Accelerated magnetic resonance thermometry in the presence of uncertainties

R Madankan¹, W Stefan¹, S J Fahrenholtz¹, C J MacLellan¹, J D Hazle¹, R J Stafford¹, J S Weinberg², G Rao² and D Fuentes¹

¹ Department of Imaging Physics, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA
² Department of Neurosurgery, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA

E-mail: dlfuentes@mdanderson.org

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Abstract
A model-based information theoretic approach is presented to perform the task of magnetic resonance (MR) thermal image reconstruction from a limited number of observed samples on k-space. The key idea of the proposed approach is to optimally detect samples of k-space that are information-rich with respect to a model of the thermal data acquisition. These highly informative k-space samples can then be used to refine the mathematical model and efficiently reconstruct the image. The information theoretic reconstruction was demonstrated retrospectively in data acquired during MR-guided laser induced thermal therapy (MRgLITT) procedures. The approach demonstrates that locations with high-information content with respect to a model-based reconstruction of MR thermometry may be quantitatively identified. These information-rich k-space locations are demonstrated to be useful as a guide for k-space undersampling techniques. The effect of interactively increasing the predicted number of data points used in the subsampled model-based reconstruction was quantified using the L2-norm of the distance between the subsampled and fully sampled reconstruction. Performance of the proposed approach was also compared with uniform rectilinear subsampling and variable-density Poisson disk subsampling techniques. The proposed subsampling scheme resulted in accurate reconstructions using a small fraction of k-space points, suggesting that the reconstruction technique may be useful in improving the efficiency of thermometry data temporal resolution.
1. Introduction

Laser induced thermal therapy (LITT) is a non-ionizing and minimally invasive treatment alternative for patients who have reached maximum radiation dose or have surgically unresectable tumors (Schwarzmaier et al 2006, Stafford et al 2010, Carpentier et al 2012, Jethwa et al 2012, Fahrenholtz et al 2013, Norred and Johnson 2014). The approach is being used clinically to rapidly treat focal diseased tissue in the liver, prostate, bone, and brain, and in other types of diseases such as epilepsy (Anzai et al 1995, Rhim and Dodd 1999, Chen et al 2000, Simon and Dupuy 2006, Curry et al 2012). Magnetic resonance thermometry is often integrated with the LITT procedure to provide temperature estimates of the target tissue and surrounding critical structures during the treatment. Currently, MR thermometry is acquired primarily through quantitative phase-sensitive techniques based on the proton resonance frequency (PRF) shift. The information provided by the integrated system, often called MR-guided laser thermal therapy (MRgLITT), improves safety and allows the clinician to reduce power or stop delivery if safety thresholds are exceeded (McNichols et al 2004).

The idea of combining MR thermometry signals with a mathematical model to better represent the temperature field has been explored in various works (Fuentes et al 2012, Roujol et al 2012, De Senneville et al 2013). The essence of all these works is to provide a better estimate of the temperature image based on model-data fusion in a Kalman filtration (Kalman 1960) framework. However, these studies did not provide any guidelines about optimal $k$-space sampling.

The current study presents a model-based information theoretic approach to increase both the accuracy and efficiency of thermal image acquisition and reconstruction. The key question is whether there exist optimal locations on $k$-space that provide maximum information regarding the temperature image, and if such optimal locations exist, how to develop a general framework to find these locations on $k$-space.

Numerous studies have examined the effect of data undersampling on temperature image reconstruction, and image reconstruction in general (Hennig 1999, Willinek et al 2002, Stafford et al 2004, Lustig et al 2007, Vogt et al 2007, Candès and Wakin 2008, Lim et al 2008, Chartrand 2009, Song et al 2009, Todd et al 2009, 2010, Todd et al 2012, Vasanawala et al 2011, Majumdar et al 2012, Gaur and Grissom 2015, Odén et al 2014). Hennig (1999) performed a comprehensive study on the effect of rectilinear and non-rectilinear methods for $k$-space sampling. Odén et al (2014) also performed a comprehensive study of various $k$-space subsampling strategies for MR temperature monitoring in particular. Stafford et al (2004) demonstrated that interleaved echo planar imaging (EPI) using asymmetric sampling undersampling in the phase-encode direction achieves a three-fold increase in slice coverage. Willinek et al (2002) suggested a randomly segmented central $k$-space ordering for high-spatial-resolution-contrast enhanced MR Angiography. Lustig et al (2007) proposed a sparse sampling technique based on compressed sensing theory (Candès and Wakin 2008) to reconstruct MR images from undersampled $k$-space. Vasanawala et al (2011) developed a practical parallel imaging compressed sensing MRI using Poisson-disk random undersampling of the phase encode. Majumdar et al (2012) also applied the compressed sensing theory for real
time dynamic MR image reconstruction. Chartrand studied the performance of compressed sensing in non-convex optimization context for sparse sampling of k-space (Chartrand 2009). Stochastic sampling of k-space has also been used in contrast-enhanced MR renography and time-resolved angiography (Vogt et al 2007, Lim et al 2008, Song et al 2009). Todd et al (2009) and (2012) presented a temporally constrained reconstruction algorithm for reconstruction of the temperature image from undersampled k-space data in an optimization framework.

Model-based reconstruction of temperature data has also recently been explored in a few studies. Todd et al (2010) provided a model predictive filtering approach for temperature image reconstruction during MR-guided high intensity focus ultrasound (MRgHIFU). The key idea of this work was to use a mathematical model to predict the spatiotemporal variations of temperature, in which the parameters of the model are identified on the basis of observed k-space data. The identified mathematical model was then combined with a set of under-sampled k-space data (by replacing the model predictions with observed data) to provide an estimate of temperature image. Geometric techniques were used for under-sampling of k-space in this work.

Gaur and Grissom (2015) proposed an accelerated MR thermometry approach using model-based estimation of the temperature from undersampled k-space. For this approach, a constrained image model whose parameters were learned from acquired k-space data points was used. The fitted image model was then used to reconstruct data-informed temperature maps. However, no scheme was provided for selection of the k-space samples used to find model parameters.

Information theoretic approaches have also been used for optimal experiment design in MRI and medical imaging in general (Marseille et al 1996, Reeves and Zhe 1999, Brihuega-Moreno et al 2003, Cercignani and Alexander 2006, Ji et al 2008, Poot et al 2010, Seeger et al 2010). In several studies (Marseille et al 1996, Brihuega-Moreno et al 2003, Cercignani and Alexander 2006, Poot et al 2010), optimal experimental parameters were based on minimizing the Cramer–Rao lower bound, which provides a reliable technique for determining the optimal parameters. However, the major drawback of this technique is that the Fisher information used in the Cramer–Rao lower bound can be a function of uncertain parameters. Hence, one needs to use an estimate of the parameters of interest (e.g. prior mean estimate of the parameter) to approximate the Fisher information in the Cramer–Rao lower bound, resulting in possible sub-optimalities.

