Noninvasive Magnetic Resonance Thermography of Recurrent Rectal Carcinoma in a 1.5 Tesla Hybrid System

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Abstract
To implement noninvasive thermometry, we installed a hybrid system consisting of a radiofrequency multiantenna applicator (SIGMA-Eye) for deep hyperthermia (BSD-2000/3D) integrated into the gantry of a 1.5 Tesla magnetic resonance (MR) tomograph Symphony. This system can record MR data during radiofrequency heating and is suitable for application and evaluation of methods for MR thermography. In 15 patients with preirradiated pelvic rectal recurrences, we acquired phase data sets (25 slices) every 10 to 15 minutes over the treatment time (60-90 minutes) using gradient echo sequences (echo time = 20 ms), transformed the phase differences to MR temperatures, and fused the color-coded MR-temperature distributions with anatomic T1-weighted MR data sets. We could generate one complete series of MR data sets per patient with satisfactory quality for further analysis. In fat, muscle, water bolus, prostate, bladder, and tumor, we delineated regions of interest (ROI), used the fat ROI for drift correction by transforming these regions to a phase shift zero, and evaluated the MR-temperature frequency distributions. Mean MR temperatures (⁴MR), maximum ⁴MR, full width half maximum (FWHM), and other descriptors of tumors and normal tissues were noninvasively derived and their dependencies outlined. In 8 of 15 patients, direct temperature measurements in reference points were available. We correlated the tumor MR temperatures with direct measurements, clinical response, and tumor features (volume and location), and found reasonable trends and correlations. Therefore, the mean ⁴MR of the tumor might be useful as a variable to evaluate the quality and effectiveness of heat treatments, and consequently as optimization variable. Feasibility of noninvasive MR thermography for regional hyperthermia has been shown and should be further investigated. (Cancer Res 2005; 65(13): 5872-80)

Introduction
Regional hyperthermia is applied to heat tumor–loaded anatomic regions such as the extremities or pelvis by radiative or capacitative techniques. Of the different regional hyperthermia approaches, particularly radiofrequency regional hyperthermia has become a well-established treatment option for patients with various (locally advanced) epithelial and mesenchymal malignancies. Together with the conduction of randomized trials that showed the efficacy of regional hyperthermia in certain clinical situations, the proof of a clearcut dose-response relationship (with thermal variables) as well as standardization of the thermometry has largely contributed to the acceptance of this approach (1-7). However, one unresolved problem of regional hyperthermia as an adjunct to radiotherapy and/or chemotherapy is that its efficacy may largely differ between individuals and tumor entities. We can roughly classify tumors as “easy-to-heat” and “difficult-to-heat”. Consequently, a reliable method to recognize tumor diseases, where patients probably benefit from regional hyperthermia, would be highly valuable. Therefore, one strategy to further improve regional hyperthermia is development of a monitoring technique, thus allowing a better navigation of regional hyperthermia systems and a more precise judgement of the heating quality in an individual patient (8, 9).

Magnetic resonance (MR) imaging has been used for monitoring of thermoablative interventions for more than a decade. MR signals are influenced by a mixture of tissue effects (e.g., coagulation and perfusion) in addition to temperature changes (10, 11). Therefore, investigators attempted to separate temperature as an observable in laser-induced thermotherapy (12-15) and focused ultrasound (16, 17), and elucidate the reliability and limitations of MR-guided thermography. Basically, three methods are available for MR thermography and are discussed in the literature. They are based on the temperature dependency of the relaxation time T1 (18), the diffusion (apparent diffusion coefficient value; refs. 19, 20), or the proton resonance frequency shift (PFS; refs. 21-23). As T1-weighted sequences are particularly dependent on the type and status of the tissue (24, 25), they are mainly recommended in low-field systems because of their higher contrast. On the contrary, diffusion methods still suffer from technical and methodical limitations in clinical practice (26). Therefore, for magnetic fields ≥1 Tesla, PFS-based methods are preferred by most investigators today (27-32).

