Ultrasound in Med. & Biol., Vol. 42, No. 10, pp. 2457–2465, 2016

0301-5629/$ - see front matter

http://dx.doi.org/10.1016/j.ultrasmedbio.2016.06.013

● *Original Contribution*

INFLUENCE OF SKIN AND SUBCUTANEOUS TISSUE ON HIGH-INTENSITY FOCUSED ULTRASOUND BEAM: EXPERIMENTAL QUANTIFICATION AND NUMERICAL MODELING

ANTHONY GRISEY,*† MARC HEIDMANN,†‡ VERONIQUE LETORT,* PAULINE LAFITTE,* and SYLVAIN YON†

*Mathematics in Interaction with Computer Science Laboratory, CentraleSupélec, Châtenay-Malabry, France; †Theraclion, Malakoff, France; and ‡Département de Physique, École Normale Supérieure de Lyon, Université de Lyon, Lyon, France

(*Received* 4 *September* 2015; *revised* 2 *May* 2016; *in final form* 6 *June* 2016)

Abstract—High-intensity focused ultrasound (HIFU) enables the non-invasive thermal ablation of tumors. However, numerical simulations of the treatment remain complex and difficult to validate in clinically relevant situations. In this context, needle hydrophone measurements of the acoustic field downstream of seven rabbit tissue layers comprising skin, subcutaneous fat and muscle were performed in different geometrical configurations. Increasing curvature and thickness of the sample were found to decrease the focusing of the beam: typically, a curvature of 0.05 mm^{-1} decreased the maximum pressure by 45% and doubled the focal area. A numerical model based on k-Wave Toolbox was found to be in very good agreement with the reported measurements. It was used to extrapolate the effect of the superficial tissues on peak positive and peak negative pressure at focus, which affects both cavitation and target heating. The shape of the interface was found to have a strong influence on the values, and it is therefore an important parameter to monitor or to control in the clinical practice. This also highlights the importance of modeling realistic configurations when designing treatment procedures. (E-mail: anthony.grisey@theraclion.com) © **2016 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **High-intensity focused ultrasound, Treatment planning, Numerical modeling, Simulation, k-Wave, Non-linear acoustics.**

INTRODUCTION

Extracorporeal high-intensity focused ultrasound (HIFU) is recognized as a safe and effective alternative treatment for several pathologies, including benign prostate hypertrophy (Gelet et al. 1993), prostate cancer (Madersbacher et al. 1995), uterine fibroids (Tempany et al. 2003), thyroid nodules (Esnault et al. 2006), bone metastasis (Catane et al. 2007) and breast fibroadenomas (Kovatcheva et al. 2015). However, the numerical modeling of HIFU treatments remains complex, mainly because of the non-linearity arising along ultrasound propagation, the anatomical complexity, the heterogeneity of the medium, the inter-individual variability of the properties of the medium, *in vivo* tissue movements and the difficulty in relating temperature to biological damage.

Moreover, validating the simulations in clinically relevant situations is difficult as several physical quantities, such as *in situ* pressure and velocity, are practically inaccessible. Therefore, simulated acoustic fields are generally validated against analytical solutions in simple cases, other numerical simulations or hydrophone measurements in water (Canney et al. 2008; Liebler et al. 2006; Tavakkoli et al. 1998) or in another homogeneous medium (Canney et al. 2008; Wang et al. 2012). Nevertheless, some experiments have been reported that validate numerical simulations through the skull (Pernot et al. 2001) and through a piece of liver (Canney et al. 2010).

The complexity related to real treatment conditions must, however, be accounted for in the models as it can be of clinical importance. For example, cavitation is strongly influenced by the waveform and notably by the peak negative pressure amplitude (Caupin and Herbert 2006), which, by nature, depends on the quality of the focusing.

In this context, the aim of this study was to model the influence of superficial tissue layers on the acoustic field in clinically relevant geometrical configurations. It is based on needle hydrophone measurements of the HIFU field downstream of excised rabbit tissue layers comprising skin, subcutaneous fat and muscle (SFML). These measurements

Address correspondence to: Anthony Grisey, 102 rue Étienne Dolet, 92240 Malakoff, France. E-mail: anthony.grisey@theraclion.com

served to validate numerical simulations with k-Wave. Finally, the simulations were used to quantify the influence of the interface curvature at higher power levels.

