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A Feasibility Study of Soft Embalmed Human Breast Tissue for Preclinical Trials of HIFU- Preliminary Results

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Abstract. Breast cancer is the commonest cancer in women in the UK, accounting for 30% of all new cancers in women, with an estimated 49,500 new cases in 2010[1]. With the widespread negative publicity around over-diagnosis and over-treatment of low risk breast cancers, interest in the application of non-invasive treatments such as magnetic resonance imaging (MRI) guided high intensity focused ultrasound (HIFU) has increased. Development has begun of novel US transducers and platforms specifically designed for use with breast lesions, so as to improve the range of breast lesions that can be safely treated. However, before such transducers can be evaluated in patients in clinical trials, there is a need to establish their efficacy. A particular issue is the accuracy of temperature monitoring of FUS with MRI in the breast, since the presence of large amounts of surrounding fat can hinder temperature measurement. An appropriate anatomical model that imposes similar physical constraints to the breast and that responds to FUS in the same way would be extremely advantageous. The aim of this feasibility study is to explore the use of Thiel embalmed cadaveric tissue for these purposes. We report here the early results of laboratory-based experiments sonicating dissected breast samples from a Thiel embalmed soft human cadaver with high body mass index (BMI). A specially developed MRI compatible chamber and sample holder was developed to secure the sample and ensure reproducible sonications at the transducer focus. The efficacy of sonication was first studied with chicken breast and porcine tissue. The experiments were then repeated with the dissected fatty breast tissue samples from the soft-embalmed human cadavers. The sonicated Thiel breast tissue was examined histopathologically, which confirmed the absence of any discrete lesion. To investigate further, fresh chicken breast tissue was embalmed and the embalmed tissue was sonicated with the same parameters. The results confirmed the inability to produce a discrete lesion in any of the Thiel embalmed samples.

INTRODUCTION

The published clinical literature on focused ultrasound surgery to date consists of small studies evaluating the efficacy of FUS using a transducer specifically designed for the treatment of either bone metastases or uterine fibroids[2]. However, these devices impose strong constraints on the number of breast lesions suitable for FUS, since proximity of the lesion to either the ribs or overlying skin can result in painful overheating of the ribs or skin burns.

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An additional technical problem in the application of FUS to breast lesions is the frequent presence of large amounts of surrounding fat, which can hinder MRI monitoring of the local tissue temperature and thus interfere with assessment of the adequacy of the procedure. Recently, development has begun of novel US transducers and platforms specifically designed for use with breast lesions, which should improve the range of breast lesions that can be safely treated. These systems surround the breast and apply FUS radially, thus avoiding the problems found in applying transducers designed for other purposes. However, before such transducers can be evaluated in patients in clinical trials, there is a need to establish their efficacy and the accuracy of temperature monitoring of FUS with MRI, particularly in the fatty breast. This requires an appropriate anatomical model that imposes similar physical constraints to the normal or cancerous breast and responds to FUS in the same way. In this feasibility study we intend to explore the use of Thiel[3] embalmed cadaveric tissue for these purposes. These soft-embalmed cadavers are human bodies preserved with a mixture of salt components and much lower amounts of formalin than in traditional embalming processes so as to maintain tissue structure and properties, lending it life-like colors and flexibility compared to traditionally (formalin – based) embalmed cadavers. The basic components of the Thiel embalming solution is mentioned in an earlier report [4]. The work reports preliminary results in analyzing the suitability of the soft-embalmed fatty breast tissues for HIFU pre-clinical trials.

MATERIALS & METHODS

A specially developed MRI compatible HIFU chamber & sample holder was developed to secure the sample to ensure reproducible sonications at the transducer focus. The set up shows an MRI-compatible chamber with a 1.09 MHz MRI-compatible single element transducer with focal length 69 mm. Figure 1a) shows the chamber design and 1b) shows the developed chamber. The transducer beam is focused into a high intensity spot to deposit heat with the aim of thermally ablating the tissue. The chamber was characterized to determine the ultrasound pressure at the focus and the dimension of the focal region. The pressure values were measured using a needle hydrophone using the set up shown in Fig 2a). Fig 2b) shows the acoustic field map of the focal region. The acoustic pressure at the focal region was 1±0.1 MPa. The efficacy of sonication was first studied with chicken breast and porcine tissue. The tissue for sonications was placed carefully in the tissue holder and immersed in the chamber filled with degassed water at room temperature. An MRI compatible thermocouple was used to measure the temperature rise induced in the chosen tissues by sonication. The experiments were then repeated with the dissected fatty breast tissue samples from the soft-embalmed human cadavers. The experimental set up for sonication is given in Fig 3.