Temperature accuracies of MR-based thermography applied for ablation techniques are reported to be in the range ³3°C to 4.5°C even under favorable in vitro conditions with liver specimens (12–14, 33). Therefore, MR thermography during regional hyperthermia seems to be even more challenging because the expected temperature differences during such a heat treatment (37-43°C) are near the uncertainties referenced for high-temperature applications.

In a small series, Carter et al. (34) employed a self-developed cylindrical phased-array hyperthermia applicator (25 cm diameter) to treat sarcomas of the lower leg in a 1.5 Tesla MR scanner (Signa General Electric, Milwaukee, WI). They acquired phase images during regional hyperthermia and showed a satisfactory correlation with measured temperatures (SE ± 1°C) at moderate power levels of about 150 W. Peller et al. (35) described a hybrid system consisting of a SIGMA-Eye applicator (BSD Medical Corp.,...
Salt Lake City, UT) integrated in a low-field system (0.2 Tesla, Magnetom Open Viva, Siemens AG, Erlangen, Germany). With T1 imaging they claimed to control heat treatments concerning hotspot detection and presented selected cases (lower extremity) with satisfactory correlation of T1 and directly measured temperatures (36).

Our group developed a hybrid system where a SIGMA-Eye applicator (BSD Medical Corp.) was integrated into a mid-field system (1.5 Tesla, MR Symphony Quantum, Siemens) simultaneously working with amplifier power levels as high as 1,800 W (37). In phantoms and patients in the SIGMA-Eye applicator, we compared the different thermographic methods as outlined above (T1, diffusion, and PFS), and found advantages of the PFS method (26).

In experiments with an anthropomorphic phantom, we even found an encouraging absolute agreement (better ±0.5°C on average) between directly measured temperatures and MR temperatures derived from phase measurements according to the PFS method when a drift correction is done employing MR signals in specified regions of interest (ROI) of the water bolus (38).

In this study, we investigated MR thermography (as developed and already validated for phantoms in the hybrid system) for the first time in a homogenous group of patients with locally recurrent rectal cancer to estimate the potentials and limitations of in vivo MR thermography.

**Patients and Methods**

Deep pelvic hyperthermia as an adjunct to chemotherapy with capecitabine (750 mg/m² bd, d1-32) and five weekly applications of oxaliplatin (50 mg/m²) was done in 15 preirradiated patients with locally recurrent rectal cancer who were consecutively enrolled into a phase II protocol, as described by Hildebrandt et al. (39). Regional hyperthermia in an MR compatible SIGMA-Eye applicator (BSD Medical Corp.) was provided by the system BSD-2000/3D. The temporal evolution of the heating patterns was monitored in an MR scanner Symphony (Siemens). Regional hyperthermia up to a maximum power level (1,600 W amplifier power) and MR acquisitions were simultaneously operated as described by Gellermann et al. (38). In short, in the hybrid approach, we succeeded to decouple the two high-frequency systems [i.e., the high power path (amplifier to applicator at 100 MHz) from the sensitive receiving line (body coil to MR receiver)] by suitable filters and other electronic modifications. Regional hyperthermia was applied as described by Wust et al. (40), adjusting balanced phases and amplitudes and positioning the tumor region approximately in the central plane of the applicator.

We used the PFS method for MR thermometry. Before the power of the heating system is switched on, an anatomic T1-weighted data set of 25 slices (1 cm apart) is acquired using a gradient-echo-sequence with echo time of 4 ms, 256 × 256 matrix, and total acquisition time of 155 seconds (Fig. 1). Temperature-sensitive images are acquired during the entire heating session (about every 10-15 minutes), and we employed uncorrected phase distributions from a spoiled gradient-echo-sequence (echo time, 20 ms; repetition time, 600 ms; 25 slices; 128 × 128 matrix; total acquisition time, 78 seconds). A reference phase data set is acquired before power-on. From the phase differences, MR-temperature distributions are calculated and superposed as color-coded distributions with the anatomic data. The MR data sets are transferred to a planning workstation into the software platform AMIRA-HyperPlan to calculate MR-temperature distributions as described elsewhere (38).

