with the increase of DOC during ultrasound irradiation. Tuziuti *et al.*[28] indicated that cavitation was more active as the increase of DOC in a solution. Stomach and intestinal preparation including fasting and water-deprivation were necessary before the clinical treatment of liver cancer, pancreatic cancer and kidney cancer [29-31]. When treating prostate cancer and uterine fibroid, and bladder injection with degassed water as acoustic coupling

medium through the catheter was also needed [32, 33], and the DOC of degassed water should be less than 4 mg/L, according to the treatment standard issued by the State Food & Drug Administration of China [34]. In HIFU experiments, isolated biological tissues such as bovine liver were generally degassed for 1 h [35]. However, the value of DOC in bovine liver tissue was not clearly stated in literature.

Thus, the aim of this study is to investigate the influence of  $P_{\text{stat}}$  and DOC levels on the variation of HIFU-induced lesions and cavitation behavior in *ex vivo* bovine livers. The mechanism of lesion formation is also analyzed in the study.

## Results

### *Cavitation signal*

Under the condition of atmospheric pressure and sub-atmospheric pressure, the broadband emissions from *ex vivo* bovine liver exposed by HIFU in degassed water with different DOC were shown in Fig. 1. The black solid line was the baseline which was detected without HIFU exposing. The signals of broadband emissions under atmospheric pressure (Fig. 1a) were higher than that under sub-atmospheric pressure (Fig. 1b) when DOC was the same. Under the condition of atmospheric pressure (1 bar), the signal of broadband emissions at three DOC levels (1.0 mg/L, 1.5 mg/L and 2.0 mg/L) were all above the noise level of the system during HIFU exposure. Moreover, the signal of broadband noise increased with an increase of the DOC levels. Under the condition of sub-atmospheric pressure (0.1 bar), there was no signal of broadband emissions above the noise level of the system except under DOC of 2.0mg/L. The violent collapse of transient cavitation is the only source of broadband emissions[10], these results indicated that each DOC

level had transient cavitation behavior during HIFU exposure under atmospheric pressure, but under the condition of sub-atmospheric pressure, only 2.0mg/L had transient cavitation behavior.

#### *Gray level variation on B-mode ultrasound*

Fig. 2 showed B-mode ultrasound image change before and after HIFU exposure. HIFU focus was located in the center of white dotted circle during the exposure. Under the condition of atmospheric pressure (1 bar), hyper-echoic change was found in the focus after HIFU exposure under the condition of different DOC levels. Under sub-atmospheric pressure (0.1 bar), hyper-echoic changes were observed found under DOC condition of 1.5 mg/L and 2.0 mg/L, but no hyper-echo at 1.0mg/L DOC.

#### *Lesions on ex vivo bovine livers*

The morphology of lesions in *ex vivo* bovine liver exposed by HIFU was shown in Fig. 3. Under atmospheric pressure (1 bar), the morphology of lesions was very different from each other. In the 2.0 mg/L DOC group, the lesion was teardrop-shaped. In the 1.5 mg/L and 1.0 mg/L DOC groups, the lesions were approximately ellipsoidal. Under sub-atmospheric pressure (0.1 bar), in the 2.0 mg/L DOC group, the lesion was approximately cigar-shaped. In the 1.5 mg/L DOC group, the lesion was also cigar-shaped but the size of lesion was smaller than that in the 2.0 mg/L group, with homogeneous coagulation necrosis in the central part. In the 1.0 mg/L DOC group there was no significant lesion formed in the liver tissue. In addition, when the DOC level was the same, the size of lesions at atmospheric pressure (1 bar) were larger than that at sub-atmospheric pressure (0.1 bar), and damage on the central zone of lesion at atmospheric pressure (1 bar) was severer than that at sub-atmospheric pressure (0.1 bar).

