Acoustic characterization of Thiel liver for magnetic resonance-guided focused ultrasound treatment

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Published in:
Minimally Invasive Therapy and Allied Technologies

DOI:
10.1080/13645706.2016.1253589

Publication date:
2017

Document Version
Peer reviewed version

ORIGINAL ARTICLE

Full Title: Acoustic characterization of Thiel liver for Magnetic Resonance-guided Focused Ultrasound treatment

Word Count: 1,875 words

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This is an Accepted Manuscript of an article published by Taylor & Francis in *Minimally Invasive Therapy and Allied Technologies* on 27 October 2016, available online: http://www.tandfonline.com/10.1080/13645706.2016.1253589.

Abstract

Background: The purpose of this work was to measure the essential acoustic parameters, i.e. acoustic impedance, reflection coefficient, attenuation coefficient, of Thiel embalmed human and animal liver. The Thiel embalmed tissue can be a promising, pre-clinical model to study liver treatment with Magnetic Resonance-guided Focused Ultrasound (MRgFUS).

Materials and Methods: Using a single-element transducer and the contact pulse-echo method, the acoustic parameters, i.e. acoustic impedance, reflection coefficient and attenuation coefficient of Thiel embalmed human and animal liver were measured.

Results: The Thiel embalmed livers had higher impedance, similar reflection and lower attenuation compared to the fresh tissue.

Conclusions: Embalming liver with Thiel fluid affects its acoustic properties. During MRgFUS sonication of a Thiel organ, more focused ultrasound (FUS) will be backscattered by the organ, and higher acoustic powers are required to reach coagulative levels (temperatures > 56^0C).

Keywords: acoustic parameters; pre-clinical model; Thiel embalming; focused ultrasound ablation

Introduction

Magnetic Resonance-guided Focused Ultrasound (MRgFUS) is a promising technique, in which the ultrasound focuses on a desired tumour area, non-invasively, and the acoustic power transfers to heat, which can ablate the tissue at the focus area only (at temperatures > 56^0C) without damaging the surrounding structures [1]. MRgFUS has been desirable for liver treatment, however a pre-clinical testing model is required due to challenges associated with the liver motion due to respiration, which dislocates the target, and due to the fact that the liver is surrounded by the rib cage, which absorbs ultrasound.

Recent changes in the Human Tissue Act (England, Wales, and Northern Ireland) and the Anatomy Act (Scotland) have allowed the use of human cadavers for surgery in the United Kingdom. The Thiel embalming process produces tissue that is long-lasting, has excellent tissue quality, life-like characteristics, i.e. colour, elasticity and physical properties [2], and it is advantageous over existing models. Embalming human cadavers with formalin and alcohol poses health risks related to formaldehyde, which leaves the cadaver stiff, fragile and difficult to handle [3]. The usage of fresh human/animal cadavers and fresh human/animal organs poses risks due to rapid decay and contamination. Using live animals raises ethical restrictions to minimize pain, suffering, distress or lasting harm and is highly protected by legislation, i.e. the Animals (Scientific Procedures) Act 1986, and the Animal Welfare and Ethical Review Body (Available from: National Centre for the Replacement Refinement & Reduction of Animals in Research). The above stated issues have pointed out the need for an alternative *ex vivo* pre-clinical model which has similar properties to a real living patient, and the Thiel model seems a promising option.

The Thiel model can provide further insight in the treatment of moving liver that can facilitate simulation of liver surgery with MRgFUS. Previous work has indicated similar liver displacement with living humans, suggesting that the Thiel embalmed cadavers can be promising for non-invasive surgery [4]. The Thiel embalmed liver has also been scrutinized for thermometry purposes during focused ultrasound (FUS) sonications under Magnetic Resonance (MR) control [5, 6]. Additionally, an assessment of mechanical properties of Thiel tissues based on tissue stiffness was carried out and

the results indicated strong correlation with in-vivo measurements [7]. However, information on MRgFUS on Thiel embalmed tissue is still limited.

The composition of the Thiel solution is believed to have an impact on the propagation of the FUS in the tissue. To date, there is no available information about the acoustic properties of the Thiel embalmed tissue. Determining the acoustic properties of Thiel embalmed liver is crucial for understanding the response of the tissue to FUS treatment. The acoustic impedance is a highly important parameter that can affect the ultrasound propagation in the target tissue during sonication. Another key parameter is the reflection coefficient, which indicates how much of the targeted FUS energy is reflected by the organ during the treatment. Last but not the least, the attenuation is the loss of amplitude and intensity of the FUS 'travelling' in the organ and is tissue-dependent. The focus of this work was the measurement of these parameters.

