MR Monitoring of Temperature and Microcirculatory Parameters in Patients with Sarcoma in Hyperthermia/MR Hybrid System

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Introduction:

Although the healing effect of the hyperthermia (HT) therapy is from many clinical studies [1], the mechanisms behind are not yet fully understood. Besides the unquestionable thermal effect, the immunological and physiological mechanisms are no less relevant. Understanding of these mechanisms will allow further optimization of the multi-modal therapy scenarios applying HT. Knowledge of perfusion behavior under HT is also crucial for the numerical procedures of the HT planning and optimization. Until recently such investigations were only possible in hardly transferable rodent studies. After the successful combination of the deep-body HT and the whole-body MR system to the first clinical HT/MR hybrid system [2] investigation of these mechanisms can be carried out under clinical conditions in situ at patients undergoing the therapy. The objective of this contribution is to investigate the physiological response in patients with the soft tissue sarcoma undergoing HT therapy.

Methods:

Investigations were performed at three patients with soft tissue sarcoma undergoing the HT therapy in the clinical HT/MR hybrid system consisting of two simultaneously operating units: the RF HT unit (BSD-2000-3D, BSD Medical Corp., Salt Lake City, UT, USA) and the MR unit (1.5T Symphony, Siemens Medical Systems, Erlangen, Germany) [2]. HT was applied throughout 60 to 80 min. MR thermography (MRTh) monitoring was based on the proton resonance frequency (PRF) shift measured by the volume covering (multi-slice) double echo gradient-echo sequence (TR/TE1/TE2/FA=600/4/20/50). Errors caused by the B0 drifts and the thermal phase coefficient offsets due to temperature-dependent conductivity were corrected [3]. The dynamic contrast-enhanced MRI (DCE MRI) was applied to monitor the microcirculatory parameters basally before HT, immediately before power turn off of some HT fractions and basally before one of the last HT fractions. The adiabatic approximation of the tissue homogeneity model [4], which is a simplified version of the 2-compartmental distributed parameter model [5], was fitted pixel-by-pixel to the DCE MRI data (IV administration of 0.1 mmol/kg Gd-DTPA) acquired every 1 s by IR TurboFLASH sequence (TI/TR/TE/FA=820/1000/1.2/20). Arterial input function (AIF) we estimated applying the heuristic approach similar to that of [6]. Perfusion (F), fractional blood volume (V_b) and transfer constant (K^{trans}) as a measure of the extravasation were mapped and compared in tumor rim and adjacent healthy muscle tissue.

Results:

The main mechanism of the tumor kill in the poorly perfused core region is, on account of the high temperature values achieved there (mean $\Delta T>15°C$), the thermal effect (**Fig. 1**). In contrast, the highly perfused tumor rim seems to be rather responsive to the antiangiogenetic vascular steal effect as the thermoregulatory vasodilation and opening of anastomosed vessels of healthy muscle tissue occur (**Fig. 2**). This microcirculatory response shows a pronounced switch-on effect at the first HT fraction, which decreases gradually under succeeding fractions. Surprisingly, once switched on at the first fraction, this vascular steal effect remains maintained even without HT application, as the later basal measurements show (**Fig. 2,3**). The drastically increased extravasation just and only at the first fraction is likewise intriguing.

Conclusions:

Provided that these preliminary results can be confirmed by more data and in more tumor entities, one may expect some consequences for HT combinations with other therapy modalities. The switch-on of the vascular steal effect at the first HT fraction would recommend the prior application of radiation therapy and the exceptionally drastic increase of the extravasation ibidem would amplify the cancer kill, when the anticancer drugs will administered simultaneously.