Fig. 4 showed the volume of lesions in *ex vivo* bovine liver exposed by HIFU under atmospheric pressure (1 bar) and sub-atmospheric pressure (0.1 bar) with different DOC conditions. At atmospheric pressure (1 bar), the volume of lesions in the 2.0 mg/L and 1.5 mg/L DOC group were  $83.28 \pm 14.56 \text{ mm}^3$  and  $76.84 \pm 11.07 \text{ mm}^3$  respectively. There was no significant difference between two groups ( $p>0.05$ ). However, when DOC was equal to 1.0 mg/L, the volume of lesion was  $47.98 \pm 14.92 \text{ mm}^3$ , which was significantly decreased while compared with the 2.0 mg/L and 1.5 mg/L groups ( $p<0.05$ ). At sub-atmospheric pressure (0.1 bar), the volume of lesions in the 2.0 mg/L, 1.5 mg/L and 1.0 mg/L groups were  $20.53 \pm 5.54 \text{ mm}^3$ ,  $16.01 \pm 4.22 \text{ mm}^3$  and  $0.00 \pm 0.00 \text{ mm}^3$  respectively. There were significant differences between any two ( $p<0.05$ ), indicating that the volume of lesion was increased with the increase of DOC levels at either atmospheric pressure or sub-atmospheric pressure. Meanwhile, the volume of lesion in tissue at atmospheric pressure (1 bar) were larger than that at sub-atmospheric pressure (0.1 bar) while DOC level kept the same ( $p<0.05$ ).

## Discussion

The main mechanisms of coagulation necrosis induced by HIFU are thermal deposition and cavitation effect[37]. During the process of HIFU exposure, the absorption of sound energy can result in thermal deposition in tissue, leading to formation of lesions[2]. Moreover, cavitation can accelerate the rise of the in situ temperature and enlarge the size of lesions[14]. Cavitation includes stable cavitation and transient cavitation[38], and the accelerated temperature increasing during HIFU exposure comes from transient cavitation[12].

Overpressure has been proved to suppress cavitation and has been used to study the influence of cavitation on HIFU-induced lesions [13, 19, 20]. This study investigates the effect of atmospheric



pressure and sub-atmospheric pressure on the formation of the lesions. Under various DOC conditions (2.0 mg/L, 1.5 mg/L or 1.0 mg/L), the broadband noise at sub-atmospheric pressure (0.1 bar) is significantly lower than that at atmospheric pressure (1 bar). It manifests that sub-atmospheric pressure can partly suppress cavitation in liver tissue during HIFU exposure, which is different from the report that sub-atmospheric pressure can strengthen cavitation activity in water by Caupin and Herbert [21]. We think that although sub-atmospheric pressure can enhance the expansion process of cavitation bubble, the mechanical strain of sub-atmospheric pressure can also disperse the bubble distribution in tissue, resulting in that cavitation bubble cannot stably formed and concentrated in the focus and the signal of sound scattering in focus is distinctly weakened. This is demonstrated by our bovine liver experiments at sub-atmospheric pressure, which reveals that the volume of the lesions is smaller than that at atmospheric pressure ( $p < 0.05$ ). Under the experiment parameter with cavitation occurred, the central of lesions appears mechanical damage due to the collapse of cavitation bubbles. Without cavitation occurred, lesion is of homogeneous necrosis, and there is no lesion formed in bovine liver tissue while DOC is equal to 1.0 mg/L.

This study also demonstrates a certain quantity of cavitation nuclei is needed for the occurrence of cavitation. Under atmospheric pressure, PCD results showed that cavitation activities exist during HIFU exposure under the condition of three DOC levels, with the hyper-echoic changed observed on B-mode ultrasound after HIFU exposure. With the increase of DOC level, the strength of the cavitation signal enhances gradually during the process of exposure, leading to the increased volume of the lesion in bovine liver tissue. However, under sub-atmospheric pressure, cavitation signal only appeared in 2.0 mg/L DOC level group, and the B-mode ultrasound image without hyper-echoic occurred only at the DOC 1.0 mg/L group. The volume of the lesion at the condition of 2.0 mg/L

DOC is  $20.53 \pm 5.54 \text{ mm}^3$ , which is larger than the lesion volume of  $16.01 \pm 4.22 \text{ mm}^3$  at the DOC 1.5 mg/L group ( $p < 0.05$ ), but no lesion is observed at the DOC 1.0 mg/L group, indicating that lower DOC level could produce less gas content in water, and less than the critical number of cavitation nuclei that makes cavitation difficult occur during HIFU exposure. On the contrary, an increase of gas content in both water and tissues could facilitate the occurrence of cavitation and lesion formation, which could improve the efficiency of HIFU treatment through microbubbles[39]. In addition, Rabkin *et al.*[40] reported that hyper-echo on B-mode ultrasound was produced by boiling bubbles of water during HIFU exposure. But the boiling point of water at sub-atmospheric pressure (0.1 bar) is only 56°C, which is much lower than that at atmospheric pressure (1 bar). This might help understand our findings that under the condition of sub-atmospheric pressure and DOC 1.5 mg/L level, PCD showed no cavitation during HIFU exposure but a significant hyper-echo on B-mode ultrasound and homogenous lesion in bovine liver tissue.

