

Radiofrequency Safety Modelling of Parallel Transmit Magnetic Resonance Imaging



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A thesis submitted for the degree of Doctor of Philosophy
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Abstract

Radio-frequency (RF) safety plays an important role in Magnetic Resonance Imaging (MRI) with the goal of assuring patient safety and preventing excessive RF heating. Historically, RF safety in MRI has been monitored using pre-calculated specific absorption rate (SAR) limits which indicate the amount of energy that can be delivered safely to the subject. Electromagnetic (EM) simulations have usually been performed to assess the electric field and RF energy levels that are experienced by the subject. In order to validate these EM simulations, the distribution of radio-frequency (B1) field can be measured experimentally, and compared with simulation results. Also, the measurement of temperature in phantom and animal models has been used to assess RF heating directly and validate the EM simulations.

Well-characterized phantom models are needed to assess RF heating experimentally. Meat phantoms can be used for RF heating tests, but these are difficult to store and challenging for their shape to be well described. Agar-gel phantoms can also be used for RF heating tests, in which one can control their dielectric properties with use of carefully controlled ingredients, such as NaCl and polyethylene powder to achieve specific conductivity and permittivity values. Once a phantom is made, the dielectric properties can be verified experimentally using an open-ended coaxial cable.

A number of EM simulation methods have been proposed, which help one understand EM field phenomena in high-field MRI. But there are still many questions remaining which need to be further studied, including better characterization of thermal behaviours. In Chapter 3, three simulation methods are compared against experimental thermal elevation measures.

A framework of validating EM simulations using Proton Resonance Frequency Shift (PRF) based MR thermometry in the context of parallel transmit (pTx) MRI is described in Chapter 4. Also described in this chapter is a 3D gradient-echo sequence used to monitor temperature-induced phase shifts, as well as the required image reconstruction techniques and field-stabilisation methods.

The need for personalised SAR models has arisen quickly, especially in ultra-high-field pTx studies. Use of a safety margin of 1.5 (150%) to account for morphometric differences across the population has been reported previously. To reduce the need for overestimation, the development of a personalized SAR models using non-linear registration is described in Chapter 5 and assessed for robustness using three 'standard' models.

Finally, the practical advantages of using the personalised model in pTx MRI are discussed in Chapter 6. With the aid of high computing capacity the personalised model approach could help MRI users reduce safety margins, so that the scanners can operate closer to the true SAR limits representing the subject in the scanner.

Acknowledgements

First of all, I would like to thank the Old Members' Trust at University College Oxford for supporting my stipend with an Oxford Radcliffe Scholarship, as well as the Clarendon Scholarship for covering my tuition and college fees. Without your support I could not have initiated my studies in Oxford. I also would like to thank the Ministry of Food and Drug Safety in South Korea, which allowed me to suspend my job and supported me with partial wages for two years. Although I have decided to pursue my career in academia instead of returning to the job, I shall/will never forget the support from the Korean government. I hope in the future to repay the support I have been given by creating a scholarship for Korean students with poor financial means to aid their study abroad.

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Preface

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List of Publications Arising from this Thesis

Journal Articles

1. **H Jeong**, M Restivo, P Jezzard, and AT Hess. Platform for validation of parallel transmit RF coil simulations using proton resonance frequency shift (PRF)-based MR thermometry. Submitted for publication.
2. **H Jeong**, J Andersson, AT Hess, P Jezzard. A personalized SAR model for subject-specific RF safety. In preparation.

Conference Proceedings

1. **H Jeong**, AT Hess, and P Jezzard. Assessment of simulated RF heating by comparison with temperature measurement. In *Proceedings of the 3rd International Congress on MRI (ICMRI) & the 20th Annual Scientific meeting of KSMRM*, Seoul, South Korea, 2015 (abstract P052)
2. **H Jeong**, K Papoutsis, P Jezzard, and AT Hess. Faster B1 Field and SAR Estimation in Parallel Transmit Arrays without Tuning using Voltage Sources. In *Proceedings of the 23rd Annual Meeting of ISMRM*, Toronto, Canada, 2015 (abstract 1873)
3. **H Jeong**, P Jezzard, and AT Hess. MR Phantom Design for Assessment of RF Heating at 7 tesla, In *Proceedings of the 21st Annual Meeting of BCISMRM*, London, United Kingdom, Sep 9-11, 2015
4. **H Jeong**, A Hess, and P Jezzard. Investigation of the resolution effects on electro-magnetic simulation in MR safety researches", In *Proceedings of the 4th International Congress on MRI (ICMRI) & the 21st Annual Scientific meeting of KSMRM*, Seoul, South Korea, 2016 (abstract P59)