For the PFS method, the drift correction (compensating for changes of the static magnetic field B0) is a critical issue. This is especially important because the thermal load of patients to the surroundings during clinical heat sessions is higher than in case of phantom experiments (patients release in the steady state up to several hundred watts to the environment in the MR gantry). In patients it proved successful to employ the fact that the resonance frequency of protons in fat has no temperature dependency: After labeling suitable regions in the adipose tissue (Fig. 1, middle row), a linear transformation of the MR phase data sets is done in a way that the phase changes are reversed to zero in the selected fat regions. For the calculation of this linear correction function, three MR temperature gradients in lateral, vertical, and longitudinal direction are purposed and adopted in an iterative procedure until the fat is as homogenous as possible in green color (zero), as illustrated in Fig. 1 (right row). The transformation is interpolated/extrapolated to the entire data set including the water bolus.

To quantify and further evaluate the MR-temperature distributions over the full treatment course, we draw additional ROIs in selected tissues such as muscle (M. gluteus maximus, M. adductor), tumor, prostate, and bladder (as also shown in Fig. 1). We delineated the tumor volume with less extension than suspected from the anatomic MR sections (Fig. 1) to reduce errors at boundaries, in particular caused by any kind of movement or shift. Other tissues (in particular large and small intestine) are so afflicted with (susceptibility) artifacts that estimation of MR temperatures is not possible (see the marked regions in Fig. 1).

We acquired four to eight phase data sets per heat treatment in 10- to 15-minute intervals in every patient/treatment corresponding to the intervals for the thermal mapping under routine conditions. Whereas the pure acquisition time is <5 minutes, the total time for data transfer and postprocessing to generate and visualize the final MR-temperature distributions amounts to 10 minutes.

Obviously, a visual control of the (corrected) MR temperature maps is not precisely enough for treatment decisions. To perform a quantitative analysis and to obtain objective criteria, we determined in every ROI mean MR temperatures at every acquisition time and, in consequence, (mean) MR temperature-time curves as shown in Fig. 2 (top).

In addition, we used utilities of AMIRA-HyperPlan to calculate MR-temperature frequency distributions for every ROI, which show the variation of the MR temperature in the single voxels (Fig. 3). Based on these frequency distributions, we derived various statistical descriptors, not only mean values but also full width half maximums (FWHM), shown in Fig. 3, as well as index temperatures $T_x$. The index temperature $T_x$ is defined as the MR temperature exceeded by $x\%$ of the voxels of the ROI under consideration. These index temperatures have been often used to analyze thermal data and have been successfully correlated with clinical end points (1, 3).

Univariate analysis of thermal variables with their attribution to response and other tumor-related factors (e.g., location) is done by the distribution-free Mann-Whitney test in the statistical program package SPSS. Correlation analyses and graphical representations of the frequency distributions are done in the Office program Excel.

This analysis of the MR data sets of a heat treatment is time-consuming and not fully automated in the present software version. Presently, an experienced assistant needs up to 2 days for the evaluation and documentation of one heat treatment. Because in some patients only one heat session was done in the hybrid system (by logistical reasons) and in other patients MR data sets were incomplete and/or disturbed (by various technical reasons), we limited our analysis to one representative hyperthermia session per patient with the best series of MR data sets available. A few patients must be excluded from the study because we failed to record even one set of MR data useful for evaluation.

**Results**

**Magnetic resonance–temperature distributions in tissues at steady state.** A total of 15 heat sessions of 15 patients (5 females, 10 men) with satisfactory MR quality could be selected for the analysis. In these patients with presacral recurrences, the tumor volumes have a large variation from 13 to 420 mL (mean, 77 mL). The longitudinal tumor position (along the patient axis) is variable, ranging from ~2 cm below the symphysis to +7 cm above the
symphysis (mean, 2.5 cm). We assigned also the position of the central plane of the applicator with respect to the symphysis, ranging from −2 to +4 cm. We did the treatments applying a total amplifier power of 1,000 to 1,600 W (mean, 1,300 W) with different standard adjustments of phases and amplitudes (38).

The total treatment time (power-on) ranged from 62 to 92 minutes (mean, 80 minutes). At steady state time between 40 and 88 minutes (mean, 66 minutes), a variety of statistical descriptors of the MR-temperature distribution in the ROI (see Discussion and Figs. 1–3) were derived for the tumors and the normal tissues, which are summarized in Fig. 4.