## Conclusions

Using *ex vivo* bovine livers, we investigated the effect of  $P_{\text{stat}}$  and DOC levels on the formation of HIFU-induced lesions in this study. Our results showed that the occurrence of cavitation could be suppressed through sub-atmospheric pressure and low DOC level in liver tissue. This could provide a method of controlling cavitation in HIFU treatment which could avoid unpredictable lesions. Conversely, coagulation necrosis could be enhanced by increasing the quantity of cavitation nuclei in tissues.

## Methods

### *Experimental equipment*

As shown in Fig. 5, all HIFU exposing experiments were performed in a stainless chamber (50 cm  $L \times$  50 cm  $W \times$  70 cm  $H$ ) which filled with degassed water of different DOC. The major experimental system (Jisheng 1#, Chongqing Haifu Technology Co., Ltd, Chongqing, China) includes a 1.0MHz HIFU transducer (12-32, Chongqing Haifu Technology Co., Ltd, Chongqing, China), with an aperture diameter of 220mm and a focal length of 170mm. The probe of the B-mode ultrasound (PA230E, ESAOTE Co., Genova, Italy) was mounted in the central hole of HIFU transducer, sharing the same focus with HIFU transducer, so that its imaging plane intersected the HIFU axis along its axial length. Data cables connected to a computer through the hermetic feedthrough. A HIFU drive system, a water processing system, which can prepare for degassed water of different DOC, and sample holder are all provided by Chongqing Haifu (HIFU) Technology Co., Ltd. A rotary vane vacuum pump (2XZ-2, Taizhou Qiushi vacuum pump Co., Ltd, Zhejiang, China) was used to control the condition of  $P_{\text{stat}}$  in the chamber. DOC in water and tissue was monitored by a portable dissolved oxygen meter (LDOTM 550A-12, YSI Co., Yellow Springs, OH, USA), with measurement range of 0~50 mg/L and resolution of 0.01 mg/L.

### *Cavitation detection*

A passive cavitation detection (PCD) (V309-SU, Olympus Panametrics NDT Inc, Waltham, MA, USA) with a central frequency of 5 MHz was used to detect the cavitation characteristics to compare the cavitation behavior. The broadband focusing PCD transducer with the diameter of

13mm and focal length of 40mm was fixed on the sample holder, shown in the Fig. 1. Acoustic signal from *ex vivo* bovine liver was recorded by the high-speed data acquisition card with sampling rate of 20MHz (PXie-5122, National Instruments Co., USA). The corresponding spectrum of obtained signal was analyzed via fast Fourier transform on the LabView development platform (v10.0.1, National Instruments Co., Austin, TX, USA), and the sampling step length was 15ms. The broadband noise was calculated after band-pass filter (3~7 MHz) and band-stop filter (filter stopped the signals around harmonics  $\pm 30$  kHz), to minimize the error caused by the contributions from the HIFU fundamental, second, third and fourth harmonic frequencies arising from nonlinear sound propagation.

#### *Dissolved oxygen concentration and hydrostatic pressure detection*

Degassed water at different DOC levels was prepared by regulating the water flow of a water processing system. The experimental chamber was filled with degassed water at DOC of 1.0 mg/L, 1.5 mg/L and 2.0 mg/L respectively with the temperature kept at 37°C, according to the standard protocol of HIFU treatment system[34]. The degassed bovine liver specimens were mounted in the sample holder, and then placed in the experimental chamber. Ten minutes later, the DOC of degassed water and inside the tissue was detected for five times, shown in Table 1. The DOC in water was in accord with the DOC inside the tissue. Therefore, we used the DOC in water to present the DOC inside the tissue.  $P_{stat}$  in sealed experimental chamber was changed by a vacuum pump which was turned off after five minutes to keep the experimental chamber under the  $P_{stat}$  of 0.1 bar, which was the maximum negative pressure that vacuum pump could stably support.

### *HIFU exposure*

The liver specimens were taken from the portion of fresh bovine liver with less connective tissues and blood vessels within 6 hours after the animal was sacrificed. It was then cut into blocks of 12 cm × 6 cm × 4 cm, soaked in 0.9% saline, and degassed by vacuum pump for 60 min. Acoustic spatial and temporal averaged intensity ( $I_{\text{sata}}$ ) was 6500 W/cm<sup>2</sup> for ultrasound applied to *ex vivo* bovine livers, which cavitation could be detected clearly under atmospheric pressure. Before the exposure experiment, the acoustic power generated was measured by the radiation force method[36], and the sound field was scanned by needle-type hydrophone (HFO-660, ONDA, Sunnyvale, CA, USA), in order to ensure every experiment had the same acoustic output.