Although most work in the field of MR thermometry has focused on randomly selected or geometrically undersampled k-space points for image reconstruction, herein we tackle the problem of k-space under-sampling and temperature image reconstruction from a Bayesian experimental design perspective (Reeves and Zhe 1999, Ji et al 2008, Seeger et al 2010). We first apply a probabilistic mathematical model to describe the spatiotemporal evolution of the temperature field and corresponding manifestation of k-space measurements. The key contribution of the current work is to provide a general framework to quantitatively select the samples on k-space that result in the best estimate of the corresponding temperature image. This has been achieved by maximizing the entropy of model outputs or maximizing the information gain (Cover and Thomas 2012) between model uncertainties and data observations. We use this framework to quantify the information content of alternative random or geometric subsampling strategies and we demonstrate that the optimally selected observations on k-space may be useful in guiding model based reconstruction of the temperature field estimates. Within this context, the various reconstruction strategies discussed in literature (Hennig 1999, Willinek et al 2002, Stafford et al 2004, Lustig et al 2007, Vogt et al 2007, Candès and Wakin 2008, Lim et al 2008, Chartrand 2009, Song et al 2009, Todd et al 2009, R Madankan et al Phys. Med. Biol. 62 (2017) 214)
2010, Todd et al 2012, Vasanawala et al 2011, Majumdar et al 2012, Gaur and Grissom 2015, Odén et al 2014) are expected to produce similar accuracies when comparable information content sampling of $k$-space is used.

The structure of this paper is as follows: first, mathematical description of the problem is provided in section 2.1. Then, we describe the overall picture of the proposed approach in section 2.2. The basic idea for optimal $k$-space sampling is then elucidated in section 2.3. In section 3, performance of the proposed algorithm is demonstrated using in silico and in vivo examples. Results and discussion conclude the manuscript.

2. Methods

2.1. Problem statement

Consider the problem of temperature field estimation during the MRgLITT process. According to the Pennes bioheat equation (Pennes 1948), the spatio-temporal behavior of temperature $u(x, t)$ at a given time $t$ and spatial location $x$ is given by:

$$
\frac{\partial u}{\partial t} - \nabla \cdot (\Lambda(u, x) \nabla u) + \omega(u, x) c_{\text{blood}}(u - u_d) = Q_{\text{laser}}(x, t), \quad \forall x \in \Omega
$$

$$
Q_{\text{laser}}(x, t) = P(t) \mu^2 e^{-\mu_0 ||x - x_0||} / 4\pi ||x - x_0||
$$

$$
u(x, 0) = u_0(x), \quad x \in \Omega$$

$$
u(x, t) = u_P(x), \quad x \in \partial \Omega_D$$

$$
-\Lambda(u, x) \nabla \cdot u(x, t) = g_N(x), \quad x \in \partial \Omega_N
$$

$$
-\Lambda(u, x) \nabla \cdot u(x, t) = h(u - u_\infty), \quad x \in \partial \Omega_c
$$

where parameters $\rho$ and $c$ are density and specific heat of the tissue, and $\Lambda(u, x)$ represents thermal conductivity, $c_{\text{blood}}$ represents the specific heat capacity of blood, and $\omega(u, x)$ represents perfusion rate. Note that $x$ is an $n$-dimensional spatial domain in general, i.e. $x \in \mathbb{R}^n$. For instance, if $n = 2$, then $\Omega$ is a 2D domain and $x = (x, y)$.

$Q_{\text{laser}}(x, t)$ denotes the optical-thermal response to the laser source and is modeled as the classical spherically symmetric isotropic solution to the transport equation of light within laser-irradiated tissue (Welch 1984). $P(t)$ is the laser power as a function of time. Parameter $x_0$ denotes the position of the laser photon source and $\mu$ is the effective optical attenuation coefficient. Note that $\mu$ can be a function of tissue properties in general, i.e. $\mu = \mu(x)$.

The initial temperature of the tissue is denoted by $u_0(x)$, which is typically assumed to be 37 °C for the human body. Also, $u_0(x)$ represents Dirichlet boundary condition. Possible effects of blood flow on temperature are also modeled as convection $h(u - u_\infty)$, where $h$ denotes the convection coefficient and $u_\infty$ represents the blood temperature. Note that $u_\infty = u_0$.

One of the key challenges to using equation (1) is that the associated parameters are often unknown and their values are different from patient to patient. Hence, it is a reasonable assumption to treat these parameters as uncertain parameters with some a priori information. On the basis of previous sensitivity analysis (Fahrenholtz et al 2013), we focus on the effective optical attenuation coefficient as the dominant uncertainty, with some uncertainty from the prior probability density function, $p(\mu)$. Furthermore, tissue heterogeneities are incorporated using finite spatial variations of the attenuation coefficient:
\[ \mu(x) = \sum_{i=1}^{d} \mu_i U(x - \Omega_i) \]  

(2)

where, the unitary function \( U(.) \) is defined as follows:

\[ U(x - \Omega_i) = \begin{cases} 
1, & x \in \Omega_i \\
0, & \text{otherwise} 
\end{cases} \]  

(3)

In equation (2), \( d \) is the total number of tissue types and \( \mu_i \) is the corresponding attenuation coefficient for the \( i \)th tissue. Note that each \( \mu_i \) is assumed to be uncertain. \( \Omega_i \) represents the corresponding sub-domain of the \( i \)th tissue on spatial domain \( \Omega \). Note that \( \Omega_i \) values are mutually disjoint. Hence, the overall optical attenuation coefficient \( \mu \) is a piecewise continuous function of spatial coordinate \( x \), where the \( \mu_i \) on each sub-domain \( \Omega_i \) is considered to be uncertain. A Gaussian mixture model was assumed to obtain the tissue segmentation (Avants et al 2011) of each domain, \( \Omega_i \). K-means clustering was used to initialize a \( d = 4 \) tissue intensity model representing gray matter, white matter, cerebrospinal fluid (CSF), and an enhancing lesion on contrast-enhanced \( T_1 \)-weighted imaging. The segmentation problem was solved using expectation maximization of a parametric formulation of the mixture model. Piecewise homogeneity across tissue types was enforced using Markov random fields.

PRF shift is induced by fluctuations in the temperature field (Hindman 1966). We assume that the changes in the PRF are observed through noise-corrupted \( k \)-space measurements of a steady-state gradient echo sequence:

\[ z \propto \mathcal{U}(\mu, \bar{k}) + \nu \quad \nu \sim \mathcal{N}(0, \sigma) + i \mathcal{N}(0, \sigma) \]

\[ \mathcal{U}(\mu, \bar{k}) = \int_{\Omega} (M(x)e^{-\mu(x)}e^{-2\pi i \bar{k} \cdot x})d x \]  

(4)

where, \( \bar{k} = (k_x, k_y, k_z) \) and

\[ s(\mu, x) = \frac{T_E}{T_2(x)} + i\{2\pi\gamma\alpha B_0 T_E \Delta u(\mu, x) + T_E \Delta x_0(x)\} \]  

(5)

Transverse magnetization \( M(x) \) is determined by the repetition time, \( T_R \), as well as \( T_1 \)-relaxation and flip angle, \( \theta \):

\[ M(x) = \frac{M_0 \sin \theta (1 - e^{-\frac{T_s}{T_1}})}{(1 - \cos \theta e^{-\frac{T_s}{T_1}})} \]  

(6)

Note that relaxation parameters such as \( T_1 \) can be a function of temperature in general. As equation (4) represents, observation data are polluted with some normally distributed white noise \( \nu \) (with mean 0, and standard deviation \( \sigma \)). Gaussian noise is a reasonable assumption for imaging with a sufficient signal to noise ratio (SNR > 10) (Fuentes et al 2011). One should note that complex measurement data \( z \) is a function of \( k \)-space parameters \( \bar{k} = (k_x, k_y, k_z) \). Table 1 summarizes the parameters involved in equation (4) to equation (6).

