Published in final edited form as:

Phys Med Biol. 2016 August 7; 61(15): N373–N385. doi:10.1088/0031-9155/61/15/N373.

Sensitivity of tissue properties derived from MRgFUS temperature data to input errors and data inclusion criteria: ex vivo study in porcine muscle

Y C Shi¹, D L Parker², and C R Dillon²

¹Department of Engineering Physics, Tsinghua University, HaiDian District, Beijing 100084, China

²Department of Radiology, University of Utah, 729 S Arapsee Dr, Salt Lake City, UT 84108, USA

Abstract

This study evaluates the sensitivity of two magnetic resonance-guided focused ultrasound (MRgFUS) thermal property estimation methods to errors in required inputs and different data inclusion criteria. Using ex vivo pork muscle MRgFUS data, sensitivities to required inputs are determined by introducing errors to ultrasound beam locations ($r_{error} = -2$ to 2 mm) and time vectors ($t_{error} = -2.2$ to 2.2 s). In addition, the sensitivity to user-defined data inclusion criteria is evaluated by choosing different spatial ($r_{fit} = 1$ to 10 mm) and temporal ($t_{fit} = 8.8$ to 61.6 s) regions for fitting. Beam location errors resulted in up to 50% change in property estimates with local minima occurring at $r_{error}=0$ and estimate errors less than 10% when $r_{error}<0.5$ mm. Errors in the time vector led to property estimate errors up to 40% and without local minimum, indicating the need to trigger ultrasound sonications with the MR image acquisition. Regarding the selection of data inclusion criteria, property estimates reached stable values (less than 5% change) when $r_{fit}>2.5\times FWHM$, and were most accurate with the least variability for longer t_{fit} . Guidelines provided by this study highlight the importance of identifying required inputs and choosing appropriate data inclusion criteria for robust and accurate thermal property estimation. Applying these guidelines will prevent the introduction of biases and avoidable errors when utilizing these property estimation techniques for MRgFUS thermal modeling applications.

1. Introduction

Accurate knowledge of tissue properties is an essential part of thermal modeling used for treatment planning, monitoring, and control of magnetic resonance-guided focused ultrasound (MRgFUS) therapies. Recently two new methods to estimate ultrasound and tissue thermal properties from MRgFUS temperature data have been developed (Dillon *et al* 2012, 2016). In both methods, properties are estimated by fitting an analytical temperature solution for a one-dimensional radial Gaussian heating pattern to experimental temperature versus time data. But the methods use slightly different analytical solutions and yield different properties. The first method estimates the initial heating rate (*IHR*) and full width at half maximum (*FWHM*) of the applied heating pattern and the tissue thermal diffusivity (α). The second method estimates those three properties and the tissue perfusion (w). In this study, these are termed the *No Perfusion Method* (NPM) and the *Perfusion Method* (PM), respectively.

When implementing these methods, users must identify required inputs, including the ultrasound beam axis location ($r=0$) and the time vector (t) associated with temperature measurements, whose accuracy may affect property estimate results. Users also decide which spatial and temporal MR temperature data to utilize by choosing the data inclusion criteria of fitting radius (r_{fit}) and fitting time (t_{fit}).

This paper aims to evaluate sensitivities to 1) required inputs by introducing errors into the radial beam axis positions (r_{error}) and the time vector (t_{error}) and 2) different selections of r_{fit} and t_{fit} . The study utilizes eight different MRgFUS datasets in ex-vivo pork muscle with known thermal diffusivity, beam axis location, and a well-triggered MR time vector. Results demonstrate how parameter selection during data acquisition and analysis affect estimates and can guide users in obtaining consistent and reliable properties for patient-specific thermal modeling of MRgFUS treatments.