During the experiment, 1MHz HIFU transducer was used to generate a continuous wave of exposure parameter of  $I_{\text{sata}}$  6500 W/cm<sup>2</sup> for two seconds to expose bovine liver specimens. Experiments were done under two  $P_{\text{stat}}$ : atmospheric pressure ( $P_{\text{stat}} = 1$  bar) and sub-atmospheric pressure ( $P_{\text{stat}} = 0.1$  bar). Experiments with same exposure conditions were repeated for ten times. The gray level variation bovine livers at HIFU focus was monitored by B-mode ultrasound before and after HIFU exposure. Moreover, the DOC of water was detected by the portable dissolved oxygen analyzer before and after each experiment. The deviation of DOC in each group was within  $\pm 0.1$  mg/L.

Sections of the bovine liver specimens with their cross section perpendicular to the direction of acoustic propagation of HIFU were cut immediately after exposure to observe the lesion size and shape. The lesion was photographed digitally under every exposure condition. The *HIFU measurement* software (1.0, Chongqing Haifu Technology Co., Ltd, Chongqing, China) was used to set the scale and mark the boundary of the lesion region. The SPSS software (19.0, IBM, Camp

Takajo, NY, USA) was used for statistical analysis. The final measurement results were expressed by mean  $\pm$  standard deviation. Statistical significance of differences was evaluated using paired-sample  $t$  test. If  $p < 0.05$ , a significant difference between two groups was specified.

### **List of abbreviations**

DOC: dissolved oxygen concentration;

HIFU: high intensity focused ultrasound;

PCD: passive cavitation detection;

P<sub>stat</sub>: ambient hydrostatic pressure.

## **Declarations**

### **Ethics approval and consent to participate**

Not applicable.

### **Consent for publication**

Not applicable.

### **Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### **Competing interests**

The authors declare that they have no competing interests.

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### **Authors' contributions**

MH, FL and ZW designed the study, MH and ZZ performed the experiments, collected and

processed the data, XG and DZ maintained the experimental setup, MH wrote the manuscript, FL revised the manuscript. All authors read and approved the final manuscript.

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## Figure captions

**Fig. 1** Broadband noise during HIFU exposure, (a) atmospheric pressure, (b) sub-atmospheric pressure. The black solid line was the baseline which was detected without HIFU exposing. The red, blue and purple solid line represent the broadband noise signal at the DOC of 2.0mg/L, 1.5mg/L and 1.0mg/L respectively.

**Fig. 2** B-mode ultrasound image before and after HIFU exposure. The white dotted circle flagged the HIFU focus zone. Hyper-echoic occurred under all the condition except at sub-atmospheric pressure with the DOC of 1.0mg/L.

**Fig. 3** Morphology variation of lesions in *ex vivo* bovine liver. The first row was experimented under the condition of atmospheric pressure, and the second row was experimented under the condition of sub-atmospheric pressure. The column represented the HIFU exposure conducted under the DOC of 2.0mg/L, 1.5mg/L and 1.0mg/L. Lesion appeared under all the condition except at sub-atmospheric pressure with the DOC of 1.0mg/L.

**Fig. 4** Lesion volume variation in *ex vivo* bovine liver after HIFU exposure. At atmospheric pressure (1 bar), the volume of lesions in the 2.0 mg/L and 1.5 mg/L DOC group were  $83.28 \pm 14.56 \text{ mm}^3$

and  $76.84 \pm 11.07 \text{ mm}^3$  respectively. At sub-atmospheric pressure (0.1 bar), the volume of lesions in the 2.0 mg/L, 1.5 mg/L and 1.0 mg/L groups were  $20.53 \pm 5.54 \text{ mm}^3$ ,  $16.01 \pm 4.22 \text{ mm}^3$  and  $0.00 \pm 0.00 \text{ mm}^3$  respectively. Lesion volume under atmospheric pressure was significant different from that under sub-atmospheric pressure when DOC kept the same. \*represents  $p < 0.05$  for significance of difference between the two group, \*\*represents  $p > 0.05$  for no significance of difference between the two group.

**Fig. 5** Schematic diagram of the experimental system. The HIFU transducer was driven by the HIFU drive system. The input power was set on the PC. The PCD signal was acquired by the data acquisition card and shown on the PC. The ultrasound diagnostic scanner, which was controlled by PC, was used to scan the B mode image of tissue.