Our final goal is to accurately estimate the temperature field over the spatial domain, given a limited number of measurement data \( z \) values. The key challenge to achieve this goal is to find the optimal set of frequencies \( (k_x, k_y, k_z) \) that provide the maximum amount of information for accurate estimation of uncertain parameter \( \mu \) and consequently temperature field \( u \).
As outlined in figure 1, the methodology presented in the current study consists of 4 distinct components that are combined together to perform the task of model-based thermometry image reconstruction. These components consist of (i) uncertainty quantification (UQ), (ii) optimal $k$-space sampling, (iii) model-data fusion, and (iv) model-based image reconstruction. A schematic view of the whole estimation process is shown in figure 1. We focus on (ii) optimal $k$-space sampling and provide references to the mathematical details of the remaining steps.

Briefly, the overall process starts with given uncertainties in the parameters of the Pennes bioheat equation. The first step to perform the estimation is to quantify the effect of these uncertain parameters on the spatio-temporal distribution of the temperature. A quadrature method (conjugate unscented transform (Nagavenkat et al 2012)) is used to capture the uncertainty in the temperature field due to the presence of uncertain optical attenuation coefficients, $p(\mu)$. In the current study, a single quadrature point represents a carefully selected realization of the optical parameter. The weighted average of propagated quadrature points is then used to determine the statistics of the temperature (mean and covariance) over the spatial domain at a given time and the resulting statistics of the signal model shown in equation (4).

$$m_t = \hat{U} \equiv \mathbb{E}[U] = \int_{\xi} (U(\mu(\xi), x, t) p(\xi)d\xi = \mathbb{E}(U - \hat{U})^2 = \int_{\xi} (U(\mu(\xi), x, t) - \hat{U})^2 p(\xi)d\xi \quad (7)$$

The methodology for UQ is discussed in further detail elsewhere (Nagavenkat et al 2012, Fahrenholtz et al 2013, Madankan et al 2013, 2014a, 2016).

In addition to precise quantification of uncertainty, useful measurement data are also highly important to ensure accurate estimation. This is the focus of the current study and we achieved this through optimal $k$-space sampling. The key goal of optimal $k$-space sampling is to locate a set of samples over $k$-space that ensure measurement of the most useful data. This is achieved by maximizing the mutual information between measurements $z$ and model parameters $\mu$. Our approximation to the solution of this problem is presented in the next section.

To improve our level of confidence about the present uncertainties in the Pennes bioheat equation, we combined prior statistics obtained from UQ with observed data from optimal $k$-space sampling within a model-data fusion (data assimilation) framework. This generated posterior statistics (e.g. mean and covariance) of uncertain parameters. An overview of the mathematical details of this process is provided in appendix B. Further details may be found elsewhere (Fuentes et al 2012, Madankan et al 2014a, 2016).
The obtained posterior statistics were then used to refine the parameter values in the Pennes bioheat equation, and simulation results provided by this updated mathematical model were used to reconstruct the spread of temperature over the tissue. Further details about the model-based temperature image reconstruction are provided in appendix C.

2.3. Optimal k-space sampling

As mentioned earlier, one of the main challenges in MRI is to effectively determine the optimal sampling locations on k-space to provide the best estimate for the image. In other words, measurement data that provide the most confident estimates of uncertain parameters are needed. This is equivalent to finding measurement data that result in the most reduction of uncertainty in parameter estimates. According to information theory (Cover and Thomas 2012), the reduction of uncertainty in one parameter due to the knowledge of the other variable is known as mutual information. Hence, good measurement data provide the maximum amount of mutual information. Information theoretic approaches and the concept of mutual information have been used in numerous works for optimal sensor placement and sensor management (Bourgault et al 2002, Martínez and Bullo 2006, Tharmarasa et al 2007, Williams et al 2007, Krause et al 2008, Choi and How 2010, Julian et al 2012, Madankan et al, 2014b, 2016). The concept of mutual information has also recently been used for optimal measurement design in functional MRI (Yan et al 2014). In the following section, we describe the concept of mutual information and present the mathematical details for finding the optimal locations on k-space.
2.3.1. Mutual information as a measure of sensor performance. According to information theory, the mutual information (Cover and Thomas 2012) between the model forecast $U$ and measurement $z$ can be equivalently written in terms of the entropy, $H(U)$, $H(Z)$, and conditional entropy, $H(Z|U)$.

$$I(U(\mu, \hat{k}); z) = H(U) - H(Z|U) = H(Z) - H(U|Z)$$

By assumption, the conditional probability of the data measurement given the model predictions, $H(Z|U)$, is Gaussian distributed such that maximizing the entropy of the distribution is equivalent to maximizing the mutual information.

$$\max_k I(U(\mu, \hat{k}); z) = \max_k H(U)$$

2.3.2. Optimal locations on k-space  Note that owing to the dependence of observation data $z$ on k-space parameters, the mutual information $I(U; z)$ is also a function of $(k_x, k_y, k_z)$ parameters. Hence, our goal was to look for a set of optimal locations $(k_x^j, k_y^j, k_z^j)$, $j = 1, 2, \ldots, N$ that maximize the mutual information. This can be mathematically described as the following optimization problem:

$$\max_k J(K) = \max_k I(U; z)$$

where, $K = \{(k_x^1, k_y^1, k_z^1), \ldots, (k_x^N, k_y^N, k_z^N)\}$ denotes the coordinates of $N$ observations on k-space and $z = \{z_1, z_2, \ldots, z_N\}$ is the set of all $N$ observations in hand.

We should emphasize here that obtained k-space points are completely independent from noise realizations, whereas noise statistics affect the location of k-space points. For instance, if the standard deviation of noise increases, the estimate of parameter $U$ will be less confident, and vice versa. In an extreme case, when the standard deviation of noise reaches infinity, i.e. when the signal-to-noise ration (SNR) approaches 0, no useful information can be gleaned from k-space measurements and the proposed algorithm returns the same prior estimates of $U$. On the other hand, when SNR reaches infinity (i.e. standard deviation of noise is 0), the proposed algorithm generates a much more confident temperature estimate.

2.3.3. Computational challenges. Unfortunately, solving the above optimization problem is not computationally affordable owing to a couple of issues. First, evaluation of mutual information $I(U; z)$ is computationally intractable for most practical MRI applications. For instance, when scanning 100 lines over a $256 \times 256$ k-space (which is very common in MRI), the measurement data $z$ is a vector of 25,600 elements. Consequently, a $(25600 + d)$ dimensional integral needs to be evaluated to calculate the mutual information $I(U; z)$.

Second, a large set of measurement data makes it computationally intractable to solve the optimization problem in equation (8) for most practical applications. For instance, referring back to the previous example, when scanning 100 lines over a $256 \times 256$ k-space, measurement data $z$ is a vector of 25,600 elements. Consequently, the maximization in equation (8) needs to be performed on a function of more than 25,000 variables, which is computationally intractable. Hence, one needs to simplify the original optimization problem and find the approximate solution for optimal location of each observation.