We find a higher range of temperatures (and fluctuations) in tumors in comparison with the various ROI muscles. In one third of the tumors, an effective hyperthermia seems difficult with a mean value of <3.5 MR-deg (i.e., <41°C). In one third of the tumors (5 of 15), mean MR temperatures of >5 MR-deg (i.e., >42.5°C) are achieved corresponding to easy-to-heat tumors.

The mean MR temperatures in the presacral tumors have considerable variation extending from nearly 0 (0.6 MR-deg) up to cytotoxic values of 8.9 MR-deg. The fluctuations of the MR-temperature distributions (FWHM) are also quite high in the tumors and of the same range (2.2-7.6 MR-deg). In the tumor ROIs, nearly always some spots with high MR temperatures were found. Therefore, we ascertained the mean temperature in the 5 mL of the tumor ROI with the highest MR temperatures (32 voxel of 0.16 mL; ~5 mL). Only in 2 of 15 tumors the mean MR temperature in this high-temperature region was below 6 MR-deg (corresponding to <43.5°C); in 10 of 15 tumors we achieved considerable elevations above 8.5 MR-deg (corresponding to 45-46°C). For the estimation of the physical temperature (in degree Celsius), we neglect perfusion at this time (see Discussion).

Evidently, areas (necroses?) exist in tumors, which are heated to higher MR temperatures. Muscles are more homogeneous and the MR temperatures are below critical values. Only in a minority of the muscle ROI (<10%) we found elevations >8.0 MR-deg in appreciable portions of the volume (5 mL). In fact, 8.0 MR-deg would correspond to a potentially harmful temperature elevation of 45°C to 46°C. However, a fraction of 1 to 4 MR-deg can be

**Figure 1.** Part of a three-dimensional data set for a patient with extensive necrotic presacral recurrence. The color-coded MR temperatures are fused with the anatomic data set (left). Middle, without drift correction. Right, after drift correction according to fat labels. The ROIs of some muscles, tumor, and bolus (top left/right, bottom left/right) are shown and assigned.
attributed to the increase of perfusion (41, 42) via increased oxygenation (blood oxygen level-dependent effect) as further elucidated in Discussion.

In muscle tissue, we identified lower mean MR temperatures ($T_{MR}$) with less fluctuations. Whereas the mean value in muscle is only slightly below the mean tumor MR temperature (3.8 versus 4.2 MR-deg), the fluctuations are considerably lower (FWHM, 3.8 versus 4.8 MR-deg). Topmost is the difference of the high-temperature parts ($T_{max(5 \text{ mL})}$) (i.e., 5.3 MR-deg in muscle versus 8.5 MR-deg intratumorally). We found no single measurement (0 of 60) in the muscle with a $T_{max(5 \text{ mL})}$ above 8.5 MR-deg.

We also differentiated the muscle MR temperatures with respect to anatomic regions (see Fig. 1). Whereas the MR temperatures in the glutaeal muscles were found slightly below the average value (right region, 3.5 ± 1.0; left region, 3.8 ± 1.2), the adductor muscles achieved slightly higher temperatures (right region, 4.2 ± 1.6; left region, 4.0 ± 1.8). No differences between right and left were found.

In organs such as prostate and bladder, the variations were considerably higher as in the muscle. Whereas the MR-temperature distributions of the prostate glands (determined in 10 men) are quite stable (Fig. 4) and seem to reflect true physiologic features, the distributions achieved for the bladders seemed unreliable and were removed from the analysis (see Discussion). The contoured ROIs of the fat tissue (Fig. 1) were used for the drift correction. The FWHMs in fat are consequently low per construction, and the MR temperatures in fat oscillate around 0 (0.0007 ± 0.015 SD) and are the main source of statistical error.

Figure 2. Time sequences of corrected MR-temperature distributions in a central plane of the tumor. MR temperature-time curves of some tissues (mean, values of the ROI according to Fig. 1). Note the different behavior in the necrosis (increase over the whole treatment time) and other tissues (transition into a plateau).
From the FWHM in fat, we estimate the statistical error for the MR temperatures, resulting from the drift or other spatial variations, to be better than $\pm 1.4\ \text{MR-deg}$.