## Table captions

**Table 1** The comparison of DOC in degassed water and inside the tissue

# Figures

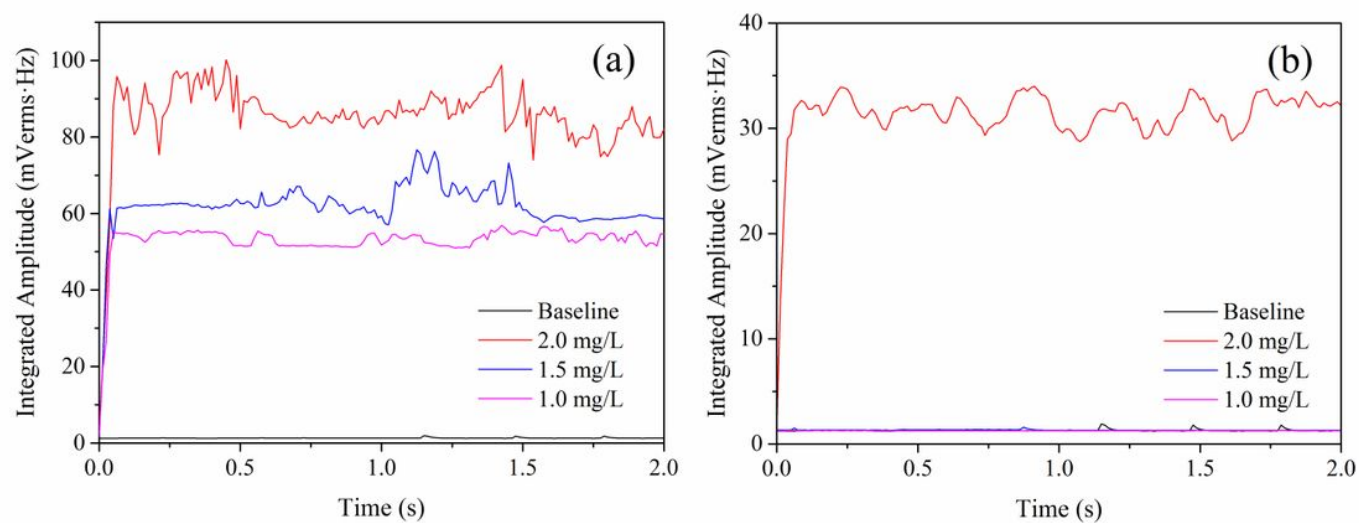


Figure 1

Broadband noise during HIFU exposure, (a) atmospheric pressure, (b) sub-atmospheric pressure. The black solid line was the baseline which was detected without HIFU exposing. The red, blue and purple solid line represent the broadband noise signal at the DOC of 2.0mg/L, 1.5mg/L and 1.0mg/L respectively.