2.3.4. A simpler alternative: maximizing variance. As presented in appendix A, maximizing the variance, $m_2$, may be used to approximate the maximal entropy.

$$\max_k h(U) \simeq \max_k m_2(U)$$ (9)
subject to:

$$|K^i - K^j| \geq N_d, \quad \forall \ i, j \in 1, 2, \ldots, N, \quad i \neq j$$

(10)

where $|K^i - K^j| = |(k^{i}_x, k^{i}_y, k^{i}_z) - (k^{j}_x, k^{j}_y, k^{j}_z)|$ denotes the distance between the $i$th and $j$th locations on $k$-space and $m_2 = \text{Var}(U)$ is defined from equation (7). Hence, one can simply calculate the variance of $U$ over all $k$-space and then locations on $k$-space that possess the highest value of variance for $U$ are good approximation of optimal locations for data observations.

Equation (10) is considered to ensure that every distinct pair of $k$-space observations is at least a distance of $N_d$ apart from each other. This constraint is used to compensate for possible dependencies that can be introduced owing to approximation of the original problem. We assumed $N_d = 1$ throughout our analysis.

The intuition behind the idea of maximizing the variance is that the points on $k$-space with lower variance values are less sensitive to model perturbations (resulting from parameter uncertainties) and vice versa. Hence, it is better to select the points on $k$-space with the highest sensitivity with respect to model uncertainties. For instance, a point with 0 variance on $k$-space is not a good candidate for data observation because no matter what the values of uncertain parameters are, model output is always the same at that specific point. On the other hand, a large variance value for a point on $k$-space means that the model output at that location is highly sensitive to model uncertainties. Hence, a measurement at that $k$-space location is of more interest. Therefore, the points with the highest variance values of $U$ are better candidates for data observations.

2.3.5. Adaptation to practical $k$-space sampling. It is well known that practically, $k$-space sampling occurs along readout lines rather than just at sparse points on $k$-space. Hence, one needs to modify the idea of variance maximization to make it applicable to practical $k$-space sampling. To accomplish this, we propose to perform $k$-space sampling along the readout lines on which $k$-space points possess the highest variance values. For instance, in 2 dimensions, we have:

$$\max_{k_x} \sum_{k_y=1}^{N_y} m_2(k_x, k_y)$$

(11)

where, $K_y = \{k^{1}_y, \ldots, k^{N_y}_y\}$ and $N_y$ denotes the total number of points along the $k_y$ axis on $k$-space. Similarly, in 3D $k$-space sampling, one can write

$$\max_{k_x} \sum_{k_y=1}^{N_y} \sum_{k_z=1}^{N_z} m_2(k_x, k_y, k_z)$$

(12)

where, $K_y = \{(k^{1}_y, k^{1}_z), \ldots, (k^{N_y}_y, k^{N_z}_z)\}$ and $N_y$ denotes the total number of points along the $k_z$ axis on $k$-space. Further, the relative information (IC) content used in each reconstruction is estimated as the sum of the information content of each read out line normalized by the information content of the entire $k$-space.

$$\text{IC} = \frac{\sum_{k_x \in \text{acquisition}} \sum_{k_y=1}^{N_y} m_2(k_x, k_y, k_z)}{\sum_{k_x=1}^{N_x} \sum_{k_y=1}^{N_y} \sum_{k_z=1}^{N_z} m_2(k_x, k_y, k_z)}$$

(13)

The major benefit of using equations (11) and (12) instead of maximizing equation (9) is that this provides a more practical scheme for $k$-space undersampling by providing the most informative readout lines, rather than the most informative points. In addition, less
computational effort is required to solve equations (11) and (12) than equation (9). Note that after the readout lines identified by maximizing equations (11) and (12), all points along those readout lines are used for model-data fusion.

3. Results

To validate the performance of the proposed approach, we performed in silico, agar phantom, and in vivo experiments. The in silico experiment evaluated the performance of the proposed approach in a simulation of temperature dispersion in the human brain over a 3D space. The methodology was further validated in 3D temperature imaging of a tissue-mimicking agar phantom and planar temperature image reconstruction in a human brain. A detailed description of each of these experiments follows.

3.1. Volumetric image reconstruction

We initially studied the performance of the proposed technique in a mathematical phantom. Fully sampled volumetric temperature imaging of MRgLITT was simulated. Figure 2 shows the position of the tumor in the brain for this example.

Figure 2(b) illustrates the tissue segmentation in one of the slices within the region of interest (ROI). Segmentation was registered to the thermal imaging using DICOM coordinate and orientation information. Figure 2(b) shows all 4 tissue types were evident within the ROI: CSF, gray matter, white matter, and tumor tissue. We considered the corresponding optical attenuation for each of these tissues to be uncertain. Hence, we had 4 uncertain parameters. The optical attenuation coefficient for the CSF, denoted by $\mu_1$, was assumed to be uniformly distributed between $10 \frac{1}{m}$ and $300 \frac{1}{m}$ (Custo et al 2006), i.e. $\mu_1 \sim U[10, 300]$, whereas all other optical attenuation coefficients were assumed to be uniformly distributed between $10 \frac{1}{m}$ and $400 \frac{1}{m}$ (Welch and Van Gemert 2011), i.e. $\mu_i \sim U[10, 400]$, $i = 2, 3, 4$. All other physical properties, such as conductivity, perfusion, etc, are assumed to be known and are given in table 2. For the LITT process, we assumed the laser power to be 11.5 watts, and the heating time period was considered to be 90 s.
To perform the estimation process, we generated fully sampled synthetic measurement data using a random realization of the optical attenuation coefficient $\mu$. In detail, we used $(\mu_1, \mu_2, \mu_3, \mu_4) = (111.39, 218.75, 383.01, 385.96) \frac{1}{\text{m}}$ to generate the temperature field through the Pennes bioheat model. The obtained temperature field was then used in equation (4) to generate the corresponding fully-sampled measurement data. The SNR is assumed to be 25 in this experiment. Table 3 shows the numeric values of the parameters involved in the simulated sensor structure.

A set of 161 conjugate unscented transform (CUT) points (Nagavenkat et al. 2012) (which accurately evaluate up to 8th order polynomial integrals) were used to capture the uncertainty in the temperature field due to the presence of uncertain optical attenuation coefficients. Figure 3 illustrates the mean and standard deviation of the temperature field over an $x - z$ slice co-planar with the laser fiber.

As discussed in section 2.3, the variance maximization technique is used to approximate $k$-space locations with the highest information content for data acquisition. Figure 4 illustrates 100 lines in $k$-space with the highest variance. Most of the points lie in the center of the $k$-space. The number of points projected on the $k_x - k_y$ plane is very small compared with the total number of points used in data observation. For instance, in the case of using 100 lines on $k$-space for data observation, the proposed technique uses only $100 \times 128 \approx 0.6\%$ of the points on the $k_x - k_y$ plane. Note that this is equivalent to almost 164 times faster data acquisition compared with full-sampling of 3D $k$-space. This can be seen in figure 4(b).
We performed the model-data fusion using acquired $k$-space samples with the predicted highest variance. Within the context of the minimum variance framework (appendix B) posterior statistics of optical attenuation coefficients were then found by merging these selected measurements ($k$-space samples) with model predictions. Figure 5(a) illustrates the convergence of the posterior estimates of optical attenuation coefficients with varying amounts of measurement data, ranging from 0 to 100 lines. As is shown in figure 5(a), posterior estimates of parameters converged on their actual value (denoted by dashed lines) as the number of data observations increased.