2. Methods

2.1. Analytical solution of NPM and PM

Integrating a series of instantaneous heating solutions (no axial conduction, radial Gaussian power distribution) yields the temperature changes during finite duration heating T_{heat} [°C] as a function of the radial distance from the beam axis r [m] and the time t [s] since the ultrasound heating began (Cline *et al* 1994)

$$T_{heat}(r, t) = \int_0^t \left[\frac{IHR \cdot \exp(-t'/\tau_{bl}) \exp(\frac{-r^2/\beta}{1+t'/\tau_c})}{1+t'/\tau_c} \right] dt' \quad (1)$$

where IHR is the ultrasound initial heating rate [°C s⁻¹], β is the ultrasound Gaussian variance [m²], and time constants $\tau_{bl} = \rho c_p / (w c_{bl})$ and $\tau_c = \beta / (4\alpha)$ [s] are related to tissue density ρ [kg m⁻³], thermal diffusivity α [m² s⁻¹], blood perfusion w [kg m⁻³ s⁻¹], β , and the specific heat capacity of tissue c_p and of blood c_{bl} [J kg⁻¹ °C⁻¹]. Tissues properties are assumed to be constant and uniform. The exponential perfusion term $\exp(-t'/\tau_{bl})$ must be modified before the integral in (1) can be evaluated analytically.

In the NPM, perfusion is assumed to be zero, making τ_{bl} infinitely large and the exponential perfusion term of (1) becomes unity. The analytical temperature solution for this simplified case is (Dillon *et al* 2012)

$$T_{heat,NPM}(r, t) = IHR \cdot \tau_c \left[Ei\left(\frac{-r^2}{\beta}\right) - Ei\left(\frac{-r^2/\beta}{(1+t/\tau_c)}\right) \right] \quad (2)$$

where Ei represents the exponential integral.

The PM includes estimation of blood perfusion by replacing the perfusion exponential term in (1) with its third-order Taylor series approximation (Dillon *et al* 2016). The resulting analytical solution is expressed by

$$\begin{aligned}
T_{\text{heat},PM}(r,t) = & \frac{IHR \cdot \tau_c}{\tau_{bl}^3} \left\{ \left(\frac{(r^4 + 8r^2\beta + 11\beta^2)\tau_c^2}{36\beta^2} + \frac{(r^2/\beta + 3)\tau_c\tau_{bl}}{4} + \tau_{bl}^2 \right) \tau_c \exp\left(\frac{-r^2}{\beta}\right) \right. \\
& - \left[\frac{(r^4 + 8r^2\beta + 11\beta^2)\tau_c^2}{36\beta^2} + \frac{[-t(r^2 + 5\beta) + 9\tau_{bl}(r^2 + 3\beta)]\tau_c}{36\beta} \right. \\
& \left. \left. + \frac{2t^2 - 9t\tau_{bl} + 36\tau_{bl}^2}{36} \right] (t + \tau_c) \exp\left(\frac{-r^2/\beta}{1+t/\tau_c}\right) \right. \\
& + \left(\frac{(r^6 + 9r^4\beta + 18r^2\beta^2 + 6\beta^3)\tau_c^3}{36\beta^3} + \frac{(r^4 + 4r^2\beta + 2\beta^2)\tau_c^2\tau_{bl}}{4\beta^2} \right. \\
& \left. \left. + \frac{(r^2 + \beta)\tau_c\tau_{bl}^2}{\beta} + \tau_{bl}^3 \right) \left[Ei\left(\frac{-r^2}{\beta}\right) - Ei\left(\frac{-r^2/\beta}{1+t/\tau_c}\right) \right] \right\} \quad (3)
\end{aligned}$$

While the PM solution is more complex than NPM, it has the same required inputs and only one additional fitting parameter, τ_{bl} .

For either method, the analytical cooling solution can be obtained by the superposition of heating solutions according to:

$$T_{\text{cool}}(r, t > t_{\text{heat}}) = T_{\text{heat}}(r, t) - T_{\text{heat}}(r, t - t_{\text{heat}}) \quad (4)$$

2.2. MRgFUS experiments and property estimation

MRgFUS experiments were performed in ex vivo pork muscle and include 4 datasets at 2 locations, 8 datasets in total. Heating was performed using a MR-compatible 256-element FUS phased array system (Imasonic, Besancon, France and Image Guided Therapy, Pessac, France). Heating time was 21.8 s with the applied power of 7.4 W, which led to a temperature rise of 8–11 °C.

