Perfusion Calculation Based on MR-Temperature Maps and Focused Ultrasound Heating. Theoretical and Experimental Study

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INTRODUCTION

An efficient thermotherapeutic procedure requires a sufficient heating of the pathologic tissue [1]. However, local blood perfusion and tissue thermal conductivity can compromise the therapeutic objective by important dissipative effects. The goal of this study is to quantitatively analyze the influence of perfusion on MR-based 3D temperature distribution. For this purpose *ex vivo* kidneys were perfused at different rates and heated non-invasively by High Intensity Focused Ultrasound (HIFU) under 3D rapid temperature imaging. The objectives were: 1) to propose a method for quantitative estimation of perfusion rate, thermal diffusivity and energy absorption coefficients and 2) to evaluate the pertinence of the bio-heat transfer equation to model the temperature distribution in presence of perfusion.

THEORY

The bio-heat transfer equation (BHTE) [2] describes the spatio-temporal temperature distribution as follows:

$$dT(\vec{r},t)/dt = D\nabla^2 T(\vec{r},t) - wT(\vec{r},t) + \alpha P(\vec{r},t) \qquad (1)$$

where D represents the thermal diffusivity, w the blood perfusion rate and α the energy absorption coefficient.

For a constant power heating followed by a cooling period, spatial integration of equation (1) leads to the following expression of the thermal energy:

$$\int_r T(\vec{r},t)d\vec{r} = \alpha \cdot P_{tot}\left[1 - \exp(-w \cdot t)\right]/w \qquad (2.1) \quad \text{during constant power application}$$

$$\int_r T(\vec{r},t)d\vec{r} = E_{Th\,0}\exp(-w \cdot t) \qquad (2.2) \quad \text{during cooling period}$$

where E_{Th0} represents the accumulated thermal energy in the tissue at the end of the heating period.

For perfused tissue, regional increase and decrease of thermal energy follow an exponential law depending on perfusion rate and energy absorption coefficient only (no influence of diffusion). On the contrary, absence of perfusion leads to a linear increase of thermal energy during constant power application and remains constant during the cooling period (exclusive dependence on energy absorption coefficient). In the BHTE model, the perfusion only acts as a scale factor on the temperature distribution but does not influence the spatial spread of the temperature, which only depends on thermal diffusivity. As a consequence, the spatial distribution over time can be modeled by a Gaussian distribution of half maximum intensity width $R(t)$. Simulations demonstrated that the square of $R(t)$ increases linearly in time with a slope proportional to the thermal diffusivity. A separate analysis of the evolution of spatial distribution of temperature and of thermal energy (spatial integration of 3D temperature maps) should allow for the determination of the coefficients of perfusion, energy absorption and thermal diffusivity.

MATERIALS AND METHODS

Pig kidneys (animal: weight ≈ 50 kg, number = 5) were extracted, canulated and perfused with isotonic fluid at room temperature (24 °C). After a rapid flush of blood contained in the kidney, the flow was varied to modify the tissue perfusion and to measure the effect on the thermal maps obtained by MR thermometry (Proton Resonant Frequency shift method). All experiments were performed on a 1.5 Tesla clinical scanner (Philips Medical Systems, Best, The Netherlands). A single element MR compatible spherical ultrasound transducer integrated in the MR bed was used to induce focal hyperthermia at several locations in the kidney and under different perfusion conditions. At each target location, HIFU energy was applied at constant power (115 W) for a given duration to observe heating and cooling of the tissue. Multislice EPI-segmented gradient-echo images were acquired continuously with the following parameters: TR = 300 ms, TE = 18 ms, flip angle = 35 degrees, EPI-factor = 11, FOV = 128×128 mm^2, matrix = 128×128, eight coronal slices, slice thickness = 5 mm, leading to 2.4 s acquisition time per volume. Images were processed offline with an in-house developed software written in IDL language to calculate the thermal maps. Each temperature map of the temporal series was fitted to a 2D Gaussian function to analyze the evolution of $R(t)^2$ with time [3]. The thermal energy curves were computed from thermal maps and fitted according to eq. (2.1) and (2.2) to derive the perfusion rate and the energy absorption coefficient.

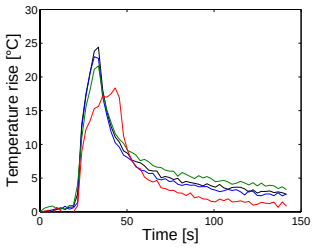

Fig. 1(a)

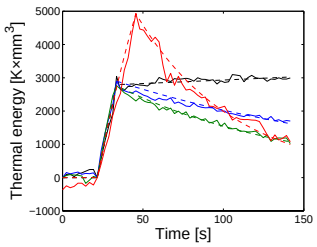

Fig. 1(b)

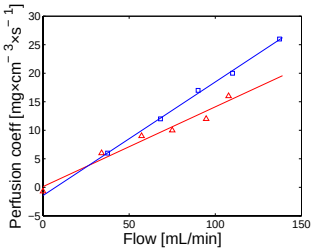

Fig. 1(c)

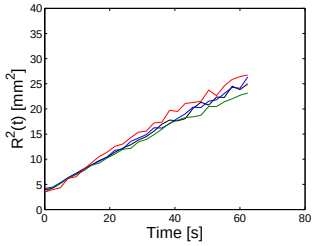

Fig. 1(d)

Figure 1: **(a)** temperature rise at the focal point: black – no perfusion, blue – 34 mL/min, green - 57 mL/min, red – 114 mL/min.
(b) thermal energy evolution vs. time measured values – solid line, fitted values – dashed line for the same flow values as in (a).
(c) perfusion rate vs. flow for two different regions in kidney; solid lines represent the result of the linear fit.
(d) Gaussian radius squared vs. time during the cooling period for the same flow values as in (a).

RESULTS

Fig. 1(a) shows temperature evolution at the focal point under different perfusion conditions. As expected, the maximal temperature decreases with increasing flow rate. Fig. 1(b) shows the thermal energy for the corresponding data and the fitting results according to eq. (2.1) and (2.2) displayed in dashed lines. The perfusion coefficient derived using the presented method showed linear flow dependence, while the absorption coefficient remained constant (2.17 ± 0.066 K/J). Similar properties were found for tissue heating in the cortex and in the medulla (see Fig. 1.c). For the two different regions in the cortex, the slope values of the linear fit were derived: $a_1 = 8.39 \times 10^{-3}$ cm^{-3} and $a_2 = 11.95 \times 10^{-3}$ cm^{-3}. $R(t)^2$ (Fig. 1.d) shows linear dependence versus time with a slope proportional to the thermal diffusivity (equal to $2 \cdot D$) [3], but is independent of the tissue perfusion rate as expected: the value of D was 0.17 ± 0.01 mm^2/s.

CONCLUSIONS

The excellent correspondence between rapid MR-based 3D temperature images and the BHTE obtained in this study demonstrates that this model is applicable for describing the temperature evolution in space and time in highly perfused organs like kidneys. The thermal diffusivity can be calculated from the analysis of the spatial temperature distribution whereas the perfusion rate and the absorption coefficient can be derived from the analysis of the thermal energy. This theoretical and experimental approach would allow for determining these parameters *in vivo* and would therefore be helpful for defining the treatment procedures for obtaining the desired therapeutic effect, taking into account the influence of perfusion on resulting thermal maps and thermal dose.

REFERENCES

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