5. **H Jeong**, P Jezzard, and AT Hess. Comparing RF heating simulations and experimental results in pTx coils: an evaluation of three simulation methods, In *Proceedings of the 24th Annual Meeting of ISMRM*, Singapore, 2016 (abstract 2219)
6. **H Jeong**, AT Hess, P Jezzard. Modelling the RF safety of tattoo pigment ink for subjects undergoing 7 Tesla MRI, In *Proceedings of the 24th Annual Meeting of ISMRM*, Singapore, 2016 (abstract 2221)
7. **H Jeong**, J Andersson, AT Hess, P Jezzard. A personalised SAR model for subject-specific RF safety", In *Proceedings of the 25th Annual Meeting of ISMRM*, Honolulu, USA, 2017 (abstract 0479)
8. **H Jeong**, P Jezzard, AT Hess. Optimisation of RF heating assessment at 7 Tesla with proton resonance frequency (PRF)-MR thermometry. In *Proceedings of the 34th Annual Scientific Meeting of ESMRMB*. Barcelona, Spain, 2017 (abstract 282)
9. **H Jeong**, M Restivo, P Jezzard, AT Hess. Platform for Validating pTx RF Coil Simulations Using Proton Resonance Frequency Shift MR Thermometry. In *Proceedings of the Joint Annual Meeting of ISMRM-ESMRMB*, Paris, France, 2018 (abstract 4394)

1 Aims and Thesis Overview

1.1 Motivation of Project Aims and Thesis Direction

The radio-frequency (RF) energy used in magnetic resonance imaging (MRI) is non-ionising, thus the effects to human tissues are generally weak, but can elevate the temperature of tissue in subjects due to the radio-frequency range being used. Direct temperature monitoring is not usually performed during MR imaging due to patient inconvenience and the complexities of thermal patterns in perfused tissue, although temperature elevation can in theory be captured during an MRI examination using Proton-Resonance Frequency (PRF) shift based MR thermometry. Whilst some studies are ongoing to develop such methods to monitor temperature during scanning, this is still a challenging task in practice, and does not easily measure absolute temperature.

While studies on temperature monitoring methods during experiments are still under development, there are established procedures to estimate the delivered energy deposition to the patient per unit mass, known as specific absorption rate (SAR) (1–3). A method to simulate SAR with different parameters and conditions to verify sensitivities to each parameter has been demonstrated (4), which demonstrated the requirement of widely accepted safety margins according to known inaccuracies. Although, each simulation solves Maxwell’s equations to estimate the electric field (E-field) and the B_1 transmit field, small differences in practical conditions can change the result, so that a proper validation method is required. Proper characterization of the sample’s dielectric properties also plays an important role, so the careful design and measurement of phantom studies are required.

In this thesis, a method of assessing RF safety in parallel transmit (pTx) MRI is developed and discussed. To accomplish this a robust workflow of RF safety assessment is described from experimental measures to computational simulation. A well-characterised cylindrical phantom is proposed in the thesis, which was targeted to have similar dielectric properties to the human brain using agarose, NaCl, and polyethylene powder. The dielectric properties of the phantom were measured using a reflection method with an open-ended coaxial probe. The measured dielectric properties were then used in EM simulations so that the level of errors arising from uncertainties in the dielectric properties could be reduced. In this thesis, methods are described to measure the dielectric properties of the phantom and EM simulations and performed using the commercial software package Sim4Life (ZMT Medtech, Switzerland).

Although there is an existing robust RF safety assessment workflow, there remain uncertainties generated from the subject's or patient's morphometric differences, which require additional safety margins in actual MRI scans. In this thesis, a method is proposed to generate a personalised voxel model for RF safety simulation, and this is subsequently assessed in the context of a pTx MRI system. Linear and non-linear registration methods were used to align a high-resolution electromagnetic voxel model onto a subject-specific model, and the differences in SAR prediction are compared in diverse B_1 shimming conditions for a pTx system. Furthermore, practical ways to generate subject-specific voxel models are proposed, which use T1-weighted MR images to warp a high-resolution voxel model into subject-specific space.

It is hoped that these projects will contribute to having a greater confidence in RF safety assessment in MRI research leading to more efficient use of available

hardware and more accurate results.

1.2 Overview of the Thesis

The thesis contains the following contents across seven chapters.

- Chapter 1: Aims and thesis overview
- Chapter 2: Background theory and current methods in the literature
- Chapter 3: Assessment of the validity of different RF coil simulations
- Chapter 4: RF heating assessment of a pTx head array coil
- Chapter 5: Development of a personalized voxel model: Validation of non-linear registration
- Chapter 6: Practical utility of the personalized voxel model
- Chapter 7: Discussion and conclusions

Chapter 1 describes the aims of this thesis and its overview. Chapter 2 explains the background theory and reviews the relevant literature, from the general background of magnetic resonance imaging, to radio-frequency coils and their safety. Chapter 3 describes several ways to assess electro-magnetic simulations and uncertainties caused by parameters and conditions used in the simulations. Chapter 4 describes the experimental aspect of RF heating assessment. This chapter explains how to design a phantom for RF heating assessment and characterize the dielectric properties of the phantom. Chapter 5 describes a method to create a personalised voxel model and its evaluation method along with information about the required image reconstruction, tools for registration and the registration process itself. The practical utility of the personalised voxel model is described in Chapter 6. SAR evaluation using the proposed personalized model is discussed, and the way in which the personalized

voxel model can be used is described in this chapter. Finally, in Chapter 7, a general discussion and conclusions are provided and future work is also proposed. Each chapter will be composed in the format of introduction, methods, results, discussion and conclusion.