Materials and Methods

Embalming the livers with Thiel fluid

All the human livers used in the context of this research were donated according to standard procedures as set out in the Human Tissue (Scotland) Anatomy Act 2006, and the Thiel Advisory Committee (University of Dundee, UK) has approved all procedures involving human cadavers. The cadavers were embalmed according to the Thiel soft-fix embalming method as currently in use at the Centre for Anatomy and Human Identification (CAHID) in Dundee [3]. However, the embalming of the animal livers was performed by the authors in the animal tissue laboratory in the Institute for Medical Science and Technology (IMSaT) at the University of Dundee. Five fresh livers, taken from freshly slaughtered sheep were embalmed for the scope of this research. To embalm the fresh organs, access was formed from the portal vein, the inferior vena cava and the hepatic artery. Thiel fluid was injected through the vascular access and the organ was immersed in Thiel solution for a minimum period of 2 weeks, until there was a colour change (more yellowish) and a soft texture.

Measurement of acoustic impedance and reflection coefficient

A commercial immersion transducer (Sonatest Ltd. UK) single element transducer of 2 MHz frequency, made of metaniobate and with an aperture of 0.5 inches, was used as the transmitter and receiver, and the received signal was used to measure the acoustic parameters of the tissue, using the contact pulse-echo method. Three excised Thiel embalmed human livers and three excised Thiel embalmed ovine livers were used in the present experiment. Multiple measurements were taken in each liver.

The molecules or atoms in an organ (or solid object) are elastically bound to each other. The acoustic impedance is defined by the following equation:

$$Z = \rho \times c, \tag{1}$$

where Z is the acoustic impedance (N × s / m^3; rayls) ρ is the density of the organ (Kg / mm^3) and c is the speed of sound (m / s) in the Thiel embalmed tissue [8]. To measure the density the following equation was used:

$$\rho = \frac{Weight}{Volume}. \tag{2}$$

The livers were scaled to find the weight and the water displacement method was applied to measure their volume. The average thickness of the liver (d) was calculated using a 1.5T MR scanner console (Signa HDx, GE Healthcare, Waukesha, WI, USA) which had a tool that can measure the thickness. For this purpose, anatomical Fast Recovery Fast Spin Echo (FRFSE) images, with TE: 79.7 ms, TR: 4160 ms, flip angle: 90^0, slice thickness: 5 mm and acquisition matrix: 256 × 192 were taken (Figure 1). A fast spine echo (FSE) MR sequence is a Spin Echo pulse with multiple echo readouts (per excitation) separated by 180^0 refocusing pulses (an echo train). Fast Recovery Fast Spin Echo (FRFSE) is a Fast Spin Echo (FSE) sequence with a -90^0 flip-back pulse before the excitation, to achieve T2-weighted imaging with shorter TR (faster scanning). For more information on MR sequences, please refer to the book by Bernstein (2004) 'Handbook of MRI Pulse Sequences' [9].