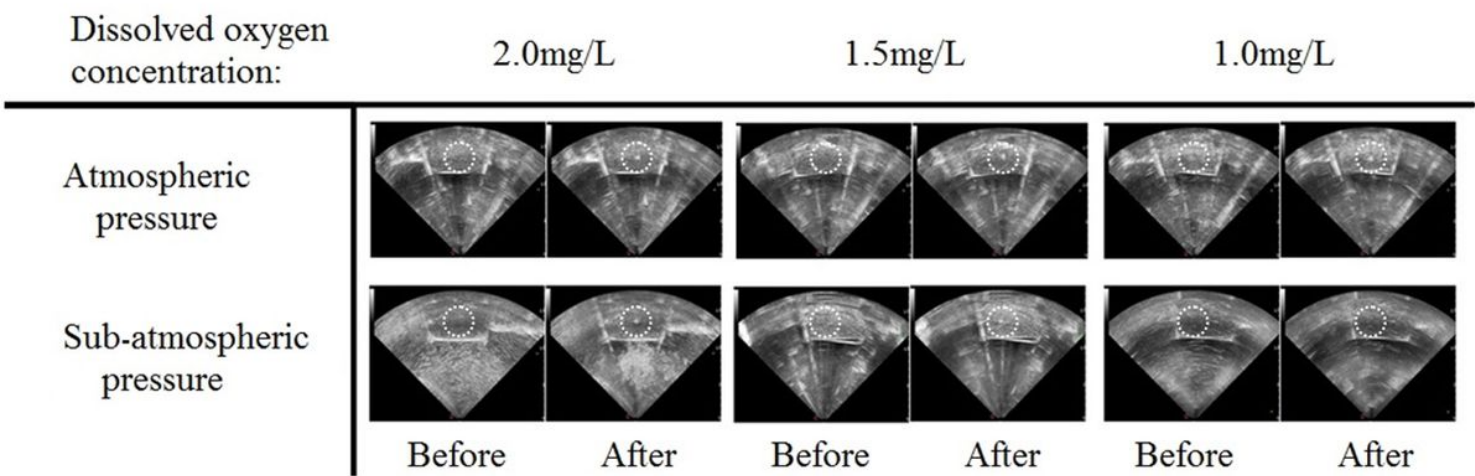
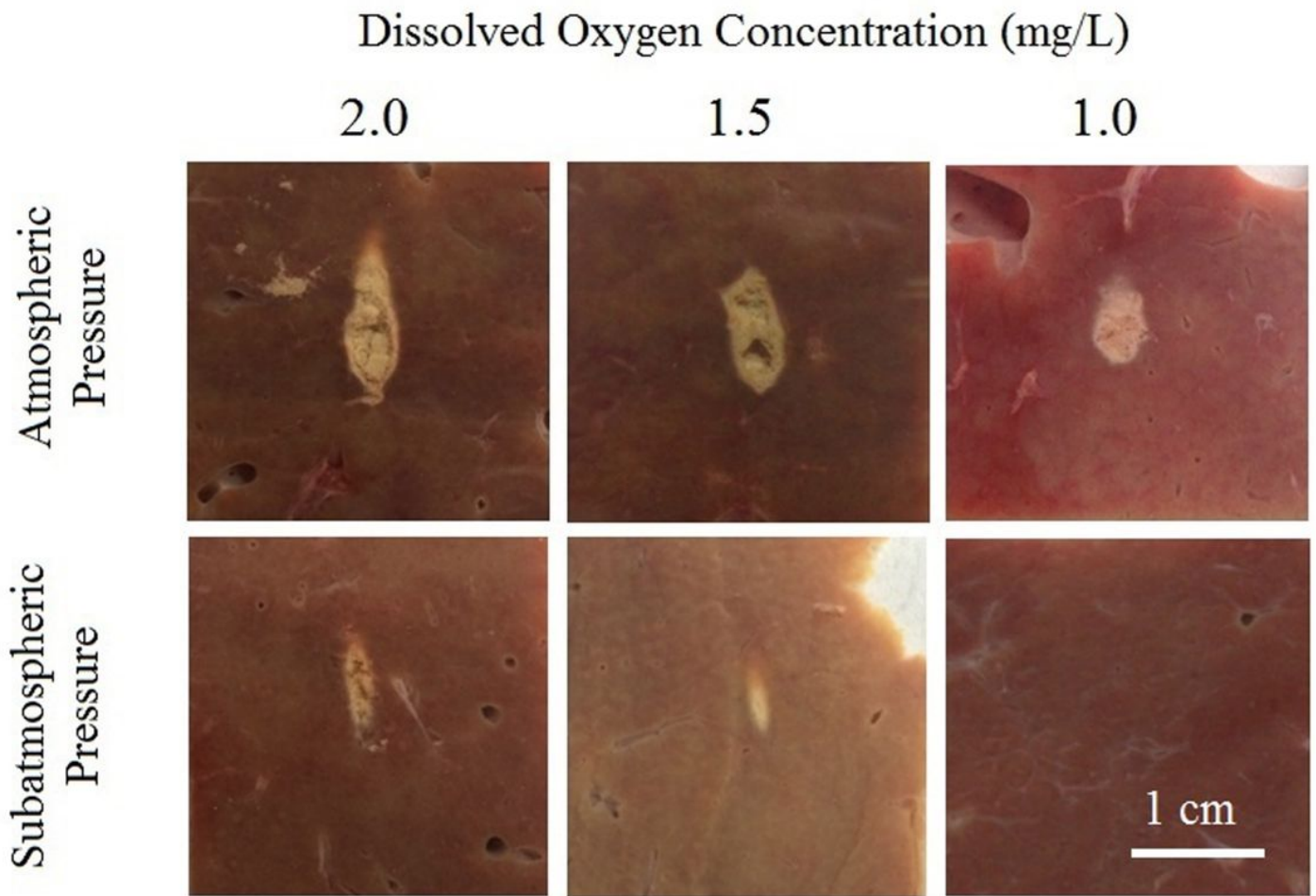