2 Background Theory and Current Methods in the Literature

2.1 Magnetic Resonance Imaging

The nuclear induction phenomena was first discovered in 1946 by Bloch et. al. of Stanford University and Purcell et al. of Harvard University by adjusting the main magnetic field using a fixed RF (5,6). The phenomenon was later studied by Erwin Hahn as an oscillating signal when an RF field is pulsed on and off at the Larmor frequency within a constant main magnetic field, the observation of which is known as a free induction decay (FID) or nuclear magnetic resonance (NMR) signal (7).

In 1973, Paul Lauterbur identified that spatially varying gradients can be used to reconstruct images from nuclear magnetic resonance (NMR) signal, called projection NMR Tomography (8). NMR uses the natural phenomena of atomic nuclei to resonate in a magnetic field when they have an odd number of protons and/or neutrons. Due to the abundance of water in the human body, hydrogen nuclei, containing a single proton, are the nuclei of choice for imaging. Using a strong main magnetic field, B_0 , there is a tendency for the protons to align to the direction of B_0 where they are otherwise randomly oriented. Protons remain in equilibrium in the presence of a main magnetic field (B_0). However, when an oscillating magnetic field, B_1 , is applied perpendicularly to B_0 at the protons' Larmor frequency, ω , they rotate around an axis perpendicular to the main magnetic field, this rotational movement is called precession.

The Larmor frequency is proportional to the main magnetic field B_0 , so that the higher the main magnetic field strength, the higher will be the Larmor frequency, given by:

$$\omega = \gamma B_0 \quad (2.1)$$

where $\gamma = 42.58 \text{ MHz/T}$ is the gyro magnetic ratio of protons, and B_0 is the main magnetic field.

There are numerous excellent text books on MRI (9,10) in which thorough explanations can be found. Magnetic resonance imaging (MRI) uses static and oscillating magnetic fields to non-invasively image the human body. With increasing strength of the main magnetic field there is an increased tendency for protons to align which in turn increases the net magnetization observed in the NMR signal. The NMR signal scales as B_0^2 ; a factor of B_0 due to the magnetization increase, and a factor of B_0 due to the increased induced voltage due to a higher Larmor frequency (11). However, the thermal noise also increases proportionally to B_0 such that the net benefits of signal-to-noise ratio for ultra-high-field MRI (≥ 7 Tesla) is proportional to B_0 by assuming that the coil losses are negligible (11,12). Also, SAR deposition via RF radiation goes up with B_0^2 , which needs to be carefully assessed to assure safety of the scan.

There are two predominant types of relaxation processes in NMR, firstly a longitudinal relaxation process called spin-lattice (T_1) relaxation, which is the time for spins to return to their equilibrium status. Secondly a transverse relaxation process called spin-spin (T_2) relaxation, which is the time for the observable FID to disappear. The idea of using magnetic relaxation times to differentiate different tissues was introduced by Raymond Damadian in his paper to separate six different tissues (13). Images collected with different T_1 and T_2 weighting can produce different tissue contrast. This means that different imaging techniques are to be chosen for the specific needs of a study. At higher main magnetic field, a higher longitudinal relaxation time (T_1) is expected (14). The T_1 - and T_2 - weighted image

contrast can be produced by choosing a different duration of echo time (TE) and repetition time (TR). TE is the time between the RF pulse and echo signal, whereas TR is the time between subsequent excitation RF pulses applied to the same slice. By having different combinations of TR and TE, different image contrast can be achieved (14–16). $T2^*$ defines the observed decay of an FID, observed in gradient-echo (GRE) sequences. $T2^*$ is shorter than $T2$, and is predominantly a result of local magnetic field inhomogeneity. These effects of field inhomogeneity that contribute to $T2^*$ can be refocused using a 180 degree flip-angle pulse as in a spin-echo sequence (17). By using spin-echoes and manipulating the timing of the pulse sequences, different tissue contrasts can be achieved. Erwin Hahn discovered the phenomenon of an RF echo in 1949, which can be observed when transmitting multiple RF pulses (i.e. spin-echo). The concept of a spin echo signal acquisition is to realign transverse magnetization to obtain spin-phase information which is lost during the decay of the FID. The spin-echo sequence uses a 180 degree pulse to refocus magnetisation vectors as described in Figure 2.1.