Figure 5(b) shows the variance for each of the parameter estimates with varying amounts of readout lines. As expected, the variance was reduced as the number of observations increased. Note that the associated variance of posterior parameter estimates was much smaller than the prior variance of the parameters, i.e. applied model-data fusion significantly increased our level of confidence about the optical attenuation parameters.

Posterior estimates of $\mu$ were then used in the Pennes bioheat equation to estimate the true temperature field. Figure 6 illustrates temperature field estimates in a representative $x - y$ plane.

3.1.1 Comparison with other under-sampling schemes. To validate the performance of the proposed undersampling technique, we compared our approach with two additional data
acquisition schemes. Data acquisition sampling shown in figures 7 and 8 was motivated by interleaved echo planar imaging (EPI) variable-density Poisson disk undersampling techniques (Stafford et al 2004, Mitchell et al 2012). The 16 shot interleaved EPI, echo train length \(= 10\), is equivalent to a partial k-space acquisition in the phase encode direction and assumes that the information content is symmetrically distributed throughout k-space. For constant readout time comparison with our model-based reconstruction, we utilized 100 k-space lines uniformly distributed over the \(k_x - k_y\) plane in the reconstruction, as shown in figure 7. Variable-density Poisson disk undersampling was used to model asymmetric data acquisition that is sampled relatively more dense near the k-space center. These acquisition points are illustrated in figure 8. To be consistent in our comparisons, we used variable-density Poisson disk sampling to generate 100 points over the \(k_x - k_y\) plane, and then all points on the lines passing through these points were considered for data acquisition. Using equation (13), the relative information content of each acquisition was \(\text{IC}_{\text{model}} = 72.4\%\), \(\text{IC}_{\text{uniform}} = 0.2\%\), and \(\text{IC}_{\text{poisson}} = 24.4\%\), table 4.

3.1.2. Error analysis. Obtained posterior estimates of \(\mu\) from each of these data acquisition techniques were then used in the Pennes bioheat equation to estimate the true temperature field. Figure 9 represents the error between the true temperature field and its estimate in a representative \(x - y\) plane, obtained using different data acquisition schemes. As illustrated in figure 9, when the variance maximization is used for data acquisition, the maximum discrepancy between the estimated and true temperature field is less than 4 °C, whereas both other undersampling schemes result in higher values of maximum error.

To further study the performance of the proposed technique, we determined the convergence of the root mean square error (RMSE) between the temperature estimate and its actual value while using the proposed technique for data acquisition. As shown in figure 10, the RMSE in the temperature field estimate was consistently reduced as the number of readout lines increased.

To summarize, table 4 shows the maximum error and the RMSE between the true temperature field and its estimate, calculated over all voxels in the full 3D volume, when maximum heating occurs. Note that without any observation data, the maximum difference between the actual temperature map and its estimate was more than 33 °C, and as the number of readout lines increased, the maximum temperature difference was consistently reduced until it reached to almost 4 °C, when 100 readout lines (obtained using the proposed data acquisition
technique) were used. Also, the RMSE between the temperature estimate and its actual value was reduced by a factor of 9. Table 4 also shows the maximum error and RMSE for rectilinear undersampling and variable-density Poisson disk undersampling. It is clear that variable-density Poisson disk undersampling performed better than rectilinear undersampling, but a comparison of these values with corresponding error metrics for the variance maximization technique clearly demonstrates the performance of the proposed subsampling technique.

### 3.2. Phantom experiment

To further validate the proposed approach, we designed a phantom experiment for 3D temperature imaging. A tissue-mimicking agar phantom (1.5% gel by weight) was used to simulate
the thermal ablation process. The LITT procedure (power = 1 watt for a period of 10 min) was monitored in real-time using the temperature-sensitive PRF shift technique acquired with EFGRE3D to generate temperature measurements using a GE scanner every $\Delta t = 15$ s ($T_{1g}/ FA = 5$ ms $/5^\circ$, frequency $\times$ phase = $256 \times 256 \times 26$, FOV = 12.8 cm $\times$ 12.8 cm $\times$ 26 mm, BW = 390.62 Hz pixel$^{-1}$, slice thickness = 1 mm). Temperature images were recorded over 26 slices in the $z$ direction (each with a thickness of 1 mm). Figure 11 shows the position of the laser fiber and corresponding ROI. The parameters used in the phantom experiment are shown in tables 5 and 6. Note that we assumed a linear dependence between $T_1$ and temperature to incorporate possible changes of $T_1$ due to changes in temperature (Vesanen et al 2013). Also, a normalized MR image (without any heating involved) was used to account for the effect of inhomogeneities in magnetization $M(\mathbf{x})$.

We considered the only uncertain parameter to be the optical attenuation coefficient, which is assumed to be uniformly distributed between 0 and 200 $\mu$m$^{-1}$, i.e. $\mu \in \mathcal{U}(0, 200)$. We used a set of 11 Gauss–Legendre quadrature points (Hildebrand 1987) (which accurately integrates up to the 21st order polynomials) to quantify the effect of uncertain parameter $\mu$ on the temperature.
field and $k$-space signal. Then, the proposed technique was used to approximate $k$-space locations with the highest variance. Figure 12 illustrates the $k$-space points found by this approach. Obtained $k$-space points were then used in the minimum variance framework to provide posterior statistics of optical attenuation coefficient $\mu$. Similar to the previous experiment, we considered SNR = 25 while using the minimum variance framework. Figure 13(a) represents the convergence of mean and variance of $\mu$ estimates with varying amounts of readout lines. Similar to the previous example, we performed a global optimization to find the value of $\mu$ that results in the least discrepancy between the predicted and fully sampled temperature measurement data (over the ROI). This is shown with a dashed black line in figure 13(a). As is evident in the figure, the mean estimate of $\mu$ approached to its optimal value as the number of readout lines increased. The posterior estimate of the temperature map over one of the slices, obtained using optimally acquired $k$-space points, is shown in figure 13(b).

### 3.2.1 Comparison with other undersampling schemes

We also performed model-data fusion using 2 other sets of data observations, which were obtained using rectilinear and variable-density Poisson undersampling techniques. These points are shown in figure 14. Note...
that the same number of points, i.e. 100 readout lines, were used for data acquisition for each scheme. In the rectilinear scheme, lines were homogeneously distributed over the \( k_{x} - k_{y} \) plane, whereas most of the lines were concentrated in the center of the \( k_{x} - k_{y} \) plane with variable-density Poisson disk undersampling. A summary of the information content of each acquisition scheme was calculated according to equation (13) and is provided in table 7.
3.2.2. Error analysis. Figure 15 illustrates the discrepancy between the posterior temperature estimate and the temperature data acquired from fully sampled $k$-space over one of the slices, using different data acquisition techniques. As is evident in the figure, rectilinear undersampling performed the worst (highest maximum error values) among the applied techniques. Variable-density Poisson disk undersampling performed better than rectilinear scheme, but it resulted in slightly higher maximum error values over the 9th slice than the proposed approach.