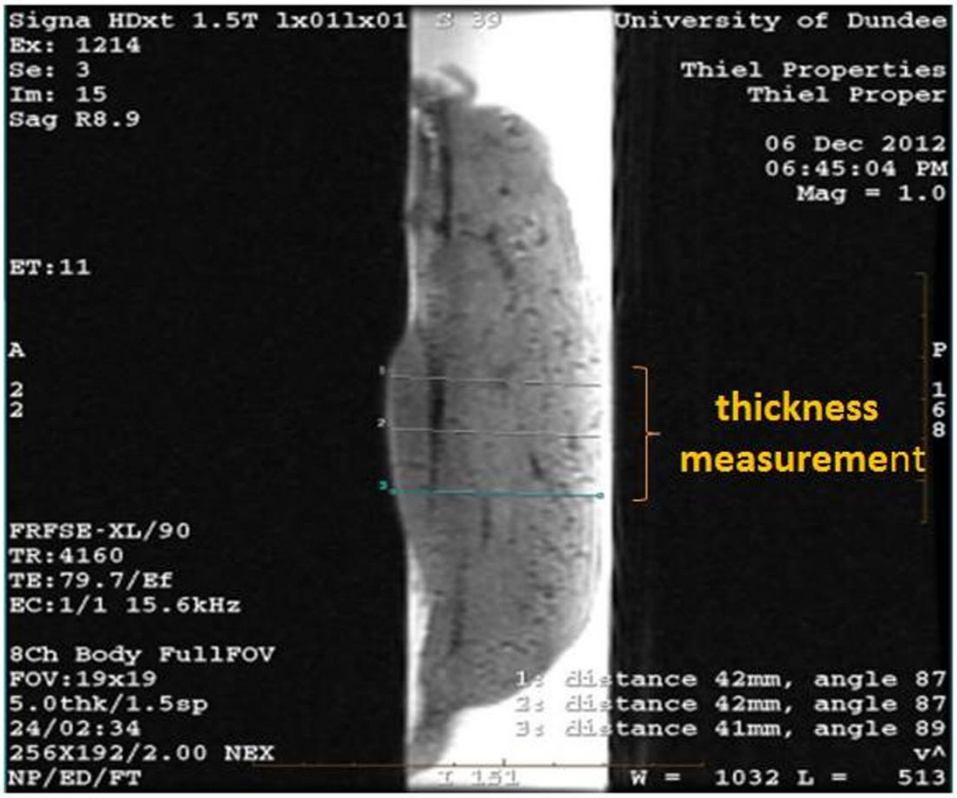

Figure 1. Sagittal MR image of the Thiel embalmed ovine liver, used to measure its average thickness, aveL. The MR console had a tool that can measure the length of lines (mm) drawn across the organ.

Figure 2 is showing the experimental arrangement. The speed of sound was assessed via time-of-flight measurements trough a tissue sample of known thickness (2cm – 4cm).

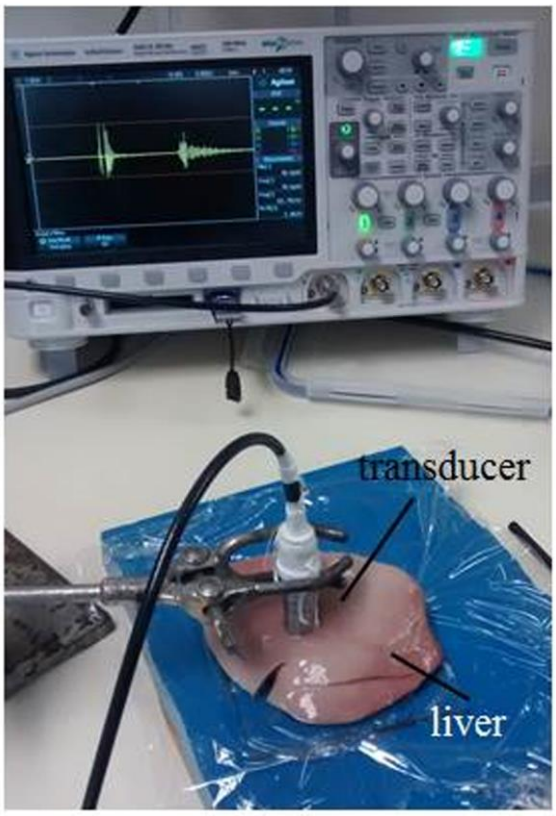

Figure 2. Photograph of acoustic characterisation set-up of Thiel embalmed liver using contact pulse-echo testing, showing the liver, the transducer and the pulser-receiver.

A container with a steel reflector (glass) was set-up in order to calculate the time for ultrasound to pass through the tissue (time data from the received signal). The liver samples were positioned on the top of the steel reflector and the transducer was placed on the top of the tissue. In order to avoid signal loss, good coupling between the transducer and the liver was applied using ultrasound gel. The speed of sound in the liver, c_l, was measured via the following equation:

$$c_l = \frac{2d}{\Delta T_l}, \tag{3}$$

where d is the liver thickness and ΔT_l is the round trip time of the pulse (time between the first and second echo signals). Since the thicknesses of the livers varied, time data was obtained at different thicknesses, and the velocities were averaged.

After calculating the round trip time, Equation (3) was used to measure the speed of sound in the organ.

The calculation of the reflection coefficient on the liver-water interface was based on the following formula:

$$R = \left(\frac{Z_2 - Z_1}{Z_2 + Z_1}\right)^2, \quad (4)$$

where Z_2 is the acoustic impedance of the distal side of an interface and Z_1 is the acoustic impedance of the proximal side of the interface [10]. In the present section, Z_2 was the acoustic impedance of the Thiel embalmed liver and Z_1 was the aco ustic impedance of the water.