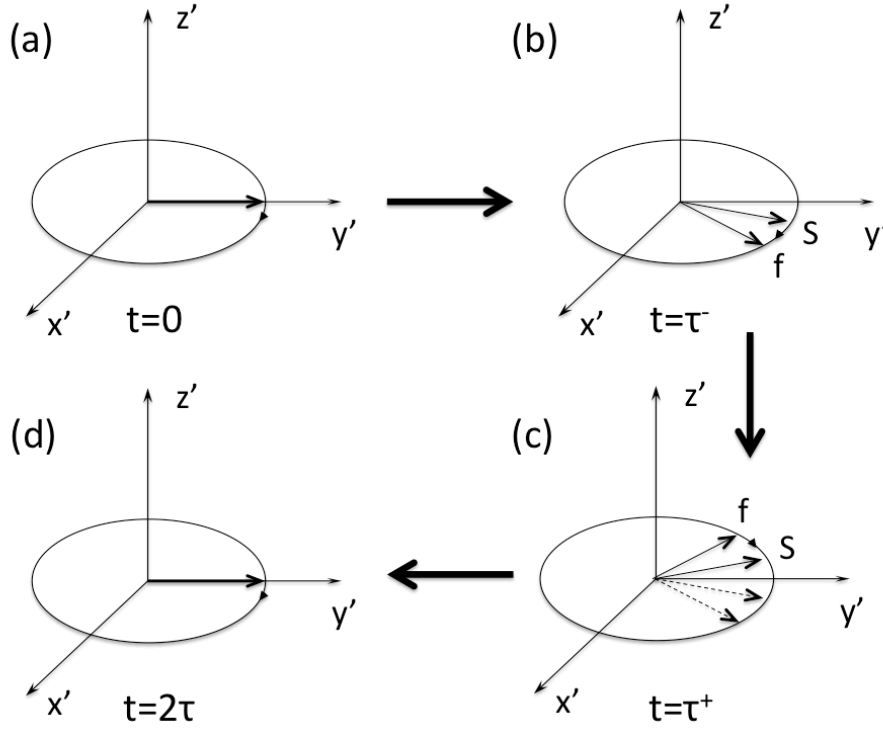


Figure 2.1: Vector diagram illustrating the refocusing of magnetisation in a spin-echo experiment, taken from Liang *et al.* 2000. Reproduced with permission.

Peter Mansfield introduced a way of using field gradients for slice selection (18),

which was incorporated into pulse sequences for 2D imaging and later further developed to achieve 3D imaging.

Gradient coils provide a mechanism to spatially vary the magnetic field and thus the Larmor frequency in three dimensions, a Fourier-transform can then be used to reconstruct the image. The magnetic field gradient system is composed of three orthogonal gradient coils made with loops of wire or a thin conductive sheet arranged on a cylindrical surface, inserted inside of the main MRI magnet. By applying a current in the gradients, a secondary magnetic field is produced resulting in a predicted alteration in the main magnetic field. A spatial variation of resonance frequency can be caused in any of the three dimensions by the gradients, which are used for selective excitation (or reception) and spatial encoding of the MR signal.

Equation (2.1) can be rewritten as Equation (2.2) when secondary magnetic field

gradients are applied:

$$\omega_i = \gamma(B_0 + \mathbf{G} \cdot \mathbf{r}_i) \quad (2.2)$$

where ω_i is the frequency of the proton at position $\mathbf{r}_i$, B_0 is the main magnetic field, $\mathbf{G}$ is a vector representing the total gradient amplitude and direction, and $\mathbf{r}_i$ is the position of proton.

The x-, and y-gradients provide a linear variation of the z-component of the magnetic field as seen in equation (2.3):

$$G_x = \frac{\partial B_z}{\partial x}, G_y = \frac{\partial B_z}{\partial y}, G_z = \frac{\partial B_z}{\partial z} \quad (2.3)$$

where G_x, G_y are transverse gradients in the x-, y- directions, and G_z is longitudinal gradient in z-direction.

The effects of x-,y-,z- gradients on the main magnetic field in the z-direction is further described in Figure 2.2.