Similar to the previous examples, we studied the effect of increasing data observations on the performance of the proposed approach. Figure 16 represents the RMSE between the posterior temperature estimate and the acquired temperature data from fully sampled $k$-space with varying amounts of readout lines used for data acquisition. As expected, RMSE was reduced as the number of readout lines increased.

Finally, Table 7 represents the RMSE (over all voxels inside the ROI) between temperature estimates and acquired temperature data, with a varying number of readout lines and different data acquisition schemes. Note that the RMSE value did not change during the rectilinear undersampling. This is expected because none of the acquired $k$-space points in rectilinear undersampling covered regions with high information content.

### Table 6. Phantom experiment: parameter values involved in sensor model (Stafford et al 2004, Duck 2013, Vesanen et al 2013).

| Parameter          | Value       |
|--------------------|-------------|
| $\theta$ (degree)  | 5           |
| $T_1$ (seconds)    | $2.56 + 0.1\Delta u$ |
| $T_2^*$ (ms)       | 30          |
| $\Delta\omega_0$ (radians) | 0          |
| $T_E$ (ms)         | 1.676       |
| $T_R$ (ms)         | 5           |
| $\gamma$ (MHz Tesla$^{-1}$) | 42.58     |
| $\alpha$ (ppm C$^{-1}$) | -0.0102 |
| $B_0$ (Tesla)      | 3           |
| $u_0$ ($^\circ$C) | 19          |

### Table 7. Phantom experiment: convergence of RMSE (over all the voxels inside the ROI) and information content, equation (13), given varying amounts of $k$-space samples for model-data fusion (numbers over the columns on the right indicate the number of readout lines). Prior values of error are provided as a reference (with zero observations).

| Technique                                | 0     | 5     | 20    | 50    | 100   |
|------------------------------------------|-------|-------|-------|-------|-------|
| Proposed technique                       |       |       |       |       |       |
| RMSE °C                                  | 2.6682| 2.5149| 2.3814| 2.3301| 2.3205|
| IC equation (13)%                       | 52.12%| 88.99%| 98.69%| 98.69%|       |
| Rectilinear undersampling                |       |       |       |       |       |
| RMSE °C                                  | 2.6682|       |       |       |       |
| IC equation (13)                         |       | 3.76% |       |       |       |
| Variable-density Poisson disk undersampling |     |       |       |       |       |
| RMSE °C                                  | 2.4014|       |       |       |       |
| IC equation (13)                         |       | 24.00%|       |       |       |
was mainly concentrated in the center of the $k$-space). Hence, almost no information was obtained by performing the model-data fusion. Also, as can be seen in table 7, the proposed technique resulted in similar values of RMSE compared to those obtained with the variable-density Poisson disk undersampling method.

3.3. Planar image reconstruction

The performance of the proposed subsampling approach was retrospectively validated in fully sampled planar temperature imaging acquired during the thermal ablation process in vivo in the human brain. The LITT procedure (power = 11.85 watts for a period of 94s) was monitored in real-time using the temperature-sensitive PRF shift technique acquired with a 2D spoiled gradient-echo to generate temperature measurements using a GE scanner at every $\Delta t = 5$ s ($T_R/F_A = 38 \text{ ms}/30^\circ$, frequency × phase = $256 \times 128$, FOV = $26 \text{ cm}^2$, BW = 100 Hz pixel$^{-1}$, slice thickness = 5 mm). Figure 17 shows the position of the tumor and the
temperature resulting from laser irradiation in the region. Equation (4) was used to model the MR signal. Numerical values of the parameters involved in the sensor structure are shown in table 8. As shown in table 8, we assumed $T_1$ to be a linear function of tissue temperature (Rieke and Butts Pauly 2008) to incorporate the possible changes in its value caused by heating. The value of $T_1$ at body temperature, denoted $T_1^0$, was considered to be 1.05 s. Also, a

**Figure 14.** Phantom experiment: acquired $k$-space points used for data observation ((a) and (b)) rectilinear scheme, ((c) and (d)) variable-density Poisson disk undersampling. (a) 3D view. (b) Projection over $k_x - k_y$ plane. (c) 3D view. (d) Projection over $k_x - k_y$ plane.

**Figure 15.** Phantom experiment: the error between the posterior estimate and actual measurement of temperature field over the 9th slice, using (a) the proposed approach, (b) rectilinear undersampling, and (c) variable-density Poisson disk undersampling (ROI = 18 mm × 13 mm × 26 mm).
normalized MR image (without any heating involved) was used to incorporate the effect of inhomogeneities in magnetization $M(x)$. Here, we assumed that the optical attenuation coefficient $\mu$ was spatially homogeneous and uniformly distributed between 100 $\frac{1}{m}$ and 400 $\frac{1}{m}$ (Fahrenholtz et al 2015), i.e. $\mu \sim \mathcal{U}[100, 400]$. Note that $\mu$ is the only uncertain parameter while solving the Pennes bioheat equation; all other parameters are assumed to be known from the physical properties of the tissue, table 2. A set of 15 Gauss–Legendre quadrature points (Hildebrand 1987) (which accurately integrate up to the 29th order polynomials), spread over the range of uncertain parameter $\mu$ values, were
used to quantify the uncertainty in the temperature field. Figure 18 illustrates the mean and standard deviation of the associated temperature field within the (ROI).

The proposed technique in section 2.3 was used to approximate the observation points on $k$-space with the largest information content. Given uncertainties in the model, as shown in equation (1), figure 19(a) shows 20 readout lines that are predicted to have the highest variance in data acquisition. Note that as expected, readout lines passed through the points in the center of the $k$-space, i.e. the points with the greatest information content. This corroborates the fact that the points in center of the $k$-space contain more information regarding the main features of the image.

The predicted $k$-space measurements were then retrospectively extracted from the fully sampled data and used in a minimum variance framework to estimate posterior statistics of parameter $\mu$, as described in appendix B. We considered SNR = 25 while using the minimum variance framework. Figure 20(a) demonstrates the convergence behavior for the mean and variance of $\mu$ for a varying number of observations. Note that only $\frac{20}{250} \approx 0.08$ of the total number of readout lines on $k$-space were used for estimation of $\mu$. This results in a speedup factor of 12 (based on the number of selected readout lines divided by the total number of readout lines) compared with full-sampling of $k$-space, as shown in figure 19(a).

As a reference, a global optimization to find the value of $\mu$ that results in the least discrepancy between the predicted and fully sampled temperature measurement data was performed. This is shown with a dashed black line in figure 20(a). Results obtained using the proposed

| Parameter | Value |
|-----------|-------|
| $\theta$  | $\pi/6$ radians |
| $T_2^*$    | 70 ms |
| $T_E$      | 20 ms |
| $\gamma$   | 42.58 MHz Tesla$^{-1}$ |
| $\alpha$   | $-0.0102$ ppm C$^{-1}$ |
| $B_0$      | 1.5 Tesla |
| $T_1$      | $T_1 = T_1^0(1 + 0.01\Delta \mu)$, $T_1^0 = 1.05$ ms |

Figure 18. Planar image reconstruction: statistics of temperature field over ROI (ROI = 55 mm x 60 mm), resulting from uncertain $\mu$. (a) mean (°C), (b) standard deviation (°C).
approach converged with the result obtained using the global optimal and fully sampled techniques.

