T_1 Relaxation Time at 0.2 Tesla for Monitoring Regional Hyperthermia: Feasibility Study in Muscle and Adipose Tissue

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It was the purpose of this study to improve T_1-mapping and to characterize T_1 particularly in the hyperthermia temperature range. A new multi-slice TOMROP-sequence was used for fast T_1-mapping in a clinical MRI-hyperthermia hybrid-system. In muscle and adipose tissue, T_1 and temperature can be adapted by a linear relationship below a breakpoint of 43 °C. Above this breakpoint muscle tissue shows irreversible tissue changes; these effects were not visible in adipose tissue. The *ex vivo* results were confirmed *in vivo* under clinical conditions. T_1 in combination with fast mapping is suitable for the investigation of hyperthermia at 0.2 T.

Purpose: Hyperthermia in combination with chemotherapy or/and radiotherapy has proven to be an effective treatment concept for local advanced deep-seated tumors [1,2].

The purpose of our project is the investigation of regional hyperthermia induced tissue effects in deep-seated tumors with a MRI-hyperthermia hybrid-system at a low magnetic field strength of 0.2 T [3]. This study was focused on the characterization of the T_1 relaxation time specifically in the hyperthermia temperature range (ca. 37 °C – 44 °C). With the aim of a 3D characterization, a new fast T_1 mapping MR-method that we extended to multiple slices was used [4]. In order to acquire comparable and reproducible results we concentrated on healthy tissue such as muscle and adipose tissue. Both types of tissue are important for a clinical treatment monitoring because both are usually present within the enlarged target area and have to be protected from overheating.

Methods: All imaging experiments were carried out on a MRI hyperthermia hybrid system [3] that allows simultaneous operation of MRI (8.25 MHz; Magnetom Open Viva, Siemens, Erlangen, Germany) and RF hyperthermia (100 MHz; Sigma-Eye applicator and BSD-2000 3D System, BSD Medical, Utah).

Before, during and after heating MR-data were acquired by a new multislice TOMROP ("T One by Multiple Read Out Pulses") pulse sequence [4]. TOMROP pulse sequence parameters were: TI= 13-2247 ms; TR = 5 s, TE = 6 ms, $\alpha = 10°$, FOV = 400 mm, matrix = 64x64, SI = 10 mm, 1 or 5 slices.
Based on the TOMROP-data, T_1 relaxation-time parameter-maps were retrospectively calculated [5,6]. For correlation purposes, up to four temperature probes were placed in the heated area. The temperature probes were either MR compatible probes of a fluoroptic thermometry system (Mod. 3000, Luxtron, USA) or resistance temperature probes (Bowman probes, BSD, Utah, USA).

Muscle samples (≈ 225 cm^3) from pig and turkey and subcutaneous adipose tissue from pig were examined. The tissue phantoms were heated or cooled by a tube system wrapped around the specimen. The tube system was filled with circulating water dotated with 0.5 g/l $MnCl_2$. T_1 measurements were made first during heating and then during cooling phases in order to detect non-reversible tissue changes. The maximum measured temperature was 63 °C.

One patient was examined with simultaneous MRI and regional hyperthermia according to the EORTC 62961 protocol for high risk soft tissue sarcomas (approved by the Ethical Committee of the Ludwig-Maximilians-University: 1995) [7]. The patient was treated 3 months after tumor resection in the thigh (recurrent liposarcoma).

Results: For the assessment of temperature changes by MRI, it is important to locate the temperature probes in the MR-images. In cases with accurately localized temperature probes a correlation of T_1 and temperature could be achieved. In muscle and adipose tissue, T_1 and temperature can be adapted by a linear relationship below a breakpoint of 43 °C.

Origin of tissue		T_1/T [ms/°C]	R^2	N
Turkey muscle	e.v.	4.7 ± 0.6	0.98 ± 0.02	16
Pig muscle	e.v.	4.1 ± 1.0	0.91 ± 0.09	6
Patient muscle	i.v.	3.1	0.88	1
Pig adipose tissue	e.v.	5.3 ± 0.7	0.97 ± 0.01	6
Patient adipose t.	i.v.	5.1	0.98	1

Table 1: Temperature sensitivity of T_1; e.v. denotes *ex vivo*; i.v. = *in vivo*; R^2 correlation coefficient, *N* number of ROIs

Above this breakpoint muscle tissue show irreversible tissue changes demonstrated by a hysteresis; these effects were not visible in adipose tissue. The table shows the high correlation coefficients in ex vivo tissue samples. The assumption proposed in literature that in a small temperature range the dependency of T_1 and temperature may be adapted by a linear relationship is not necessarily true even for the small hyperthermia temperature range. Especially at ca. 43 °C adipose tissue and muscle tissue samples show completely different response to temperature increase. The *in vivo*, clinical data confirm the results determined in the tissue phantoms below the breakpoint of 43°C.

Conclusion: T_1 offers sensitivity to temperature and tissue changes simultaneously. Both effects provide important information about effects in tissue induced by hyperthermia. Detailed investigations were performed in important model tissues such as muscle and adipose tissue to test the temperature sensitivity of tissue. Yet there is no *in vivo* data available for human muscle or adipose tissue in the temperature range above 43 °C. Our preliminary data in the patient increases the temperature range investigated in healthy human tissue and may serve as a reference for the evaluation of hyperthermia in pathological tissue.

Further investigations will have to focus on thermal dose effects. The approximately linear correlation of T_1 and temperature for adipose tissue in a wide temperature range, is important for the detection of so called "hot spots" in subcutaneous adipose tissue during hyperthermia therapy.

We consider MR thermometry based on T_1 to be best suited for the investigation of regional hyperthermia in deeply seated tumors at 0.2 Tesla.

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