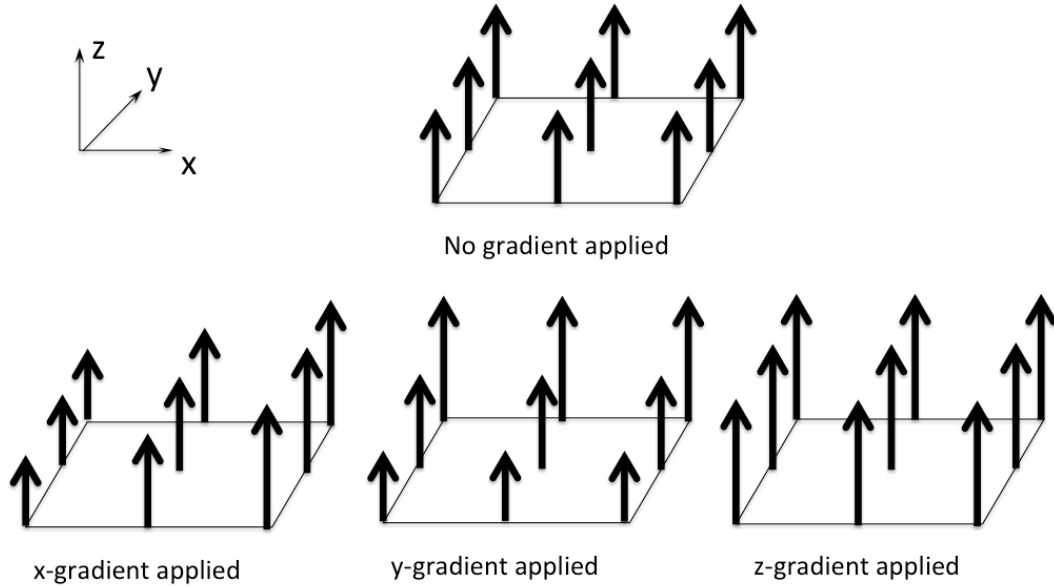


Figure 2.2: Diagram of the z-component of the main magnetic field changes by x-,y-, z- gradients

2.2 Radio-Frequency Coils

2.2.1 Basic theory of RF coils

A radio-frequency (RF) coil acts as an antenna in the MRI experiment. Typically, they operate in a radio-frequency range between 64.3 MHz to 400 MHz, depending on the main magnetic field strength (1.5 T to 9.4 T). They can have one of two functions, transmission or reception, thus we denote them transmit or receive coils, respectively. In transmit mode they transmit an electro-magnetic radio frequency (RF) field. The spatial amplitude of the magnetic component is the B_1^+ field. In receive mode they receive the returned NMR signal at a specific frequency in order to send it to the image reconstruction console.

Conventional RF coils are composed of inductors (L) and capacitors (C), forming an LC circuit which generates LC resonance tuned and matched around the Larmor frequency. (Equation (2.4))

$$f = \frac{1}{2\pi LC} \quad (2.4)$$

where L is the inductance, C is the capacitance in the circuit.

The basic type of RF coil is called a surface loop coil and has a high sensitivity for samples placed near the coil (20). It usually has a circular or rectangular shape, with smaller coil dimensions resulting in higher signal-to-noise ratio near the coil and as such can be used to image local regions.

Volume coils, on the other hand, are usually made in a cylindrical shape and cover the object by surrounding it. The most popular type of volume coil is the birdcage coil (21,22), followed by other types such as the Slotted Tube Resonator or Alderman-Grant head resonator (23,24) .

2.2.2 Transmit coils

The transmit coil is the antenna used to produce a B_1^+ excitation field within the object, which excites protons at the Larmor frequency. The main purpose of the transmit coil is to generate a homogeneous B_1^+ field, and to produce a minimal E-field for the patient in order to avoid exceeding the limits of SAR, which would otherwise overheat the subject. Note that historically the same volume coil was used for both transmit and receive, but modern systems tend to employ multiple separate receive coils that have better signal sensitivity.

The birdcage (BC) coil is a volume coil composed of multiple rungs between two end rings, see in Figure 2.3 (25). Initially, birdcage coils had one feeding port in one of the end-rings to feed the source, but a two-port feeding method has now become more popular. By feeding the same amplitude input with $\pi/2$ phase differences to the two ports, at 90 degree radial separation from the reference feeding point (26), it is possible to deliver energy more efficiently. This mode of operation is called the circularly polarised (CP) mode. By using CP mode, up to 50 % of input power reduction can be achieved by not exciting the non-productive counter-rotating mode (26). There are three common types of birdcage coil with different capacitor locations: a) high-pass birdcage coils have the capacitors located in the end-rings; b) low-pass birdcage coils have capacitors equally placed along the rungs; and finally the c) hybrid birdcage coil has capacitors in both rungs and end-rings, see in Figure 2.3. Each type of birdcage coil utilizes different resonance modes, and its particular behaviour is described in reference (27).