**Magnetic resonance–temperature-time curves and direct temperature measurements.** The time curves of mean MR temperatures over $\sim 80$ minutes are in accordance with typical directly recorded temperature-time curves (see Fig. 2) well known from invasive or minimal-invasive thermometry in regional hyperthermia (3, 42). In the majority (11 of 15 heat sessions) we found a transition of the mean MR-temperature of the tumor into a plateau with a thermal relaxation time of 15 to 20 minutes. The plateau is typically achieved after a range of 25 to 50 minutes. In 2 of 15 patients, we found a continuous increase of the mean MR temperature over the whole treatment time (power-on), as shown in Fig. 2, for the central part in the tumor. In 2 of 15 patients, we could not show any reasonable increase of the MR temperature and found instead fluctuations in the range of 1 to 2 MR-deg or a decrease after a short increase of 1 to 2 MR-deg.

We expected an increase of the width of the MR-temperature distribution over time (caused by an accumulation of errors) and analyzed the FWHM for different tissues by comparing the mean values at the start (around 16 minutes heating time) and end (after around 80 minutes heating time) of the heat treatments. In fact, the distributions get broader in all tissues. However, the elevation is strongest in the tumors (2 MR-deg) and not fully explained by the increase of the width in fat (of only 1 MR-deg). The accuracy of the MR temperature by the PFS method (phase differences), as suggested by the fluctuations in the fat, is therefore $\pm 1\ \text{MR-deg}$ (after 20 minutes treatment time) and increases during the treatment up to a final value of less $\pm 1.5\ \text{MR-deg}$. The FWHMs in muscle exceed only a little the FWHMs in fat and are obviously also due to statistical errors.

Direct thermometry was done in the water bolus (upper bolus) and in tumor-related endoluminal reference points (rectum, vagina, and bladder) in 8 of 15 patients. In 7 of 15 patients, a tumor-related thermometry was not possible by minimal-invasive methods (status after abdomino-perineal rectum resection) and/or was refused by the patient.

Table 1 documents a good agreement on average of the directly measured temperature increase in the upper bolus (by 11.2°C) in comparison with the MR temperature increase in the ROI in the upper bolus (by 10.9 MR-deg). In single cases we found higher deviations between MR temperature and directly measured temperature by several degrees Celsius. This is explained by the vertical thermal gradient from the lower to the upper part of the bolus (Table 1, on average nearly 4 MR-deg) in conjunction with the uncertainty to find the position of the thermistor for direct thermometry in the upper bolus.

The tumor-related minimal-invasive temperatures are correlated with the mean MR temperatures in the tumor volumes.

![Figure 3. Time sequences of the MR-temperature frequency distributions in some tissues of interest delineated in Fig. 1 and visualized in Fig. 2.](cancerres.aacrjournals.org)
The correlation is not so good because in some tumors (but not in all) we found slightly higher MR temperatures in comparison with the reference temperatures (in degree Celsius). However, on the whole, the directly measured temperatures are useful indicators for the tissue response. This is an ex post apology of the earlier concept to replace intratumoral (invasive) measurements by minimal-invasive endoluminal temperature measurements for regional hyperthermia of the pelvic region (3, 43), which has been controversially discussed in the literature (44).

Dependencies of the magnetic resonance–temperature distributions. We analyzed the dependencies of FWHM (tumor), which increase continuously during the treatment time and exceed the FWHM of the normal tissues (Table 1).

We found a trend that the FWHMs in the tumor depend on the mean level of the MR temperature ($P = 0.06$, Mann-Whitney test), which we interpret as the width of the distribution increasing with the temperature level. However, the FWHM (tumor) does not at all depend on the FWHM (fat). We conclude that the fluctuations of the MR-temperature distribution in the tumors are mainly addressed to the tumor biology and/or physiology, and might be a characteristic attribute of a tumor. We did not find any dependency of FWHM (tumor) on the tumor volume, amplifier power, or, in particular, the response.