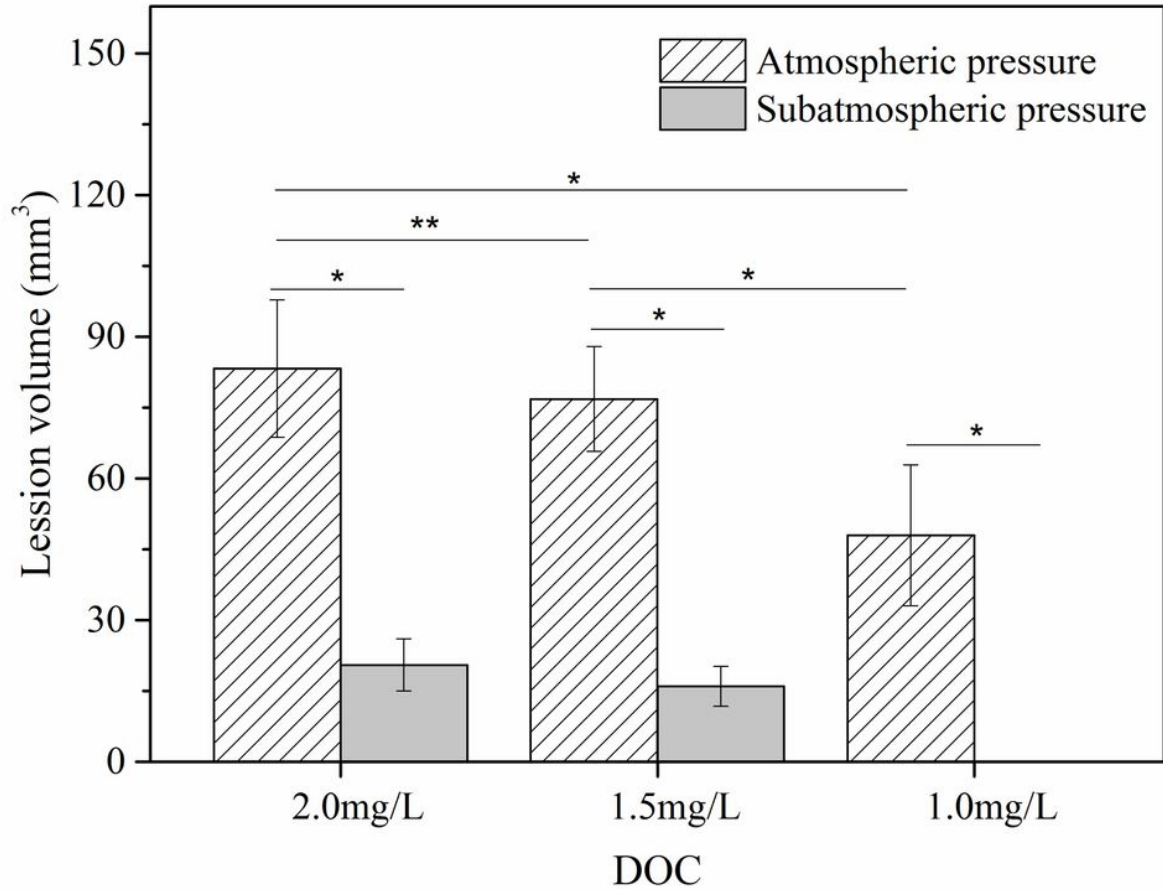
Figure 2

B-mode ultrasound image before and after HIFU exposure. The white dotted circle flagged the HIFU focus zone. Hyper-echoic occurred under all the condition except at sub-atmospheric pressure with the DOC of 1.0mg/L.