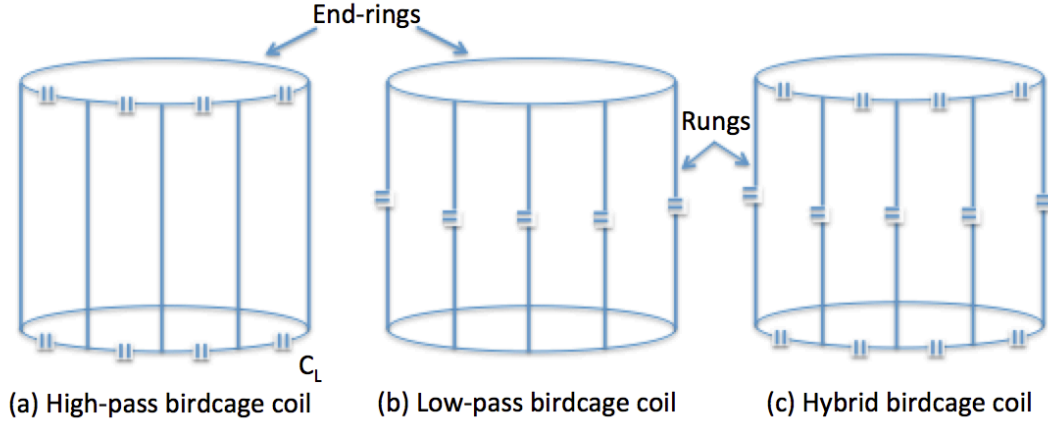


Figure 2.3: Schematic drawing of birdcage coil

A high-power amplifier is the main source of transmit energy used to supply the transmit coil. Two-port feeding of a volume transmit coil can be easily implemented by using a power splitter and phase shifter to produce a phase delay without adding extra amplifiers. Traditionally, most MR systems used only one power amplifier, but currently multiple power amplifiers are being installed to generate different transmit fields to mitigate field inhomogeneity.

For a specific transmit configuration the amount of specific absorption rate (SAR) induced by the coil can be controlled by measuring the power incident on the coil with directional couplers and converted to SAR using pre-calculated and therefore assumed EM-simulations.

Multi-array transmit coils are now widely used and enable parallel transmission (pTx) MRI, which is particularly beneficial at ultra-high-field. pTx is described in detail in Section 2.5 below.

2.2.3 *Receive coils*

The receive coil is the device which receives NMR signal from the sample. It is usually constructed of single or multiple surface coil arrays (28), or by sharing geometry with the transmit coil as a transceiver coil. Its main purpose is to receive signal with a high signal-to-noise ratio (SNR), and also to pick up the signals from multiple sources to accelerate the acquisition time (29,30). Previous studies have shown that the size of the surface receive coil has an impact on SNR (31,32). The smaller the radius of a coil, then generally the higher the SNR is expected to be in the region near the coil. Thus, it is suggested to place a number of receive coils near the object to maximize the coupling between coil and object, and to capture the signal with high sensitivity, but at the expense of depth of response (20).

The phased array coil was introduced by P. B. Roemer (28), placing the receive coils by overlapping them to minimise the coupling between neighbouring elements. Coil arrays were subsequently used to enable fast image acquisition by under-sampling k-space and using the coil sensitivities to fill in missing samples (28,29). Arrays of small coils can therefore be combined to achieve a similar performance in deep tissue structures as a single large receiver.

In general, receive coils do not have relevance to RF safety, since they are not the source of the transmit signal. However, a few studies have shown that there is an impact on SAR due to receive coil presence (33). The presence of a receive coil in a simulation could result in changing the transmit field distribution, which in turn causes different results for SAR calculation. The impact on receive coil presence in an EM simulation appeared to be larger in pTx systems than single transmit systems (33).

2.2.4 *Additional RF coil designs*

RF coil systems require several electronic circuits, such as transmit and receive (T/R) switches, pre-amplifiers, an RF-shield, and matching, decoupling and detuning circuitry. A T/R switch is usually used for a transceiver coil, where the same coil element is used both as transmitter and receiver. The switch logic is controlled by a direct current (DC) bias using a pin-diode, where the circuit with the pin-diode is normally blocked when DC current is not supplied and is only connected with a 1 Volt DC supply. Matching is achieved using an LC circuit to transform the impedance at the port (34). In order to deliver RF power at specific target frequency, transmit coil ports are matched to the system impedance, typically 50 ohms. Receiver coils on the other hand are often matched to a high impedance and connected to a low impedance pre-amplifier to facilitate coil array decoupling (28,35). RF coils within the system must be decoupled from each other, since coupling causes transmit coils to require higher power and leads to reduction of SNR in receive coils. Therefore, circuit decoupling is used to minimize crosstalk between coils through inductances and capacitances. The nearest coil element can be easily decoupled by overlapping geometrically (28) or via LC decoupling (36), but there can also be signal cross-talk coming from the next nearest element or from even further distant elements.

Cable traps are used in coil cabling to suppress current in the ground conductor of coaxial cables (37). This is achieved using a band-stop filter attached to the ground shield of a coaxial cable which is called a coaxial cable Balun. This avoids any unnecessary current being conducted through the coaxial cable from the transmit field, that would have had the potential to cause patient skin burns.

A detuning circuit is also needed to deactivate the transmit or receive coils when the two coils are used separately. A band-pass or band-stop circuit can be used to effectively detune the transmit and receive coil in an alternatingly fashion.

Finally, an RF shield is usually incorporated to reduce radiation loss from the coil by the compression of the near-zone electric field (38). The RF shield is usually made with copper mesh outside of the coil to reflect radiation or may be incorporated into the structure of the gradient coil.