The posterior estimate of $\mu$ was then used in the Pennes bioheat equation to estimate the temperature field of the tissue. Figure 20(b) illustrates the posterior estimate of the temperature field.

### 3.3.1. Comparison with other undersampling schemes.

Similar to the previous example, we used rectilinear and variable-density Poisson undersampling techniques for $k$-space data acquisition. Figures 19(b) and (c) show 20 readout lines, generated based on rectilinear and variable-density Poisson disk undersampling techniques, respectively. Using equation (13), the relative information content of each acquisition was $IC_{\text{model}} = 92.1\%$, $IC_{\text{uniform}} = 14.6\%$, and $IC_{\text{poisson}} = 44.2\%$.

Given each data acquisition scheme, the predicted $k$-space measurements were used in a minimum variance framework to estimate posterior statistics of parameter $\mu$. The obtained posterior estimate of $\mu$ was then used in the Pennes bioheat equation to estimate the temperature field of the tissue.
3.3.2. Error analysis. The error (calculated over ROI) between the posterior estimate of the temperature field and the actual temperature map is illustrated in figure 21. It is clear from figure 21 that the proposed technique resulted in less error compared with both rectilinear and variable-density Poisson disk undersampling. Note that with the proposed method most of the error occurred at the edge of ROI owing to the presence of artifacts, whereas a considerable amount of error occurred in the center of the ROI with rectilinear or Poisson disk undersampling.

Figure 21. Planar image reconstruction: (a) error between the posterior estimate and the actual measurement of temperature field, obtained using the proposed technique. Note that the maximum error occurred over the regions close to the border. The high value of error in regions near the border of the figure is due to the presence of artifacts in MR temperature data. (b) Error between the posterior estimate and actual measurement of temperature field, obtained using rectilinear undersampling. (c) Error between the posterior estimate and actual measurement of temperature field, obtained using variable-disk Poisson disk undersampling. Note the substantial amount of error in the center of ROI for cases (a) and (b) (ROI = 55 mm × 60 mm). RMSE indicates root-mean-square error.

Figure 22. Planar image reconstruction: convergence of RMSE (calculated over ROI) between the acquired temperature map from fully-sampled $k$-space and temperature estimate (obtained from the proposed technique). Note that a major portion of RMSE is due to the presence of artifacts.
To study the effect of the number of data observations on performance of the proposed technique, we calculated the RMSE between the estimated and fully-sampled temperature field figure 22. In general, the value of RMSE was reduced as the number of readout lines increased. Note that a major portion of RMSE was due to the presence of artifacts.

4. Discussion

The presented approach demonstrates that locations with high-information content with respect to a model based reconstruction of MR thermometry may be quantitatively identified. The information locations identified are a consequence of the physics based modeling of the laser induced heating and an intelligent characterization of the measurement uncertainties of the acquisition system. We further demonstrated that our mathematical model of MR thermometry acquisition may be refined using this set of judiciously selected data observations to reconstruct the thermal image. Intuitively, the accuracy and confidence of the thermal image reconstruction depends on multiple factors, including accuracy, information content, and the number of data observations. However, in each example, the presented approach created an accurate assessment of temperature data using only a subset of the full k-space data. As can be seen in figures 5(b), 20(a) and 13(a), the measurement locations chosen sufficiently reduced the posterior variance of model parameters needed to create an accurate thermal image reconstruction.

Generally, accurate temperature image reconstructions were observed in the subsampled examples figures 9, 21 and 15. Within the context of the model-data fusion, the accuracy of the Pennes bioheat equation based temperature estimations was improved by the measurement locations identified by our technique. Quantitatively, the posterior value of RMSE was less than its prior value. While the model based reconstructions are not corrupted with ‘noise’ artifacts in the traditional sense, the model based reconstruction is subject to bias from modeling errors. Intuitively, most of errors in the reconstruction may be attributed to artifacts that were not represented in the composite sensor model. For example, errors were primarily expected in neighborhood regions of the laser fiber where improved fidelity modeling of the boundary conditions are needed to account for nonlinearities at high temperatures. Ideally, RMSE modeling accuracy should be comparable to previously measured accuracy (∆1 °C) in temperature imaging (Stafford et al 2004). The RMSE observed in our model predictions may be limited by the the linear update scheme used, appendix B. Further work may consider trade-offs between improvements in model fidelity versus nonlinear parameter update schemes.

Currently, MR thermometry is acquired primarily through quantitative phase-sensitive techniques based on the PRF shift. Compared with current PRF techniques, the benefit of the proposed model-based approach is that the predicted locations of high information content represent a fraction of the fully sampled k-space observations. This implies that an accurate thermal image may be reconstructed in less time. Furthermore, the typical PRF approach is susceptible to errors from low SNR, tissue susceptibility changes, magnetic field drift, excessive heating, and modality-dependent applicator induced artifacts (Depoorter et al 1994, Poorter 1995, Kuroda et al 1997, de Zwart et al 1999). The potential data corruption and resulting information loss undermines the confidence and quality of the treatment guidance decisions provided by MR thermometry. The presented model-based approach provides a rigorous framework to include a model for each source of data corruption artifact. Improved temperature estimate accuracy in the presence of the various sources of image contamination will facilitate a safer,
more conformal laser treatment that can be performed in a variety of circumstances in which critical structures may have previously limited the use of conformal laser treatment.

Here, we pursued a computationally tractable approximation of entropy and used the concept of variance maximization to identify optimal $k$-space readout lines. It should be noted that different orders of truncation can be used to approximate the entropy in equation (A.3). Clearly, higher-order approximation with more moments leads to more accurate approximation of entropy. However, the downside of using higher-order terms is that one needs to find the corresponding coefficients for each term. Finding corresponding coefficients requires solving an optimization problem, which could increase the computational cost of the whole procedure. Hence, lower-order approximation of entropy is of more interest for real time applications of the proposed technique.

Incorporating direct parameterizations of $k$-space readout trajectories will provide the most physically meaningful models with respect to the underlying MR physics. However, given the nonlinearities in our physics model, this is computationally prohibitive. In general, maximizing the mutual information between $n$ locations over $k$-space and our thermal image model (with $m$ unknown parameters) would result in $m+n$ dimensional integrals to evaluate the mutual information, which can be computationally expensive owing to often large values of $n$. More advanced numerical methods such as Markov chain Monte Carlo techniques (Gilks 2005) for numerical integration combined with such as multi-spatial resolution calculations of the nonlinear signal model will be needed to evaluate these integrals.

We emphasize that the measurement modeling techniques presented is a general methodology that can be used with all MR-compatible thermal delivery modalities. Steady state temperature models of MRgLITT were used in the current study as a vehicle to focus modeling efforts. These models essentially represent the maximum heating time point and are a good approximation for the thermal damage (Yung et al 2010, Fahrenholtz et al 2015). These methods may be extended to incorporate transient effects and investigate sampling schemes that accurately track changes over time that are sparse with respect to sparsifying operators on the temperature field (Yan et al 2014). The methodology may also be extended to incorporate tissue motion models for thermal therapy monitoring in moving tissues of the abdomen, such as liver or kidneys (de Senneville et al 2016). The motion models would need to incorporate nonlinear changes of the MR signal induced by both tissue motion and magnetic field changes governed by Maxwell’s equations for magnetostatics (Salomir et al 2012). Moreover, current models, equation (6), consider the signal acquisition as a spoiled gradient echo at an effective echo time. Higher fidelity modeling of the signal acquisitions models and potential artifacts resulting from advanced acquisitions, such as multi-shot EPI (Stafford et al 2004), may also improve accuracy of the signal predictions.