MR temperature imaging was performed on a 3T Siemens Trio MRI with two custom-built, two channel coils using the following parameters: 3D segmented echo planar imaging (EPI), repetition time = 36 ms, echo time = 11 ms, flip angle = 30°, bandwidth = 738 Hz/pixel, voxel size = 1×1×3 mm³, field of view = 128×108 mm², 8 transverse slices with 25% oversampling, EPI factor = 9, and temporal resolution = 4.4 s. MR data were reconstructed with coil signals weighted by the inverse covariance matrix (Roemer *et al* 1990) and zero-filled interpolated to 0.5-mm isotropic spatial resolution (Todd *et al* 2011, Dillon *et al* 2013). Temperatures were calculated with the proton resonance frequency technique (De Poorter *et al* 1995, Ishihara *et al* 1995) using a 2D referenceless method with fifth-order polynomial (Rieke *et al* 2004).

Perfusion estimates require knowledge of tissue and blood properties. Tissue density was measured by the displaced-water technique (1073 kg m⁻³) and specific heat capacity was measured by a digital scanning calorimeter (3300 J kg⁻¹ °C⁻¹: Q20, TA Instruments, New Castle, DE, USA). Blood specific heat capacity was assumed from literature (3617 J kg⁻¹ °C⁻¹: Hasgall *et al* 2015). Invasive thermal diffusivity measurements provided a

standard value ($1.45 \times 10^{-7} \text{ m}^2 \text{ s}^{-1}$; KD2 Pro, Decagon Devices, Pullman, WA, USA) against which estimates were compared.

The estimation of tissue properties utilized the Nelder-Mead Simplex Method (MATLAB function *fminsearchbnd*, maximum 800 iterations and function evaluations, termination tolerance for argument and fitting parameters = $1\text{e-}4$) to optimize the following least-squares argument:

$$\text{argmin} \sum_{i=1}^n (T_{\text{exp},i}(r, t) - T_{\text{model},i}(r, t, IHR, \beta, \tau_c, \tau_{bl}))^2, \quad (5)$$

where T_{exp} is the experimental MR temperature data and T_{model} is defined by (2) or (3) (and (4) when applicable) for the NPM and PM, respectively. r and t are considered known and fixed inputs. Fitting parameters IHR , β , τ_c , and τ_{bl} are allowed to vary during the optimization and initiated with a random value between predefined constraints of IHR : 0–10, β : 0–10, τ_c : 0–25, and τ_{bl} : 10– ∞ . In a few instances, the results did not fully converge after the maximum number of iterations. Repeating the optimization led to convergence. All computations were performed on an Intel Xeon Dual-Core Processor at 2.66 GHz with 4.00 GB RAM. $FWHM$ was calculated from fitting parameter β according to $FWHM = 2(\beta \ln 2)^{1/2}$.

2.3. Required inputs

r represents the radial distance of each voxel from the ultrasound beam axis and is the first required input for each of these methods (see figure 1a). In this study, r values were obtained by fitting a Gaussian function to temperature data during heating in both x and y directions of the transverse plane. The center position of the Gaussian fit was then regarded as the beam axis position. Other approaches to finding the beam axis might produce different center positions, which in turn could affect property estimates. Sensitivity of the estimation methods to potential errors in beam axis positions (see figure 1b) was evaluated by introducing offsets to all radial positions. These r_{error} offsets were applied in the y direction and ranged from -2 mm to 2 mm with an interval of 0.1 mm .

The second required input is the time vector t associated with the MR temperature measurements. For this study, ultrasound was triggered to begin ($t=0$) with the start of an MR acquisition. For most Cartesian acquisition schemes, the data at the center of k-space, which is most relevant to temperature measurements, is acquired at the midpoint in time of the MR acquisition. Therefore, with the trigger in place and, as an example, a 4 second MR acquisition time, the first MR temperature measurement during heating would be assigned at $t=2 \text{ s}$ (see figure 1c, No error). Without an ultrasound trigger, it would be unclear how to assign the time vector in relation to the 4-second acquisition, with the potential for positive or negative t_{error} that could appreciably alter the shape of the fitted temperatures and the estimate results (figure 1c). Sensitivity of the estimation methods to t_{error} was addressed by introducing offsets to the time vector, ranging from -2.2 s to 2.2 s with an interval of 0.2 s .