2.2.5 Ultra-high-field MRI considerations

In ultra-high-field MRI (≥ 7 Tesla) B_1 transmit field inhomogeneity occurs due to the shortened electromagnetic wavelength. The wavelength of tissue at 300 MHz (7T) is about 11 cm, which is smaller than the diameter of the object being imaged, such as the brain or body, making the behaviour of the transmitting and receiving B_1 fields more complex and inhomogeneous. In particular, a skin effect is caused by the relatively high electrical conductivity of tissue, with a smaller skin depth at higher frequencies. As such, regions of dark and bright RF field distribution are manifested as a standing wave pattern, thus the penetration depth of coils is diminished. In order to overcome the B_1^+ penetration problem of a loop coil in ultra-high-field MRI, a novel transmit RF coil technique was introduced to generate an efficient and homogeneous transmit field. The transverse electromagnetic (TEM) resonator was introduced in ultra-high-field MRI systems at 4 Tesla and above, as an alternative method to the birdcage coil (39,40), see in Figure 2.4. TEM coils provide improved homogeneity by separating the inner copper strips from their closest neighbouring elements and by providing a return path for currents from the inner conductor strips (39).

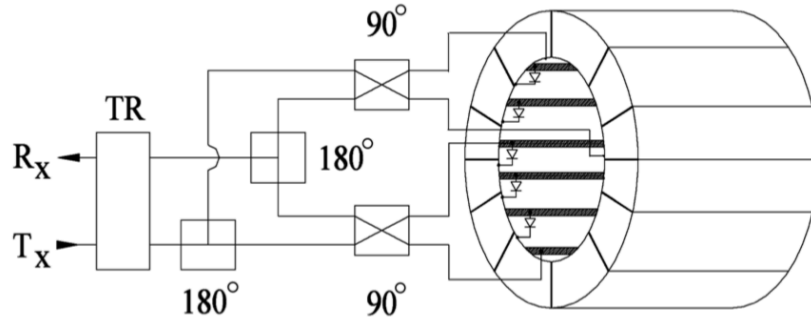


Figure 2.4: Schematic view of TEM coil, taken from J. T. Vaughan et al. 2002. Included with permission

The traveling wave antenna was introduced in 2009, which was the first method to use far-field components to deliver a transmit field to overcome the shortened penetration depth, especially in a human body at 7T and above (41). By using the RF shield inside the gradient coil as a wave-guide, the B_1^+ field delivery was efficiently made through the body with improved penetration depth compared to LC surface loop coil designs, see in Figure 2.5.

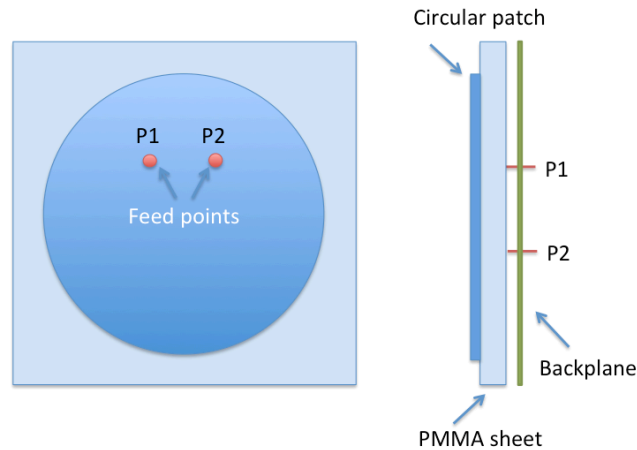


Figure 2.5: Schematic drawing of traveling wave antenna, taken from Brunner *et al.* 2009. Reproduced with permission

Another design, the dipole antenna, became one of the common transmit array techniques used for high-field MRI in order to increase the penetration depth of the transmit field (42), see in Figure 2.6.