Then we scrutinized the dependencies of the mean tumor MR temperatures, which are summarized in Table 2. Most importantly, we found a significant correlation of clinical response with the mean MR temperature in the tumor ($P = 0.04$) in correspondence to the findings for tumor-related direct thermometry in numerous phase II studies (1, 45, 46).

We found, in spite of the limited case number, additional interesting interrelationships: The proximally (cranially) located tumors (>2 cm above the symphysis) are more difficult to heat ($P = 0.05$), which agrees with phantom measurements (38) and various modeling calculations (e.g., ref. 47). The correlation between the mean MR temperatures in the muscles and the mean MR temperatures in the tumors is also statistically evident ($P = 0.02$). From these data it seems that we can categorize the patients into two groups (easy-to-heat and difficult-to-heat); in the easy-to-heat group all tissues, including the muscles, are well heated (with increase of MR temperature). No clear correlation (but a trend) was found for a correlation of $\langle T_{\text{MR}} \rangle$ with the tumor volume and the total power adjusted in the amplifier.

**Discussion**

The objective of this work is to develop a method to achieve three-dimensional data sets about heat treatments noninvasively by MR imaging (so-called MR temperatures), to analyze these data sets, and to discuss useful quality variables we can derive from them to characterize the heat treatment. Note that the identity of these MR variables with temperatures in degree Celsius is not required as long as MR variables are usable to assess the quality and effectiveness of the heat treatment under monitoring (see below).

We installed a hybrid system (37) to perform regional hyperthermia in a multiantenna applicator under simultaneous MR imaging.
monitoring and to acquire MR data sets during the entire treatment time of 90 minutes under routine conditions (37, 38). Achieving an undisturbed MR data set during radiofrequency heating is a difficult task. Therefore, in the beginning not every heating session was successful, and the number of evaluable MR data sets was limited. With increasing experience, the quality of the monitoring is more and more improving.

The data analysis to extract thermal MR variables is still time-consuming and not online yet. However, a visual MR-temperature distribution is already available during the heat treatment (after fat correction procedure, which is based on the postulate that the proton resonance frequency of fat tissue has no frequency shift during the heat treatment (21). Fat tissue (low-water content tissue) typically contains more than 70% fat and less than 10% water. During the segmentation process of the fat, we verify this low water content from the T1-weighted images (high water content, e.g., caused by edema, we expect high perfusion and especially no or low reactive perfusion increases under hyperthermia conditions (1)). Therefore, MR temperatures in the tumors should be near the real temperatures (Table 2; Fig. 4). A mean MR temperature >4 MR-deg indicates mean temperatures near 42°C, but higher temperatures are observed in parts of the tumor with $T_{\text{max}}$ (in 5 mL) approaching 45°C to 46°C. This is in agreement with our ideas of advanced tumors, which are heterogeneous and contain necrotic (i.e., low perfused) areas.

In some tumors, decrease of perfusion during radiofrequency hyperthermia is expected and, consequently, an underestimated of temperatures in degree Celsius. In fact, we find a few tumors (one third) in Fig. 4 with very low MR temperatures where we suspect that the fat temperature is underestimated. In selected patients (data not shown here), we measured temperatures directly in degree Celsius as well as perfusion changes (via contrast media dynamics) and MR temperature at the same location, and found a perfusion increase of roughly 5 mL/100 g/min, corresponding to 1 MR-deg (but this is just an estimation and thus needs further confirmation). Conversely, in case of a blood flow decrease, MR temperature might underestimate the real temperature (in degree Celsius). If preferential perfusion directions exist inside the image voxels, this can also influence the MR temperature (48). This also could be a reason for the broadening of the FWHM of tumor tissue in comparison with normal tissues, which have a well-regulated blood supply.

We should consider the interference of temperature and perfusion when interpreting MR-temperature distributions. In recurrent tumors (and either the more if preirradiated), we do not expect high perfusion and especially no or low reactive perfusion increases under hyperthermia conditions (1). Therefore, MR temperatures in the tumors should be near the real temperatures (Table 2; Fig. 4). A mean MR temperature >4 MR-deg indicates mean temperatures near 42°C, but higher temperatures are observed in parts of the tumor with $T_{\text{max}}$ (in 5 mL) approaching 45°C to 46°C. This is in agreement with our ideas of advanced tumors, which are heterogeneous and contain necrotic (i.e., low perfused) areas.