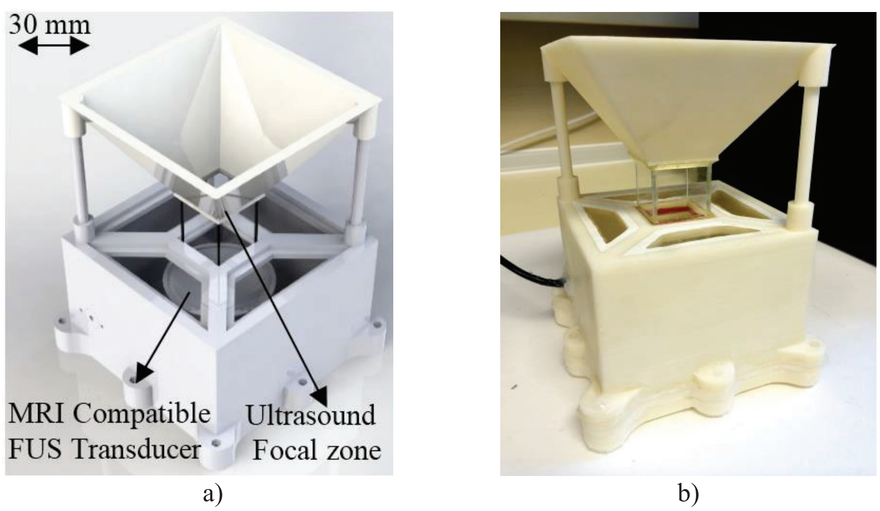
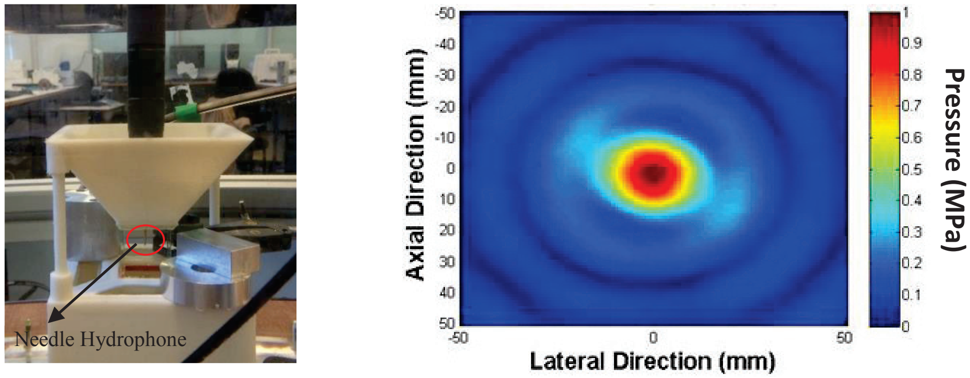


FIGURE 1. a) Design for the MRI-Compatible HIFU chamber, b) The lab- manufactured chamber as per the design.



a) b)

FIGURE 2.a) Set up for scanning acoustic field- Chamber with the needle hydrophone at the focus, b). Acoustic pressure map of the chamber focal zone