2.4. Data inclusion criteria

Property estimation results may also be affected by the choice of which spatial region (defined by fitting radius r_{fit} , include all data with $r \leq r_{fit}$) and which MR temperature images in time (defined by fitting time t_{fit} , include all data with $0 \leq t \leq t_{fit}$) to utilize in the optimization. Unlike beam location and time vector, these criteria are completely defined by the user. Ideally, property estimation methods would be completely insensitive to these user-defined data inclusion criteria. This study assessed estimation results for different fitting radii and fitting times. The fitting radius was varied from 1 mm to 10 mm with an interval of 0.5 mm and fitting times were evaluated from 8.8 s (only 2 temperature images) to 61.6 s (14 total images). Except when varying r_{fit} , the nominal r_{fit} value was set as 5 mm. The nominal (and maximum) choice of t_{fit} included all heating data and cooling data that satisfied temperature $SNR > 5$.

3. Results

In this study, there are no independently measured standard values for *IHR* and *FWHM* because no gold standard methods exist for measuring them. For each figure, the standard value of thermal diffusivity is shown with a horizontal dark line. Because experiments were performed ex vivo, the true perfusion is zero. Results are presented as the mean of estimates from all sonications ($N=8$) with error bars extending $\pm$ one standard deviation for each case.

3.1 Sensitivity to beam position errors

Figure 2(a)–(d) shows how r_{error} affects estimates of *IHR*, *FWHM*, thermal diffusivity and blood perfusion. Local maximum *IHR* values and local minimum *FWHM* values occur both in NPM and PM results when $r_{error} = 0$. An error of 2 mm in beam location leads to a decrease in *IHR* of 67% and an increase in *FWHM* of 50%. Minimal changes are evident in thermal diffusivity mean values, where the error is consistently less than 5% relative to the standard value. The perfusion estimate approaches zero as beam axis error becomes smaller with total variation less than $3 \text{ kg m}^{-3} \text{ s}^{-1}$.

3.2 Sensitivity to time vector errors

Figure 3(a)–(d) shows how t_{error} affects estimates of *IHR*, *FWHM*, thermal diffusivity and blood perfusion. As t_{error} changes from -2.2 s to 2.2 s , *IHR* and thermal diffusivity decrease but *FWHM* increases with errors of up to 40%, 39% and 30% in *IHR*, thermal diffusivity and *FWHM*, respectively. When $t_{error} = 0$, thermal diffusivity has an error of 5% compared to standard value. The perfusion estimates are consistently less than $3 \text{ kg m}^{-3} \text{ s}^{-1}$.

3.3 Sensitivity to different spatial fitting regions

Figure 4(a)–(e) shows how r_{fit} affects estimates of *IHR*, *FWHM*, thermal diffusivity and blood perfusion as well as the calculation time needed for the optimization. For both NPM and PM, *IHR* is insensitive to fitting radius, with variation less than 10%. *FWHM*, thermal diffusivity and perfusion vary when r_{fit} is small but become stable after r_{fit} is larger than 4 mm. A radius of 1 mm results in a *FWHM* 15% lower than the stable value and a 17% error in thermal diffusivity. Calculation times are larger in PM than in NPM, with an increasing disparity as r_{fit} increases.

3.4 Sensitivity to different temporal fitting periods

Figure 5(a)–(e) shows how t_{fit} affects estimates of IHR , $FWHM$, thermal diffusivity and blood perfusion as well as calculation time. Thermal diffusivity and perfusion approach true values with longer fitting times in both NPM and PM. The variability of all property estimates decreases with increasing t_{fit} . Mean values of calculation time increase with greater t_{fit} and are consistently larger in PM than in NPM.