5. Conclusion

In summary, we have presented a model-based information theoretic approach to improve the efficiency of MR thermometry for monitoring MRgLITT procedures. The approach approximates measurement locations in $k$-space with the highest information content with respect to the thermal image reconstruction. The performance of these predicted measurement locations was demonstrated retrospectively in agar phantom, in vivo, and in silico imaging and is likely to reduce the number of $k$-space measurements needed to accurately reconstruct the thermal image.
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Appendix A. Entropy approximation

On the basis of information theory, the entropy of $U$, denoted by $h(U)$, is defined as:

$$ h(U) = - \int \ln(p(U)) p(U) \, dU $$

(A.1)

where $p(U)$ is the probability density function of $U$. To proceed with maximizing the entropy $h(U)$, we first note that on the basis of maximum entropy principle (Cover and Thomas 2012), the probability density function $p(U)$ can be parametrized in terms of its central moments as

$$ p(U) = \lim_{l \to \infty} \left\{ \sum_{\lambda=0}^\infty \lambda^l \frac{(U-\hat{U})^l}{l!} \right\}, \quad \lambda \in \mathbb{R} $$

(A.2)

where $\hat{U}$ is provided by equation (7). By substituting equation (A.2) in equation (A.1), we have:

$$ h(U) = - \int_U \lim_{l \to \infty} \left\{ \sum_{n=0}^\infty \lambda_n (U-\hat{U})^n \right\} p(U) \, dU $$

$$ = \lim_{l \to \infty} \left\{ -\lambda_0 - \sum_{n=2}^l \lambda_n m_n(U) \right\} $$

(A.3)

where $m_n$ values are the central moments of $U$, defined by equation (7). Hence, entropy of $p(U)$ can be described in terms of its central moments, as shown in equation (A.3). Now, by approximating $p(U)$ with its first 2 moments and truncating the above expansion (i.e. letting $l = 2$), we have

$$ h(U) \approx -\lambda_0 - \lambda_2 m_2(U), \quad \lambda_0, \lambda_2 \in \mathbb{R} $$

(A.4)

Appendix B. Model-data fusion

Once, the most useful measurement data are extracted through the proposed technique, one can combine these data with model predictions to improve the level of confidence about the uncertain parameters and consequently temperature estimates.

Various approaches exist to perform model-data fusion (Fuentes et al 2012, Madankan et al 2014a, 2016). Here, we employ a linear unbiased minimum variance estimation method for this purpose. In detail, the minimum variance technique is used to minimize the trace of the posterior parameter covariance matrix:

$$ J = \min_\mu \text{Tr} [ \mathcal{E}[(\mu - \mathbb{E}[\mu])(\mu - \mathbb{E}[\mu]^T)] ] $$

(B.1)
where \( \mu = [\mu_1, \mu_2, \cdots, \mu_d]^T \) denotes optical attenuation coefficients for \( d \) tissues. Note that the minimum variance formulation is valid for any probability density function, although the formulation uses only the mean and covariance information. It provides the maximum a posteriori estimate when model dynamics and the measurement model are linear and state uncertainty is Gaussian. Minimizing the cost function \( J \) subject to the constraint of being an unbiased estimate, as well as using linear updating, results in the first 2 moments of the posterior distribution (Gelb 1974, Madankan et al 2013, 2014a, 2016):

\[
\hat{\mu}^+ = \hat{\mu}^- + K [z - E^-[ U(u, \mu)]]
\]

\[
\Sigma^+ = \Sigma^- - K \Sigma_{d\ell} K^T
\]

where \( z = [z_1, z_2, \cdots, z_N]^T \) is the measurement vector of \( N \) observations and the gain matrix \( K \) is given by

\[
K = \Sigma_{\nu c}(\Sigma_{d\ell} + R)^{-1}
\]

Here, \( \hat{\mu}^- \) and \( \hat{\mu}^+ \) represent prior and posterior value of the mean for the parameter vector \( \mu \), respectively:

\[
\hat{\mu}^- \triangleq E^-[\mu] = \int_{\xi} \mu^-([\xi]) p(\xi) d\xi
\]

\[
\hat{\mu}^+ \triangleq E^+[\mu] = \int_{\xi} \mu^+([\xi]) p(\xi) d\xi
\]

Similarly, the prior and posterior covariance matrices \( \Sigma^- \) and \( \Sigma^+ \) can be written as:

\[
\Sigma^- \triangleq E^-[ (\mu - \hat{\mu}^-)(\mu - \hat{\mu}^-)^T ]
\]

\[
\Sigma^+ \triangleq E^[ (\mu - \hat{\mu}^+)(\mu - \hat{\mu}^+)^T ]
\]

Also, diagonal matrix \( R \) denotes the measurement error covariance matrix in equation (B.4) which encapsulates the measurement’s inaccuracies. Note that \( R_{ii} = \sigma^2 \). The matrices \( \Sigma_{\nu c} \) and \( \Sigma_{d\ell} \) are defined as:

\[
\hat{U}^- \triangleq E^-[ U(u, \mu)] = \int_{\xi} \frac{U(u(\xi), \mu^-([\xi])) p(\xi) d\xi}{U}
\]

\[
\Sigma_{\nu c} \triangleq E^-[ (\mu - \hat{\mu})(\hat{U} - \hat{U}^-)^T ]
\]

\[
\Sigma_{d\ell} \triangleq E^[ (\hat{U} - \hat{U}^-)(\hat{U} - \hat{U}^-)^T ]
\]

where, the expectation integrals in equations (B.9)–(B.11) can be computed using suitable quadrature rules.

**Appendix C. Model-based image reconstruction**

After accurate estimation of uncertain parameters using the proposed approach, one can refine the Pennes bioheat model using obtained posterior mean of uncertain \( \mu \), i.e.
\[
\rho \left( \frac{\partial u}{\partial t} + \nabla \cdot (u \mathbf{v}) \right) - \nabla \cdot (\lambda (u, x) \nabla u) + \omega (u, x) c_{\text{blood}} (u - u_a) = Q_{\text{laser}} (x, t), \quad \forall x \in \Omega
\]

\[
Q_{\text{laser}} (x, t) = P(t) \hat{\mu}^+ e^{-\frac{1}{8} \| x - x_0 \|^2}
\]

\[
u (x, 0) = u_0 (x), \quad x \in \Omega
\]

\[
u (x, t) = u_0 (x), \quad x \in \partial \Omega_0
\]

\[
-\lambda (u, x) \nabla \cdot u (x, t) = g_N (x), \quad x \in \partial \Omega_N
\]

\[
-\lambda (u, x) \nabla \cdot u (x, t) = \delta (u - u_\infty), \quad x \in \partial \Omega_c
\]

where \( \hat{\mu}^+ \) is the posterior mean of uncertain parameter \( \mu \), obtained from the model-data fusion, equation (B.2). The reconstructed image from equation (C.1) is a data-informed temperature estimate.

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