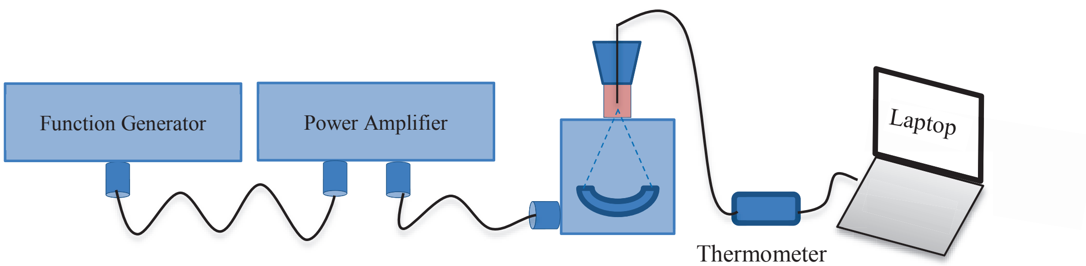
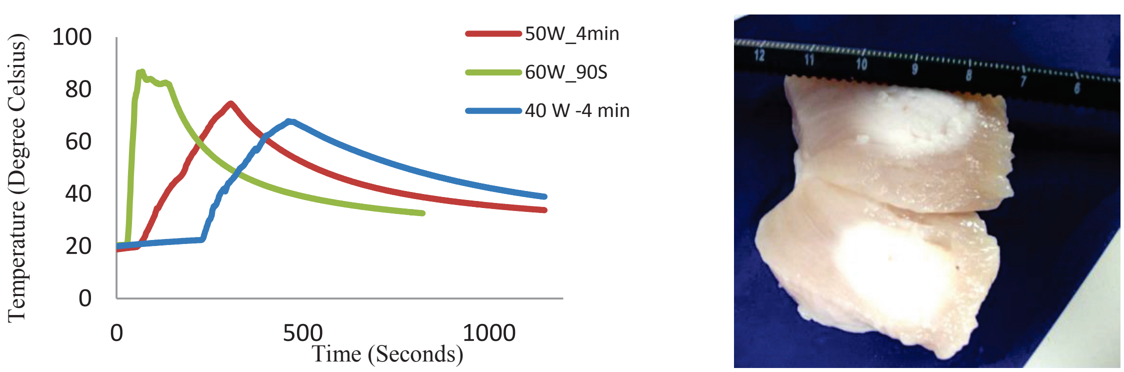


FIGURE 3. Experimental set-up for tissue sonications

RESULTS

Testing the Chamber

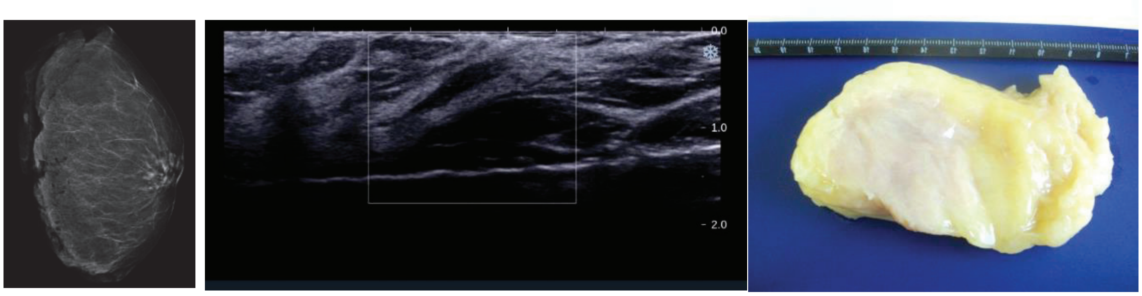
The initial testing of the chamber was conducted by sonicating fresh chicken breast and porcine samples. Sonications were carried out at different power settings (40 W, 50W & 60W) and durations. The temperature maps of these sonications are shown in Fig 4a). Figure 4b) shows the 2 cm lesion formed in fresh chicken breast as the result of sonication at 40W for 4 min.



a) b)

FIGURE 4. a) Temperature graphs for fresh chicken breast sonications at various power levels and durations b) 2cm lesion formed as a result of sonications at 40W for 4 minutes.

Sonicating Soft Embalmed Human Breast Tissue



a) b) c)

FIGURE 5. a) X-Ray image of the whole soft-embalmed human breast. b) Ultrasound image of the whole soft-embalmed human breast. c) Dissected human breast tissue before sonications.

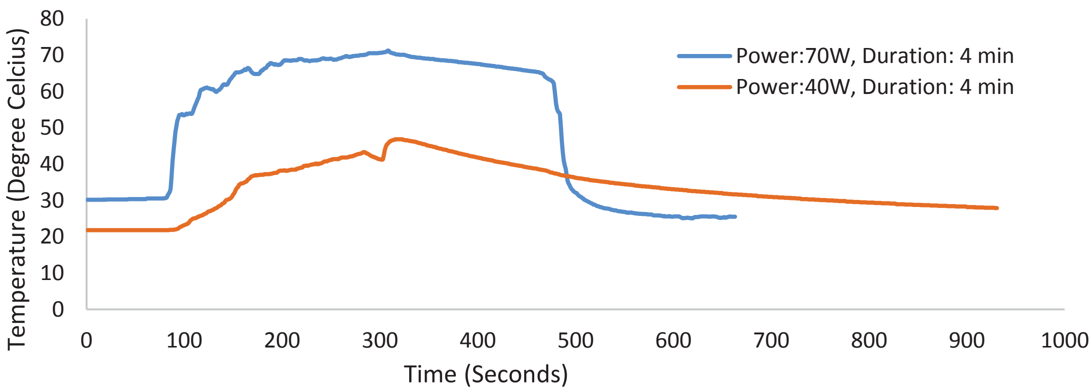


FIGURE 6. Temperature graphs for soft-embalmed human breast sonications at various power levels and durations.

