In vivo characterization of tissue thermal properties of the kidney by HIFU local hyperthermia under MR-thermometry with modulation of the arterial flow

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Introduction: The purpose of this study was to quantitatively evaluate *in vivo* the tissue thermal properties of the kidney from non destructive local heatings induced by high intensity focused ultrasound (HIFU) monitored by MRI thermometry. The temperature data were analyzed with the Bio Heat Transfer [1] model in which the absorption coefficient (α) reflects the conversion of the acoustic intensity into heat which is evacuated by the thermal diffusion (thermal diffusivity coefficient, D) and perfusion (wb). In order to validate the model *in vivo* and to analyze the influence of perfusion, several HIFU heatings were performed in the kidney of pigs and the blood flow was modulated by obstruction of the aorta with a MR compatible angioplasty balloon.

Materials and methods: *In vivo* experiments were performed on 6 pigs (50 to 70kg body weight) under general anaesthesia. An 14 mm diameter angioplasty balloon was introduced by arterial way and precisely positioned in the aorta near the renal arteries under MRI guidance (SSFP sequence). MRgHIFU experiments were performed on a 1.5 Tesla Achieva/Intera clinical scanner (Philips Medical Systems, Best, The Netherlands) equipped with a HIFU platform prototype designed for the treatment of uterine fibroids. Forty two HIFU sonications (120W, 20 sec) were performed in the kidneys under volumetric real-time MRI thermometry, 21 without and 21 with inflation of the angioplasty balloon in the aorta. A multi-slice, single shot EPI gradient-echo sequence was continuously acquired in a sagittal orientation (TE/TR=29/80 ms, 300x300 FOV, 112x112 matrix, 45° binomial (121) water selective excitation), 6 adjacent slices, leading to a temporal resolution of 480 msec/volume. The temperature images were calculated with the Proton Resonant Frequency (PRF) technique (PRF constant=0.0094 ppm.°C^{-1}). For each time point, the spatial integration of the temperature rise in the kidney was performed and the resulting thermal load (Eth) curve was fitted (Levenberg-Marquardt (LM)) to derive the absorption (α) and perfusion (wb) coefficients, using the equations of the BHT model [2]. The slice containing the hottest temperature at the end of the heating was selected and a 2D gaussian fitting routine (LM) was performed for each subsequent image in the time series acquired during the cooling period. The temporal evolution of the variance along the 2 orthogonal directions (x, y) were fitted by a linear function to determine the thermal diffusivity coefficient D ($\sigma^2 t = 2.D.t$). The accumulated thermal dose was calculated from the Sapareto model [3] by taking the rectal temperature as a reference. The lethal threshold was set to an equivalent dose corresponding to a constant heating at 43°C during 240 minutes. The Student t test was used to compare the groups.

Results: Figure 1 compares the temperature evolution at the hottest point for two sonications performed at the same location, with (red) and without (black) inflating the balloon. The maximal temperature was higher (12°C vs 8.5°C) when the flow was blocked and the time required to reach half of the maximal temperature were 35 sec and 12 sec, with and without flow obstruction, respectively. Figure 2 shows typical results of the data processing. The top row of Figure 2 displays the evolution of Eth for the two HIFU sonications shown in Figure 1. In the presence of flow, Eth decreased exponentially during the cooling period, whereas it remained nearly constant when the balloon was inflated. The fits (red curves) of the experimental data show an excellent correspondence with the BHT model. The graphs in the second row of Figure 2 display the temporal variations of the variances of the fits of the temperature spread along 2 orthogonal axis of the Gaussian function, without (left) and with (right) flow occlusion. As predicted from the BHT, a linear dependence in time can be observed. Figure 3 shows the box-and-whiskers plots of the results obtained for all the experiments. A statistically significant decrease ($p < 0.0001$) of the perfusion was observed (Figure 3, top left) when the balloon was inflated, with an average reduction of the perfusion coefficient (wb) of 85%. The statistical analysis did not revealed significant variations of the absorption coefficient (α) (p=0.965, Figure 3 top right) and of the thermal diffusivity (D) (p=0.6, Figure 3 bottom) for both conditions, in agreement with the model. No pixels reached the lethal thermal dose.

Discussion and conclusion: An excellent correspondence was observed between the BHT model and experimental data, showing that this model is relevant to describe temperature changes *in vivo* during HIFU sonication. The fit of the experimental curves of Eth provides a quantitative estimate of α and wb. The thermal diffusivity coefficient can be determined from the analysis of the spatial spread of the temperature in time. The absorption and thermal diffusivity were found independent of the flow, whereas the perfusion was directly affected by flow modifications. This non invasive method makes it possible to quantitatively evaluate the thermal parameters and may therefore improve the quality of the treatment planning during non invasive MR guided HIFU.

References
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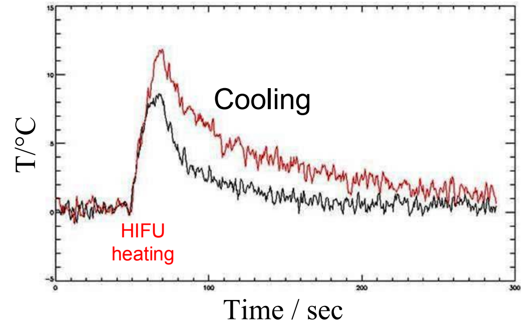

Figure 1: temporal evolution of temperature with deflated (black curve) or inflated balloon (red curve) obtained by MRI thermometry.

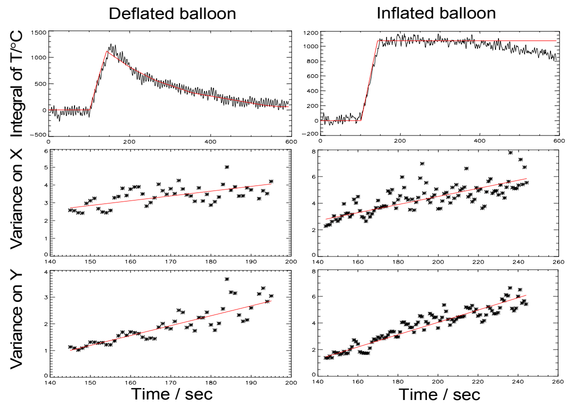

Figure 2: representative results from the data processing of evolution of the integrated thermal load and variance on x and y with deflated or inflated balloon.

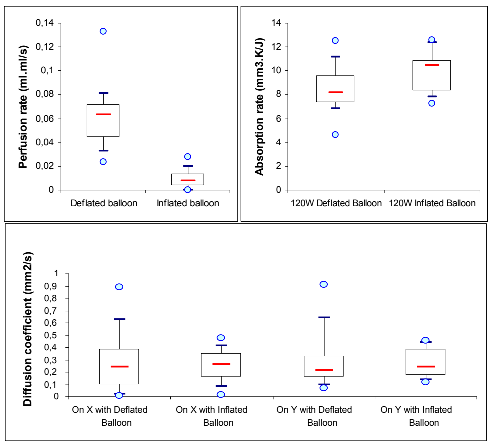

Figure 3: box and whiskers plots of the perfusion and absorption rates and diffusion coefficient on x and y with deflated or inflated balloon.