In some tumors, decrease of perfusion during radiofrequency hyperthermia is expected and, consequently, an underestimation of temperatures in degree Celsius. In fact, we find a few tumors (one third) in Fig. 4 with very low MR temperatures where we suspect decline of perfusion.

The mean MR temperatures in the specified muscle regions are only slightly lower (<4 MR-deg), predicting temperatures between 41°C and 42°C (for perfusion change zero). However, we expected lower temperatures of 39°C to 41°C (42) and, therefore, 1 to 2 MR-deg might be due to perfusion increase. Muscle is a reactive tissue where blood flow can be physiologically elevated 10- to 30-fold above the basal value (of only a few milliliters per 100 g per minute) if an adequate stimulus is done (e.g., exercise).

<table>
<thead>
<tr>
<th>Table 2. Dependence of the mean steady-state MR temperature in the tumor on certain factors</th>
<th>$(\langle T_{\text{MR}}\rangle_{\text{tumor}})$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response</td>
<td></td>
<td>0.04</td>
</tr>
<tr>
<td>Responder</td>
<td>7 of 15</td>
<td>5.5</td>
</tr>
<tr>
<td>Nonresponder</td>
<td>8 of 15</td>
<td>3.1</td>
</tr>
<tr>
<td>Volume (mL)</td>
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<td></td>
</tr>
<tr>
<td>$&lt;50$</td>
<td>9 of 15</td>
<td>4.8</td>
</tr>
<tr>
<td>$&gt;50$</td>
<td>6 of 15</td>
<td>3.3</td>
</tr>
<tr>
<td>Location</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>$\leq$2 cm symphysis</td>
<td>7 of 15</td>
<td>5.4</td>
</tr>
<tr>
<td>$&gt;2$ cm symphysis</td>
<td>8 of 15</td>
<td>3.1</td>
</tr>
<tr>
<td>Power (W)</td>
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<td></td>
</tr>
<tr>
<td>$\geq$1,300</td>
<td>9 of 15</td>
<td>5.0</td>
</tr>
<tr>
<td>$&lt;1,300$</td>
<td>6 of 15</td>
<td>3.0</td>
</tr>
<tr>
<td>$(\langle T_{\text{MR}}\rangle_{\text{muscle}})$</td>
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<td></td>
</tr>
<tr>
<td>$&gt;3.8$</td>
<td>7 of 15</td>
<td>5.4</td>
</tr>
<tr>
<td>$\leq3.8$</td>
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<td>3.2</td>
</tr>
</tbody>
</table>
In the prostate glands the MR temperatures are higher, probably due to both higher temperatures and perfusion increase. This is in accordance with direct temperature measurements in the urethra on occasion of heat treatments of prostate cancer, yielding minimum values near 41°C, which is 1°C to 2°C higher than in muscle (46).

In the bladder we found even higher MR temperatures (mean, >7 MR-deg). Because of the variable filling of the bladder during the heat treatment, we identified these variables as artificially high. A constant bladder filling must be adhered (via a catheter) to achieve reliable MR temperatures of the bladder. In this case, a direct measurement by a thermistor in the catheter seems easier.

The mean MR temperatures ($T_{MR}$) in the specified tumor ROIs correlate with directly measured reference temperatures and depend in a reasonable and statistically relevant manner on various variables, in particular on the clinical response (Table 2). We conclude that the ($T_{MR}$) of these tumors are useful to characterize the heat treatments in at least the same way as invasive or minimal-invasive thermal data published earlier (1, 3, 46). Because a three-dimensional MR-temperature distribution represents more complete information than temperature measurements in points or along scan lines, ($T_{MR}$) should be even a better predictor. This has to be validated in a larger number of patients.

For further improvements of the analysis, we have to include the perfusion, which can be determined by contrast media measurements in points or along scan lines, ($T_{MR}$) provides much more information than discussed in this article, and might much more information than discussed in this article, and might provide valuable insight into tumor physiology and biology. Further research on this innovative field is strongly desirable.

Acknowledgments

References


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