After successful testing of chamber, the experiments were conducted using soft – embalmed human breast tissue. Ultrasound and x-ray imaging was used to image the whole embalmed cadaveric breast before dissecting it for experiments. Figure 5a) and b) shows the images obtained from the ultrasound and X-ray imaging respectively. A rectangular block of breast tissue was carefully dissected from the breast sample without damaging the skin. The dissected breast sample before sonications is shown in Fig 5c. The temperature map for embalmed breast tissue sonications is shown in Fig 6.

Sonications of chicken breast and porcine tissue yielded visible lesions over 2cm in size, indicating that sonications were accurate. The thermocouple recorded temperatures up to 85º Celsius. However, sonication of Thiel breast tissue failed to produce a discrete lesion. The sonicated Thiel breast tissue (which was largely fatty as shown by mammography and ultrasound (Fig 5a & 5b) of the specimen) was examined histopathologically, which confirmed the absence of any discrete lesion. To investigate further, fresh chicken breast tissue was embalmed and the embalmed tissue was sonicated with the same parameters.

It was observed that the temperature rise in the embalmed tissue was lower and slow when compared to fresh tissue sonicated at the same power. No visible lesion was identified in the sonicated breast tissue. Histopathology analysis confirmed that there was no difference between the normal tissue and the sonicated region. Thermal ablation of tissue with HIFU causes denaturation of proteins. However, soft embalming also denatures proteins[5], which may be the reason no lesion formed in the embalmed tissue. To investigate further, the experiments were repeated with soft embalmed chicken breast tissue. Chicken breast tissue was embalmed to test the hypothesis that no HIFU lesion forms because proteins are already denatured in the soft embalmed tissue.

Sonicating Soft Embalmed Chicken Breast Tissue

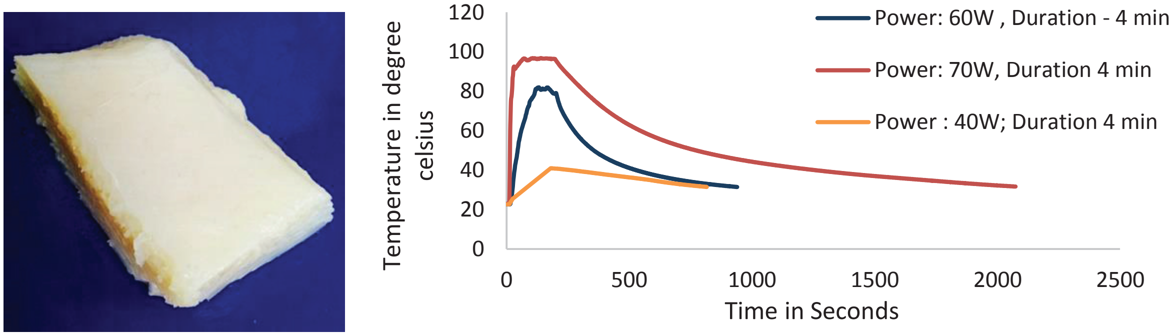


FIGURE 7. a) Soft-embalmed chicken breast tissue before sonications. b) Temperature graph showing the temperature rise during sonications at 40W power for a duration of 4 minutes.

Soft-embalming of the chicken breast followed the same procedure as for the human cadaver embalming (5). Figure 7a) shows the embalmed chicken breast tissue before sonications and 7b) shows the temperature graph for sonication at different powers for a duration of 4 minutes. The embalmed chicken breast sonications were repeated at different power levels and durations. As with the results from the human breast tissue sonications, these experiments also did not produce any visible lesions in the sonicated region. However, the temperature rise was substantially higher at higher power levels when compared to the soft-embalmed human breast tissue.

CONCLUSION

Initial experiments sonicating fatty Thiel breast tissue & Thiel chicken have not produced visible thermo-ablated zones. We suspect that this is a result of the denaturation of tissues produced by the salt solution used for Thiel embalming[5]. It may also reflect the fact that the sonicated tissues were initially at room temperature rather than body temperature. The preliminary results suggests that the best model for pre-clinical HIFU trials will be the fresh breast tissue. However, more experiments will be needed before drawing firm conclusions.

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