4. Discussion

4.1. Comparison of NPM and PM

Because there is no perfusion in the experiments and the PM reduces to the NPM when $w=0$ ($\tau_b=\infty$), the two methods are expected to have the same results in this study. In most cases presented, the results show nearly identical property estimates. The PM has longer calculation times than NPM, because it has a more complex analytical solution and an additional fitting parameter. The real benefit of the PM over the NPM would be seen in vivo, where the NPM is less reliable as tissue perfusion increases (Dillon *et al* 2012). Performing such experiments is beyond the scope of this sensitivity study, in which knowing that perfusion is zero has allowed perfusion errors to be quantified directly.

Although perfusion errors up to $3 \text{ kg m}^{-3} \text{ s}^{-1}$ are shown when varying r_{error} and t_{error} , they may not be important in the clinical setting. Figure 6 shows temperature profiles at the focal point from a simple simulation to demonstrate the effects of perfusion variability ($IHR=1.70 \text{ }^\circ\text{C s}^{-1}$, $\alpha=1.45\times 10^{-7} \text{ m}^2 \text{ s}^{-1}$, $FWHM=3.3 \text{ mm}$). For this situation, perfusion values of $10 \text{ kg m}^{-3} \text{ s}^{-1}$ affected temperatures after 20 s of heating by less than $1 \text{ }^\circ\text{C}$. Thus only for highly perfused tissues (or in situations where perfusion is suspected to play a role in the evolution of temperatures such as in uterine fibroid treatments (McDannold *et al* 2006, Lnrd *et al* 2008, Machtinger *et al* 2012)) will it be necessary to estimate properties using the PM.

4.2. Sensitivity to beam position errors

Different methods for identifying the ultrasound beam axis may provide different $r=0$ locations. However, if the beam axis can be identified to within 0.5 mm, the variability of property estimates should be less than 10%. While we would expect symmetry of results about the $r_{error}=0$ position, some deviation from our expectation is observed in thermal diffusivity estimates (figure 2c). This asymmetry is believed to arise from the non-ideal nature of experimental temperature data. In some individual datasets, thermal diffusivity estimates increased as r_{error} changed from -2 to 2 mm ; in some, it decreased; and in others, it remained stable. With a larger number of datasets, the observed asymmetry would likely be resolved. The more important and surprising take home message is that even large errors in beam location (up to $\pm 2 \text{ mm}$) had a limited impact on thermal diffusivity estimates, with changes in estimate values less than 6%.

The outcome of temperature predictions from estimates generated with different beam axis locations are seen in Figure 7. Since property estimates varied less than 10% for $r_{error}=0.5 \text{ mm}$ (see figure 3), the temperature profile and magnitude predicted in this case is very

similar to the error-free case; the primary difference is simply in the misregistration of the beam position. Larger errors in beam position amplify misregistration and provide poorer predictions of temperature profiles and amplitudes. Thus, identifying the beam axis to within 0.5 mm is important for both the accuracy of property estimates and the reliability of temperature predictions.

In the absence of bulk motion and provided that MRgFUS temperatures are acquired with an appropriate voxel size and utilize zero-filled interpolation (Todd *et al* 2011, Dillon *et al* 2013), identifying the beam axis with 0.5 mm accuracy should not be a challenge. Users might simply use the maximum temperature voxel as the beam axis location, though this would likely produce some errors. Slightly more involved methods for identifying $r = 0$ such as using Gaussian fits to the temperatures (as done in this study) or finding the temperature center-of-mass will generally provide equivalent and accurate results.

4.3. Sensitivity to time vector errors

All properties are sensitive to time vector errors. An offset of 0.6 s in time vector leads to an error up to 17% in *IHR*, 7% in *FWHM* and 11% in thermal diffusivity. Because the temporal resolution of MR temperature measurement is in the order of seconds, there is no way to identify when the ultrasound turned on from temperature measurements alone. By implementing a simple optical trigger like the one used in this study so that the ultrasound turns on at a specific time of the MR acquisition period, these errors can be eliminated. Such triggers are already utilized with sub-millisecond resolution for other MRgFUS imaging sequences such as acoustic radiation force impulse imaging (De Bever *et al* 2015).

