Feasibility of In-Vivo Cardiac HIFU Ablation

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Abstract. The potential for cardiac applications of HIFU remains largely unexplored. In order to create reproducible lesions in a beating heart, it is necessary to maintain focusing at a certain position within moving myocardial tissue. One technique is to use multiple short HIFU exposures (0.2 s) and to synchronize them with an EKG signal and respiration. In order to investigate the interaction of HIFU exposures and cardiac tissues, a series of in-vitro experiments was conducted. The left ventricular free wall (LVFW) of calf hearts were cut into 4-cm cubes, degassed in phosphate buffer saline (PBS), and heated to 37C. Several transducers were employed. Most experiments used a 33-mm diameter spherical-cap transducer with focal length of 35 mm, operated at a frequency of 5.075 MHz and a focused intensity of 13 kW/cm^2 (in-situ spatial average over the half-power points of the focused beam). The transducer was coupled to the LVFW using degassed PBS. First, the effects of pericardial fat, focal depth, and temperature on lesion size were individually evaluated. We compared the effect of different time pulse duration (0.2 s and 0.3 s) and number of applied pulses. Dimensions of all lesions were measured by visual examination of the fresh, unstained tissue. Histopathological examination of the lesions was also performed.

INTRODUCTION

High intensity focused ultrasound (HIFU) is an emerging technique that allows the creation of a lesion without direct contact with the tissue. Several investigators have investigated cardiac applications of HIFU [1,2]. However, the feasibility of creating lesions in myocardium has not been well examined. In order to evaluate the feasibility of creating lesions in myocardium, it is important to consider the typical characteristics of the heart. First and most importantly, the heart dilates, and also physically moves within the chest cavity during the cardiac cycle. A second, related factor incolves the fact that the surface of the heart is covered by pericardium. A third factor to be considered is the depth of the HIFU focal point relative to the cardiac surface.

The purpose of this study was to evaluate the above factors in order to better assess the feasibility of future HIFU applications and to elucidate the characteristics of *in-vitro* myocardial lesions. The study was designed to clarify the importance of several factors upon lesion production: 1.intervening pericardial fat, 2.depth of tissue site targeted for treatment, 3.temperature, 4.pulse parameters (a. pulse duration, b. pulse interval).

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Three HIFU transducers were employed in these studies. The following paragraphs describe each transducer and specify their *in-situ* spatial average intensity (the *in-situ* intensity spatially averaged over the -3 dB width of the focal-plane beam.) The intensity was calculated from free-field (water tank) measurements using a tissue attenuation coefficient of 0.35 dB/cm-MHz, which was measured in separate experiments.

The first HIFU transducer was an 80 mm diameter spherical-cap transducer with a 90 mm focal length; it was operated at a frequency of 4.67 MHz. The intensity for this transducer was 13.3 kW/cm^2 at a tissue depth of 10mm.

The second transducer was a 23 mm diameter, 35 mm focal length spherical-cap transducer; this transducer was operated at a frequency of 6.0 MHz, the intensity for this transducer was 10.3 kW/cm^2 at a tissue depth of 10mm.

The third transducer was a 40 mm diameter, 35 mm focal length spherical-cap transducer, which was operated at a frequency of 5.075 MHz. A 10 mm diameter A mode transducer (7.5 MHz) was affixed in the center of the treatment transducer in the same manner described above. The intensity for this transducer was 13.3 kW/cm^2 at a tissue depth of 10 mm and 7.4 kW/cm2 at a tissue depth of 25 mm.

MATERIALS AND METHODS

Refrigerated bovine hearts were obtained from a meat market. A piece of the left ventricular free wall was degassed and placed in a 37ºC degassed phosphate buffered saline bath. The transducer was coupled with the tissue from epicardial side.

HIFU pulses with 0.2 s or 0.3 s durations were delivered every 4 s; at each exposure site, the total number of pulses was varied from one to 25, depending on the experiment. Three to eight lesions were created in different areas of each tissue by moving the transducer several millimeters laterally between exposures. Following these exposures, all specimens were cut and shaved carefully to show the maximum lesion size, as determined by visual examination of the fresh, unstained tissue. As a measure of the longitudinal cross-section, the length and width of lesions were evaluated. Histopathological sections were prepared in order to assess the HIFU effect on the tissue of both the lesion and the intervening tissue.

RESULTS

In order to evaluate the effect of the thickness of pericardial fat, the fat thickness was divided into three groups: 0 mm, 1-3 mm, 3.5-6 mm. The length of the lesion was the same regardless of the thickness of the fat, whereas the width slightly decreased as the fat thickness increased. Overall, it was possible to create compatible size of lesions even through pericardial fat.

Although HIFU is fired with the same power, the intensity at the focal point is different depending on the target depth from the surface of the tissue. There were significant differences in both the lesion length and width between the lesions created 10 mm and 25 mm from the tissue surface.

HIFU lesions were created with different temperature: body temperature (37ºC) and room temperature (23ºC). As the number of pulses increased, the difference of lesion lengths and widths became more significant.

Thinking of future in-vivo or clinical applications, the effect of dividing the total HIFU exposure duration was evaluated. With the setting of 0.2 s and 0.3 s for each short pulse duration, both lesion lengths and widths were in proportion to the total exposure duration regardless of each short pulse duration. In comparing 0.8 s and 4 s as the duration between each short pulses, the lesion lengths were quite similar between those two groups, whereas the lesion widths were significantly different.

Histopathological slides were obtained with trichrome staining. Tears and vacuoles were observed in the central part of the lesion surrounded by hyperchromatic area. The vacuoles were associated with microbubbles created by the vaporization of fluid within the tissue, which was compatible with thermal effect.

DISCUSSION AND SUMMARY

HIFU can create targeted, well-demarcated thermal lesions in myocardium with protocols simulating ECG triggering system. Lesion sizes are affected by temperature, focal depth and duration between pulses. Even with dividing exposure time duration into multiple times, total exposure time duration is important rather than the duration of each short pulses under our study conditions. Although the pericardial fat attenuates ultrasound, it is possible to create a lesion through pericardial fat; acoustic refraction, however, can affect lesion properties. HIFU may allow for a non-invasive approach for ablating cardiac tissues without direct contact.

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REFERENCES

1. Strickberger SA, Takano T, Kluiwstra JA, Morady F, and Cain C. Extracardiac ablation of the canine atrioventricular junction by use of high-intensity focused ultrasound. Circulation 100, 203-208 (1999).
2. Lee LA, Simon C, Bove EL, Mosca RS, Ebbini ES, Abrams GD, and Ludomirsky A. High intensity focused ultrasound effect on cardiac tissue: potential; for clinical application. Echocardiography **17**(6), 563-566 (2000).

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