METHODS

Biological sample preparation

The samples were excised out of the low abdomen of euthanized rabbits. On each rabbit, a HIFU treatment had been delivered to the liver in the context of an *in vivo* study, which is not reported here. It was conducted in an ethical way, and the protocol was approved by the ethics committee ComEth ANSES/ENVA/UPEC. After this treatment, the subject was euthanized, immediately deep-frozen and stored at −70°C for 1 week. This process is known to preserve the acoustic properties of the tissues (Koch et al. 2011). Samples were then taken directly from entire frozen rabbits and stored at −30°C. Thus, the *in vivo* tissue architecture and geometry were preserved. Care was taken to use only portions of the SFML that had not been subjected to direct HIFU exposure. The reported study was conducted on seven samples from seven different specimens.

The measurements took one day per sample. On the day of the experiment, the remaining parts of the digestive tract were removed and the sample was cleaned. While the sample was still frozen, it was screwed to a rigid frame to maintain the same skin tension as *in vivo*. Then, it slowly thawed at ambient temperature and was degassed with a vacuum pump. Two parallel rigid metallic wires were mounted on the frame just under the skin, to enable smaller curvature radii of the SFML. Subsequently, the sample and the frame were placed into a 50-μm-thick plastic bag full of water. The water was slowly removed without allowing air to enter the bag. According to the hydrophone manufacturer, this process is necessary to prevent a bacterial film from developing on the needle, which could influence the measurements. Finally, the bag was firmly maintained with two rubber bands on a sample holder immersed into the hydrophone water tank (see Fig. 1). The water in the tank was at ambient temperature (approximately 22°C) so that the sample temperature approximately matched the temperature of the skin during actual treatments, which is cooled down to avoid skin burns.

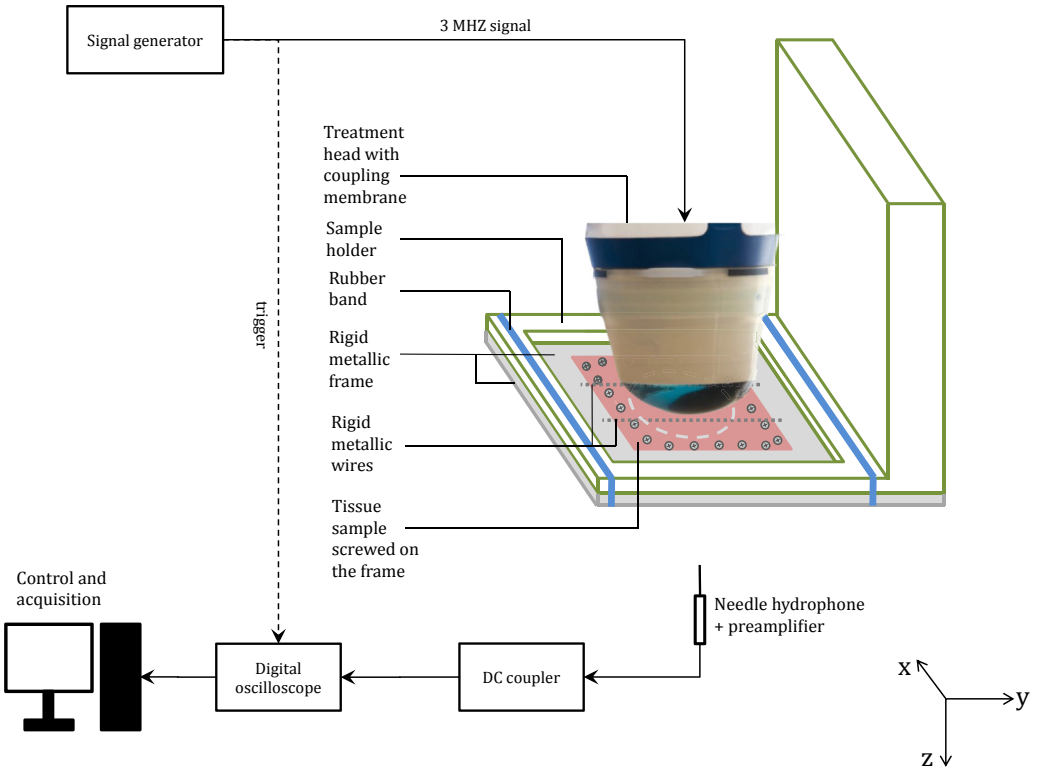

Fig. 1. Schematic of experimental assembly. The sample holder is in *green*, and the metallic frame in *gray*. The latter is placed under vacuum in a plastic bag, which is not shown. It is maintained on the sample holder by two thick rubber bands (*blue*). The sample is screwed on the metallic frame. The *light gray dashed circle* represents the opening of the frame, and the two *gray dotted lines* represent the rigid metallic wires.