Figure 8 shows how errors in the time vector affect temperature predictions. Somewhat surprisingly, errors up to 2 s in the time vector error had minimal effect on predictions of the temperature profile and magnitude at the end of heating (Figure 8b). This occurs because the optimization process adjusts fitting parameters to compensate for errors in the time vector in order to provide the best possible temperature fit. Thus, while the individual fitting parameters are inaccurate, when used in combination the predicted temperatures varied by less than 0.5 °C at the final measurement during heating.

The real impact of time vector errors would be seen if these property estimates were not used together for temperature predictions. For example, if thermal diffusivity estimates were used to predict temperatures with a power deposition pattern computed by ultrasound prediction software, results could appear like those in Figure 9 in which thermal diffusivity was varied but other parameters were unchanged ($IHR=1.70\text{ }^{\circ}\text{C s}^{-1}$, $FWHM=3.3\text{ mm}$, $w=0\text{ kg m}^{-3}\text{ s}^{-1}$). The variability in thermal diffusivity estimates seen in figure 3 leads to a predicted temperature difference of ~ 5 °C after 20 s of heating (figure 9b). Such prediction uncertainty is a strong motivator for implementing the optical trigger required to eliminate time vector errors.

4.4 Sensitivity to spatial fitting region size

It is desirable for property estimates to be as insensitive as possible to user-defined criteria like r_{fit} . In this study, all property estimates reach a stable value when r_{fit} is larger than 4 mm (figure 4). Identifying this transition value of r_{fit} and utilizing values above the transition will

help eliminate estimate variability introduced by the user's choices. However, the r_{fit} transition value may vary for different ultrasound transducers, tissues, and treatment geometries. Considering our current study's accuracy and calculation times, a conservative suggestion would be to use

$$r_{fit} > 2.5 \times FWHM \quad (6)$$

Using this recommendation requires a relatively simple approximation of the beam size. Applying it would include the entire ultrasound beam and much of the spatial region affected by thermal conduction in the optimization process, increasing the likelihood of stable and accurate property estimates.

Compared to the standard thermal diffusivity measurement used as truth, the stable estimate values overpredict thermal diffusivity by 5% in both methods. This overestimation has been observed in previous studies (Dillon *et al* 2012, 2013, 2014) and may be a result of neglecting axial conduction in the estimation process. Interpolating with figure 9, it is evident that a 5% change in thermal diffusivity will not significantly affect temperature predictions.

4.5 Sensitivity to temporal fitting periods

In the study, ultrasound was turned off after 22 s, but the most accurate thermal diffusivity estimates occur with much longer fitting times (figure 5). Estimate variability also decreases as t_{fit} increases. Thus a longer fitting time that includes both heating and cooling data is desirable. However, longer fitting times have diminishing returns; the more time the tissue cools, the smaller the temperature signal becomes relative to noise in the image. The inclusion requirement employed in this study that focal temperature $SNR > 5$ provides a reasonable cutoff to eliminate cooling data whose signal is largely affected by noise and that will not contribute significantly to the accuracy of property estimates.

4.6 Study limitations

In this study, the sensitivity of property estimation to tissue inhomogeneity is not considered and all tissue properties are treated as time/temperature independent. As such, variable properties such as those from temperature-induced vasodilation or thermal tissue damage are not accounted for with these methods. For individual short high-power sonications utilized in MRgFUS ablative therapies, such effects would likely be minimal; however, cumulative effects over longer treatments could be significant. Future studies could incorporate temperature dependency of properties via the superposition principle and would require a specific model for how properties change with temperature.

To simplify analysis and presentation, input error and data inclusion criteria sensitivities were considered individually in this study. A joint analysis of sensitivities could provide additional information and insight into the effect of combined errors.

More data from in vivo experiments where perfusion is not zero are needed, and other MR temperaturebased property estimation methods (Cheng and Plewes 2002, Dragonu *et al*

2009), which may be sensitive to similar data inclusion criteria choices, can be evaluated in future work. While the specific results may differ from those presented in this study for in vivo scenarios, in other tissues, or with different MRgFUS systems, even a qualitative awareness of how required inputs and data inclusion criteria affect results may prevent researchers from unknowingly introducing biases and avoidable errors into their property estimates and treatment predictions.