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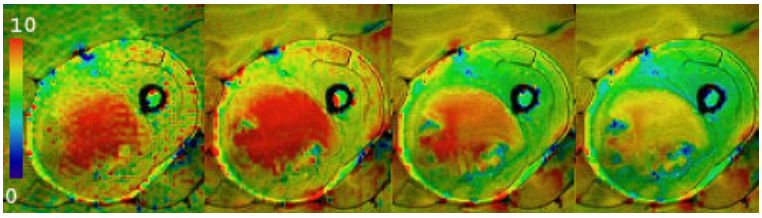
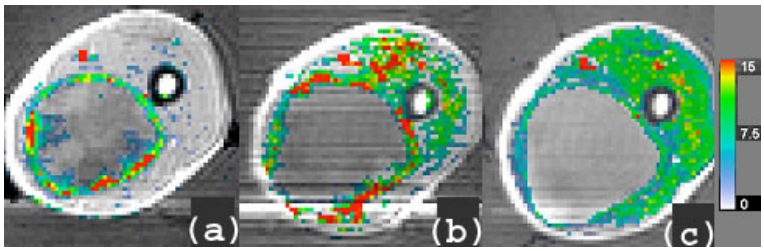
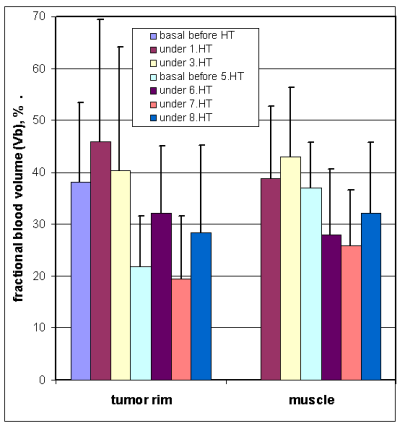


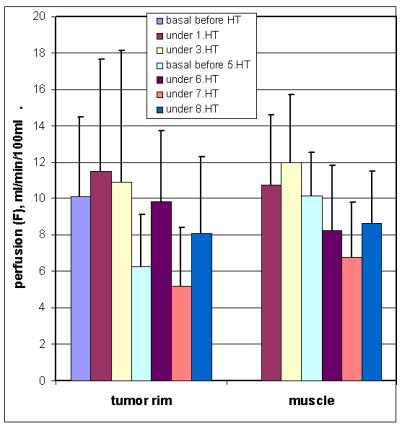


References: **1**. van der Zee J et al., *Lancet* 355:1119-1125 (2000); **2**. Wlodarczyk W et al., *Proc. ISMRM* 10:244 (2002); **3**. Wlodarczyk W et al., submitted for *Proc. ISMRM* 12 (2004); **4**. St. Lawrence KS and Lee T, *J Cereb Blood Flow Metab* 18:1365-77 (1998); **5**. Koh TS et al., *Phys Med Biol* 46:1519-38 (2001); **6**. Parker GJ et al., *Proc. ISMRM* 11:1264 (2003)

Figure 1. Maps of temperature changes ΔT (scale -10 to 10°C) in patient with soft tissue sarcoma in the left thigh 32 and 73 min after RF switch-on and 4 and 16 min after RF switch-off (from left to right).

Figure 2. Maps of perfusion F (scale 0 to 15 ml/min/100ml) measured by DCE MRI basally before HT (a), under 1st HT fraction (b) and basally before 5th HT fraction (c). Note the large vascular steal effect under the 1st HT fraction (b), which remains maintained after 4 fractions even at basal state (before 5th HT fraction).





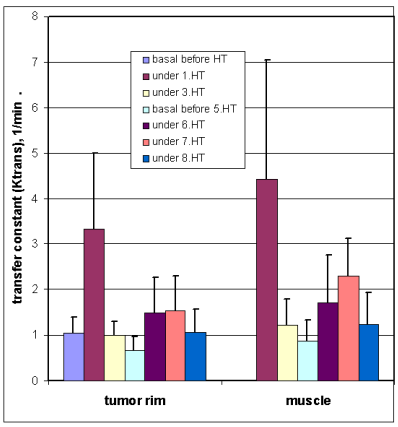


Figure 3. Comparison of fractional blood volume V_b, perfusion F and transfer constant K^{trans} (extravasation) in the tumor rim and the adjacent healthy muscle tissue. Summary of all measurements in one patient with the soft tissue sarcoma: basal before 1st and 5th HT fractions as well as under some succeeded HT fractions.