Optimization of the LITT protocol for hyperthermia treatment of prostate by means of simulations and MR-thermometry

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Introduction
Combination of hyperthermia and radiotherapy increases the efficiency of the later method. Laser induced hyperthermia of prostate allows well-controlled heat delivery and for a laser applicator placed in the urethra, the treatment will be noninvasive. However, for intra-urethral laser application special precautions should be taken in order to avoid hot spots in the urethra, i.e. the temperature at the surface of the applicator should not exceed the critical temperature. The aim of this study was to investigate the possibility of intraurethral hyperthermia and to find the optimal LITT protocol for this purpose. The protocol was optimized to achieve the largest heated volume where the temperature reached the desired value $T_c$ ($> 41^\circ$C) for a given maximum temperature $T_p$.

Methods
As a model for human tissue ex vivo porcine kidneys and an MRI phantom with tissue equivalent material were used. The phantoms were prepared according to recipe in [1]. The kidneys were perfused post mortem with an isotonic NaCl solution. ‘Arterial input’ was varied from 0.0 to 120.0 ml/min. Laser induced interstitial thermotherapy (LITT) was performed with a Nd:YAG laser with a wavelength of 1064 nm. The laser applicator (Huettinger Medizintechnik, Unkirch, Germany) with an active length of 25 mm was placed inside a 9F water-cooled catheter (Somatex GmbH, Berlin, Germany).

MR measurements were performed on a 2.0 T clinical whole body system (Bruker Medspec S200F Avance, Bruker Medical Engineering, Ettlingen, Germany). The temperature in the sample was monitored with a phase shift-based PRF method. TE/TR and the flip angle of the corresponding gradient recalled sequence were 15 ms/37 ms and 18° correspondingly. Typical temporal and in plane spatial resolutions were 4 sec and 0.9x0.9 mm². The slice thickness was 4 mm. To control the temperature in the sample, a 4-channel Luxtron fluoroptic thermometer (Model 3100) was used.

Numerical simulations were performed with a computer simulation program (LITCIT, v.1.3, Laser und Medizin Technologie, Berlin, Germany). The tissue parameters used for simulations were set according to [2].

Theory
According to the linear properties of the heat transfer equation [3], a solution for the temperature change $\Delta T$ after the series of the $N$ identical laser pulses can be found as a linear combination of the temperature response on each of these pulses:

$$\Delta T(r, t) = \Delta T_{\text{temp}}(r) + \sum_{n=1}^{N} \Delta T_{\text{app}}(r, t - (n - 1)(t_p + t_d)).$$  \hspace{1cm} \text{Eq. (1)}$$

Here $r$ is the position, $t$ is the measurement time, $\Delta T_{\text{temp}}(r)$ is the temperature distribution which is set by the applicator cooling, $\Delta T_{\text{app}}(r, t)$ is the temperature increase caused by a single pulse to the time $t$ after its onset. $t_p$ is the duration of the pulse, $t_d + t_d$ is the delay between the pulse onsets. Zero boundary conditions are assumed which is valid in infinite medium or with negligible cooling at the outer boundaries.

Results
In Fig.1 simulated and measured heat distributions in a porcine kidney can be seen. In the experiment the laser applicator was placed between two porcine kidneys with one perfused kidney. Accordingly in the simulation perfusion was set to 0 and 60 ml/(min*100g) on the left- and on the right hand sides of the applicator. Although the calculated and the experimental heat distribution were in qualitative agreement, the relative peak temperatures $\Delta T_p$ were different. In the experiment $\Delta T_p$ was $11^\circ$C in perfused kidney and $14^\circ$C in the other one. In the simulation $\Delta T_p$ was $12^\circ$C and $18^\circ$C, correspondingly.

The size of the heated volume in the gel phantom was significantly smaller than in the kidney. According to the simulations the size of the heated volume depended mainly on the tissue's thermal conductivity. For a fixed peak temperature $T_p$ the size of the heated area was almost independent of the power and duration of the laser pulses. The maximum size of the heated area was achieved with a pulsed heating (Table 1), the laser pulse parameters were found experimentally for a given peak temperature $T_p/1$ and the delay $t_d$ was determined as the time when the peak temperature dropped after the single heating pulse to $T_p/2$.

Discussion
While the PRF temperature maps were in agreement with the thermometer data, the difference between the measured and simulated temperatures are probably caused by the inhomogeneity of the kidney. The heat distribution in the kidney is more complex because of more intensive cooling by the large vessels in the center of the organ. The linear property of the temperature response function (Eq.1) simplifies the creation of a heating protocol. After measuring a temperature response on a single heating pulse it is possible to predict then temperature distribution for a series of pulses. The delay $t_d$ can be chosen as the time when a point of interest reaches the temperature $T_c$. From the maximum distance the heat will be transported by thermococonductivity the maximum size of the heated volume can be estimated.

According to the simulations and the perfused kidney model, it is impossible to heat an arbitrary target volume. If the diameter of a prostate is less than 15-25 mm a reliable heating can be performed with a laser applicator placed intra-urethral. Bigger target volumes must be treated by the implantation of applicators in several positions. However, the kidney model is not ideal for testing hyperthermia of the prostate, because the thickness of the medula is smaller than the characteristic size of the prostate. Therefore a future studies in a living animal model will provide further insights.

References