5. Conclusion

Both estimation methods used in this study can provide accurate and reliable results in ex vivo tissues, provided that the required inputs are accurately determined and the data inclusion criteria are intelligently chosen. The PM has a longer calculation time than NPM, but will likely be more useful in clinical settings with higher anticipated perfusion values. Regarding required inputs, the study shows that property estimates vary less than 10% when the beam location error is less than 0.5 mm. All properties are highly dependent upon the accuracy of the time vector, suggesting that a well-triggered time vector is essential. This study recommends user-defined data inclusion criteria of $r_{fit} > 2.5 \times FWHM$ and longer fitting times to achieve stable and accurate property estimate values.

Acknowledgments

The authors wish to acknowledge support for this study from NIH grants R01 CA172787 and F32 HD085685.

References

- Cheng H-LM, Plewes DB. Tissue thermal conductivity by magnetic resonance thermometry and focused ultrasound heating. *J. Magn. Reson. Imaging*. 2002; 16:598–609. [PubMed: 12412038]
- Cline HE, Hynynen K, Hardy CJ, Watkins RD, Schenck JF, Jolesz FA. MR temperature mapping of focused ultrasound surgery. *Magn. Reson. Med*. 1994; 31:628–636. [PubMed: 8057815]
- De Bever JT, Odéen H, Todd N, Farrer AI, Parker DL. Evaluation of a three-dimensional MR acoustic radiation force imaging pulse sequence using a novel unbalanced bipolar motion encoding gradient: 3D MR-ARFI. *Magn. Reson. Med*. 2015 Online: <http://doi.wiley.com/10.1002/mrm.25971>.
- De Poorter J, De Wagter C, De Deene Y, Thomsen C, Ståhlberg F, Achten E. Noninvasive MRI thermometry with the proton resonance frequency (PRF) method: in vivo results in human muscle. *Magn. Reson. Med*. 1995; 33:74–81. [PubMed: 7891538]
- Dillon CR, Borasi G, Payne A. Analytical estimation of ultrasound properties, thermal diffusivity, and perfusion using magnetic resonance-guided focused ultrasound temperature data. *Phys. Med. Biol*. 2016; 61:923–936. [PubMed: 26741344]
- Dillon CR, Payne A, Christensen DA, Roemer RB. The accuracy and precision of two non-invasive, magnetic resonance-guided focused ultrasound-based thermal diffusivity estimation methods. *Int. J. Hyperthermia*. 2014; 30:362–371. [PubMed: 25198092]
- Dillon CR, Todd N, Payne A, Parker DL, Christensen DA, Roemer RB. Effects of MRTI sampling characteristics on estimation of HIFU SAR and tissue thermal diffusivity. *Phys. Med. Biol*. 2013; 58:7291–7307. [PubMed: 24077026]
- Dillon CR, Vyas U, Payne A, Christensen DA, Roemer RB. An analytical solution for improved HIFU SAR estimation. *Phys. Med. Biol*. 2012; 57:4527–4544. [PubMed: 22722656]
- Dragonu I, de Oliveira PL, Laurent C, Mougenot C, Grenier N, Moonen CTW, Quesson B. Non-invasive determination of tissue thermal parameters from high intensity focused ultrasound treatment monitored by volumetric MRI thermometry. *NMR Biomed*. 2009; 22:843–851. [PubMed: 19562728]