Measurement of attenuation coefficient

To measure the attenuation coefficient of the Thiel embalmed liver samples, the pulse-echo contact technique was applied, using the set-up illustrated in Figure 2. The organs were located on the steel reflector and, after applying pulsed echoes, the amplitude of the echo signal was measured. The attenuation coefficient was calculated according to the following formula:

$$a_l = a_w - \frac{1}{2(d1-d2)}[lnA_{s1} - lnA_{s2}] \quad (5)$$

where a_l, a_w are the attenuation coefficients for the liver and the water, respectively, A_{s1}, d1 are the amplitude of the received pulse and the average thickness of the first liver sample, A_{s2}, d2 are the amplitude of the received pulse and the average thickness of the second liver sample (d1 and d2 were calculated in the same way as previously described) [8].

Results

The measured values of the speed of sound, the acoustic impedance, the reflection coefficient and the attenuation coefficient are tabulated in Table 1. For fresh human liver and fresh ovine liver, it was found in the literature that its speed of sound is 1569 m / s [11], its acoustic impedance is 1.66×10^6 rayls [12], its reflection coefficient is 0.01 [13] and its attenuation coefficient is 0.9 dB / cm [14].

Table 1. Measured values of the acoustic parameters of the Thiel embalmed human and ovine liver.

Sample	*Average value*			
	Speed of sound (m/s)	*Acoustic impedance (rayls)×10^6*	*Reflection coefficient*	*Attenuation coefficient (dB/cm)*
Thiel human liver	1667	1.89	0.014	0.1005
Thiel ovine liver	1667	1.91	0.014	0.1011

Discussion

MRgFUS is a non-invasive technique, providing closed loop feedback via real-time treatment control using MRI [15, 16]. However, research has been conducted to improve this methodology, *in vivo* and *ex vivo* [17 - 22]. As there is no realistic anatomical model for preclinical research with FUS due to drawbacks in the existing ex vivo models (organs/cadavers) and due to ethical constraints and cost effectiveness of in vivo models (live animals), this study has been undertaken using *ex vivo* Thiel embalmed explanted human and animal liver. Previous work has studied a basic field of MRgFUS treatment, which is the MR thermometry, involving temperature response of the Thiel tissue and measurement of its thermal coefficient [5, 6] The present research investigated a fundamental aspect of the MRgFUS treatment, which is the acoustic parameters of the pre-clinical Thiel embalmed human and animal liver.

Studying the acoustic properties of the Thiel embalmed tissue was important to assess how the embalming can affect the propagation of focused ultrasound during treatment. The results showed that embalming a liver (either ovine or human) with Thiel solution can influence its acoustic properties. More specifically, the acoustic impedance of the Thiel embalmed ovine liver and the Thiel embalmed human liver was found larger than that of a fresh ovine or human liver. From this observation, it could be assumed that during FUS sonication, more ultrasound will be backscattered from the embalmed organ. The reflection coefficient of the Thiel embalmed human and ovine liver (0.014) was found similar to the reflection coefficient of the fresh liver, which is 0.01 [13]. On the contrary, the attenuation coefficient of the Thiel embalmed livers was lower than the ones in fresh livers, as found in the literature [14]. This parameter should be taken into account, since the attenuation is related to the absorption (conversion of acoustic energy into heat). The obtained values show that, when sonicating a Thiel embalmed liver with focused ultrasound, higher acoustic energies are required (than the fresh liver) to achieve a desired level of heating.

This study involved experimental calculation of the acoustic parameters, i.e. speed of sound, acoustic impedance, reflection coefficient and attenuation coefficient of the Thiel embalmed human and animal liver. The Thiel embalmed model has been shown promising for pre-clinical study of MRgFUS of liver. According to the results, it was found that embalming a human or animal liver with Thiel fluid changes its acoustic properties, suggesting that higher acoustic energies are required to achieve ablation temperatures ($> 56\ ^{0}C$).

Acknowledgements

The authors are thankful for financial assistance provided by from the European Community's Seventh Framework Programmes (FP7/2007-2017) and (FP7/2014-2019) under grant agreement numbers 270186 (FUSIMO project) and 611889 (TRANS-FUSIMO project). We would also like to thank Dr. Roos Eisma from CAHID project and Mrs. Helen McLeod for providing us with Thiel embalmed human tissue.

Disclosure of interest

The authors report no conflicts of interest.

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