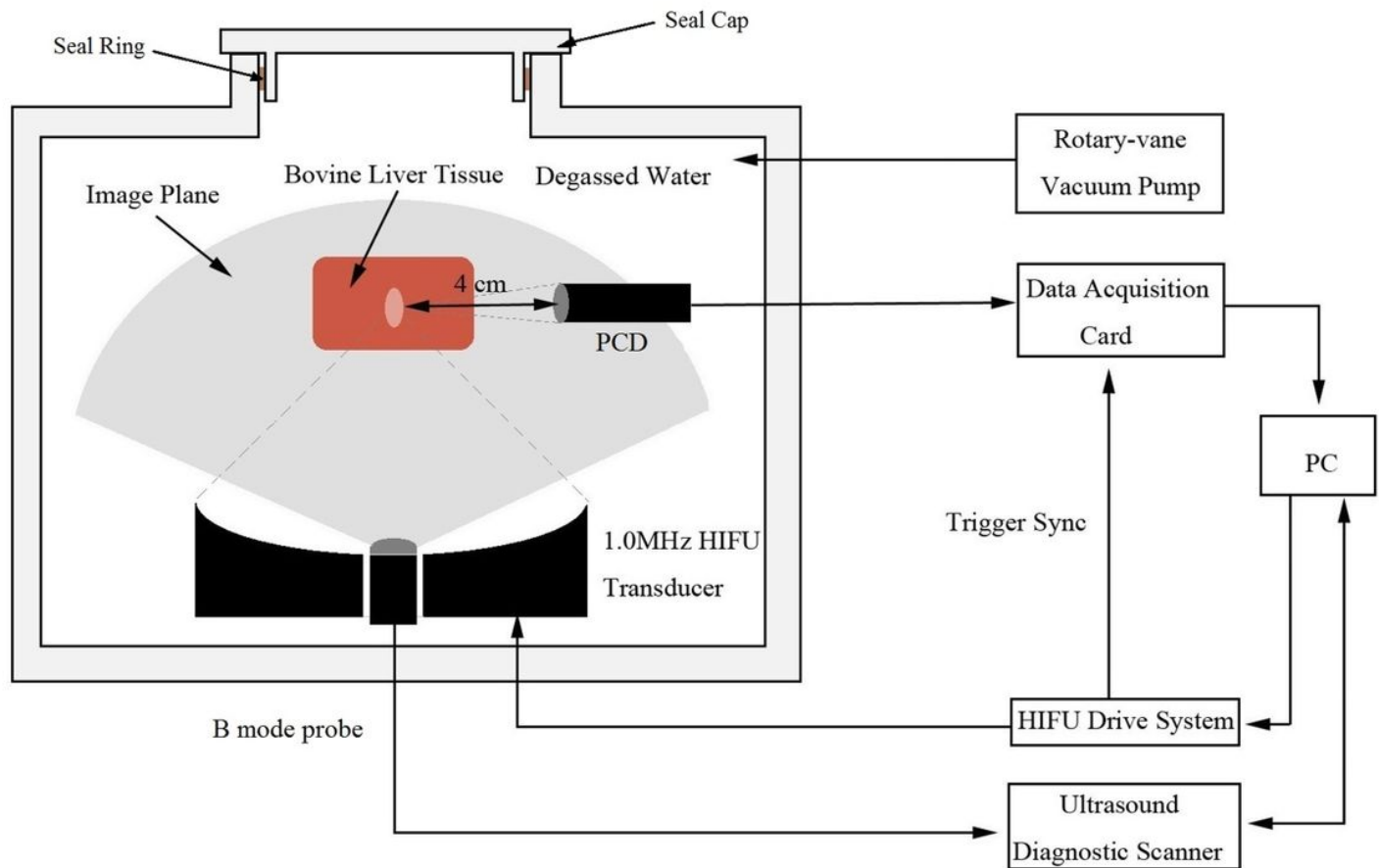
**Figure 3**

Morphology variation of lesions in ex vivo bovine liver. The first row was experimented under the condition of atmospheric pressure, and the second row was experimented under the condition of sub-atmospheric pressure. The column represented the HIFU exposure conducted under the DOC of 2.0mg/L, 1.5mg/L and 1.0mg/L. Lesion appeared under all the condition except at sub-atmospheric pressure with the DOC of 1.0mg/L.



**Figure 4**

Lesion volume variation in ex vivo bovine liver after HIFU exposure. At atmospheric pressure (1 bar), the volume of lesions in the 2.0 mg/L and 1.5 mg/L DOC group were  $83.28 \pm 14.56 \text{ mm}^3$  and  $76.84 \pm 11.07 \text{ mm}^3$  respectively. At sub-atmospheric pressure (0.1 bar), the volume of lesions in the 2.0 mg/L, 1.5 mg/L and 1.0 mg/L groups were  $20.53 \pm 5.54 \text{ mm}^3$ ,  $16.01 \pm 4.22 \text{ mm}^3$  and  $0.00 \pm 0.00 \text{ mm}^3$  respectively. Lesion volume under atmospheric pressure was significant different from that under sub-atmospheric pressure when DOC kept the same. \*represents  $p < 0.05$  for significance of difference between the two group, \*\*represents  $p > 0.05$  for no significance of difference between the two group.



**Figure 5**

Schematic diagram of the experimental system. The HIFU transducer was driven by the HIFU drive system. The input power was set on the PC. The PCD signal was acquired by the data acquisition card and shown on the PC. The ultrasound diagnostic scanner, which was controlled by PC, was used to scan the B mode image of tissue.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Table1.pdf](#)