- Hasgall PA, Di Gennaro F, Baumgartner C, Neufeld E, Gosselin MC, Payne D, Klingenberg A, Kuster N. IT'IS Database for thermal and electromagnetic parameters of biological tissues. 2015 Online: www.itis.ethz.ch/database.
- Ishihara Y, Calderon A, Watanabe H, Okamoto K, Suzuki Y, Kuroda K, Suzuki Y. A precise and fast temperature mapping using water proton chemical shift. *Magn. Reson. Med.* 1995; 34:814–823. [PubMed: 8598808]
- Lénárd ZM, McDannold NJ, Fennessy FM, Stewart EA, Jolesz FA, Hynynen K, Tempny CMC. Uterine leiomyomas: MR imaging-guided focused ultrasound surgery--imaging predictors of success. *Radiology.* 2008; 249:187–194. [PubMed: 18695211]
- Machtinger R, Inbar Y, Cohen-Eylon S, Admon D, Alagem-Mizrachi A, Rabinovici J. MR-guided focus ultrasound (MRgFUS) for symptomatic uterine fibroids: predictors of treatment success. *Hum. Reprod. Oxf. Engl.* 2012; 27:3425–3431.
- McDannold N, Tempny CM, Fennessy FM, So MJ, Rybicki FJ, Stewart EA, Jolesz FA, Hynynen K. Uterine leiomyomas: MR imaging-based thermometry and thermal dosimetry during focused ultrasound thermal ablation. *Radiology.* 2006; 240:263–272. [PubMed: 16793983]
- Rieke V, Vigen KK, Sommer G, Daniel BL, Pauly JM, Butts K. Referenceless PRF shift thermometry. *Magn. Reson. Med.* 2004; 51:1223–1231. [PubMed: 15170843]
- Roemer PB, Edelstein WA, Hayes CE, Souza SP, Mueller OM. The NMR phased array. *Magn. Reson. Med.* 1990; 16:192–225. [PubMed: 2266841]
- Todd N, Vyas U, de Bever J, Payne A, Parker DL. The effects of spatial sampling choices on MR temperature measurements. *Magn. Reson. Med.* 2011; 65:515–521. [PubMed: 20882671]

Figure 1.

Schematic diagrams representing (a) the models' setup, (b) radial position errors r_{error} and (c) time vector errors t_{error} . (a) Both estimation methods utilize radial temperature data within the transverse plane. (b) The distance between the correct (+ marker) and assumed (x marker) beam position is r_{error} , which may introduce property estimation errors due to the misalignment of temperature distributions used during the optimization process (dashed lines) from those measured experimentally (solid lines). (c) With an optical trigger, the relative timing of the ultrasound commencement ($t=0$) to each MR measurement (x markers) can be identified with no errors (solid black line). Without the trigger, property estimation errors might arise from assuming the ultrasound turned on before (+ t_{error} , blue dashed line) or after (- t_{error} , red dotted line) the true ultrasound onset.

Figure 2. Effect of beam position errors on tissue property estimates. (a) IHR , (b) $FWHM$, (c) thermal diffusivity and (d) blood perfusion.

Figure 3. Effect of errors in the MR time vector on tissue property estimates. (a) IHR , (b) FWHM, (c) thermal diffusivity and (d) blood perfusion.

Figure 4.

Effect of varying fitting radius on tissue property estimates. All data with r_{fit} are included in the estimation. (a) IHR, (b) FWHM, (c) thermal diffusivity, (d) blood perfusion. (e) shows the effect of r_{fit} in calculation time.

Figure 5.

Effect of varying fitting time on tissue property estimates. (a) IHR , (b) $FWHM$, (c) thermal diffusivity, (d) blood perfusion and (e) calculation time. To make sure all data meet the requirement that temperature $SNR > 5$, the number of data sets (N) is less than 8 after $t_{fit} > 35.2$ s. For these points, $N=7, 7, 5, 4, 3, 3$ as t_{fit} increases.

Figure 6.

Effect of varying perfusion on focal point temperature calculations. Temperature versus time curves at the location of maximum temperature rise are seen in (a), while spatial temperature profiles at the end of 20 s heating are seen in (b).

Figure 7. Effect of beam position errors r_{error} on predicting experimental temperatures (× markers). Temperature versus time curves at the location of maximum temperature rise are seen in (a), while spatial temperature profiles at the end of heating are seen in (b).

Figure 8.

Effect of time vector errors t_{error} on predicting experimental temperatures ($\times$ markers).

Temperature versus time curves at the location of maximum temperature rise are seen in (a), while spatial temperature profiles at the end of heating are seen in (b).

Figure 9.

Effect of varying thermal diffusivity on focal point temperature calculations. Temperature versus time curves at the location of maximum temperature rise are seen in (a), while spatial temperature profiles at the end of 20 s heating are seen in (b).