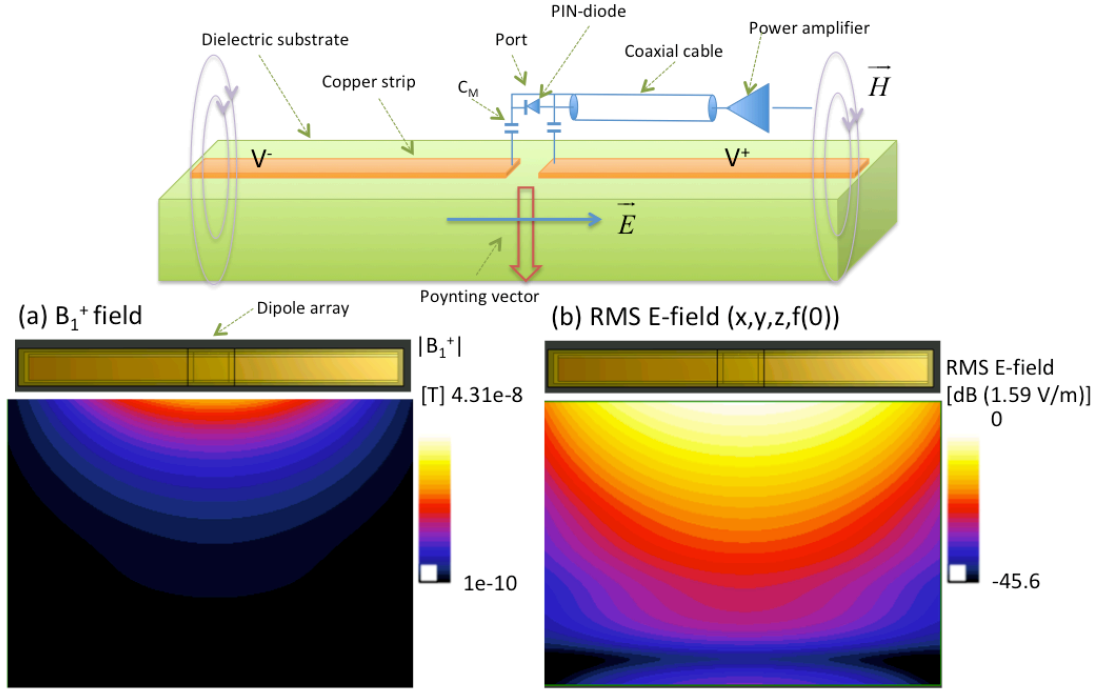


Figure 2.6: Schematic view of dipole antenna; (a) B_1^+ field distribution, (b) RMS E-field distribution in the homogeneous phantom with averaged brain properties at 297.2 MHz.

It constitutes a simple antenna concept, made of two copper strips meeting at the centre that forms a feeding point. Dielectric pads are positioned under the antenna, which helps the field travel towards the patient. Its electrical design is simpler than a loop antenna. It consists of two copper strips extend in opposite directions from the feeding point and originally mounted on a ceramic substrate to shorten their required length, and more recently have been shortened using inductive windings. Dipole arrays have higher penetration depth compared to LC loop arrays (43–45) by orienting the Poynting vector of the element toward the imaging target region as seen in Figure 2.6 (46). So it is a plausible option for use as a transmit coil at ultra-high field, especially in deep body structure imaging. Further advances have combined dipole arrays with loop arrays, in which a dipole array is positioned on top (outside) of a surface loop array. By positioning the dipole array elements coincident with the centres of the LC surface loop array elements, the coupling between the two coils is

minimized, which improves the B_1^+ field or SNR (43). A differently shaped dipole design known as the fractionated dipole was also introduced (42), which can reduce the array's physical size, resulting in an ability to position more transmit array elements on the object.

2.3 Parallel Transmission MRI

2.3.1 Overall system

The method of combining the transmit fields from multiple independent sources with independent magnitude (0-1) and phase (0- 2π) (47) is known as parallel transmission (pTx). In order to provide truly independent transmit sources, multiple waveform generators and power amplifiers are used.

Multiple RF elements are needed to generate tailored transmit fields driven with different waveforms or magnitude and phase. This can be used for transmit-only purposes, or for transmit and receive by using same elements with T/R switches. A popular pTx transmit coil uses a multi-channel transmit array surrounding the object which comprises an array of LC surface loop coils. When such an array is used in CP mode, it has been shown to offer a maximum of nine-fold increase in SNR nearest to the transceive array with the expense of 10.7 % less SNR in the centre brain region compared to an equivalent birdcage coil (48).

Work is ongoing exploring the benefits of higher numbers of Tx-channels, including up to 32 channels (49). With high such high channel count systems are being developed where the power amplifiers are mounted near the coil. This minimizes cable losses and hence the size of amplifiers, and increases the capacity to run more transmit coils (50).

2.3.2 *Parallel transmission application*

Parallel transmission MRI can be employed to accelerate or tailor spatial excitation (transmit SENSE) and to actively lower the SAR burden. This is particularly beneficial at ultra-high-fields where the SAR burden is increased and transmit fields are non-uniform.

RF shimming is the term used when only the relative phase and amplitude of transmit channels are adjusted. The phase and amplitudes can be optimised to reduce B_1^+ field inhomogeneity (51).

Parallel transmission can also be used to accelerate localised excitations using transmit SENSE (52). This can be achieved by adjusting the each channel's transmit waveform while simultaneously changing the gradient waveform(47). Such 'reduced field-of-view' imaging can significantly reduce scan time for high-resolution acquisitions.

Ultra-high field MRI provides potential advantages, including higher SNR, improved image contrast for angiography, and a higher spectral resolution for spectroscopy (53). Circularly polarised (CP) mode has been widely used for low-field RF transmission, which generates a homogeneous B_1 field with reduced excitation power (up to 50%) and improved SNR by a factor of $\sqrt{2}$. However, RF wavelengths shorten to the same dimensions as the image region at ultra-high field, resulting in volume transmit coils generating a spatially varying B_1 field, which usually presents as a centre brightening effect at 7T (54). Multi-channel transmit coils can improve the B_1 transmit field strength and uniformity by implementing different phase combinations for each transmit coil. Initially this was achieved by adjusting the phase of each transmitted signal manually by changing the length of the coaxial cables (55,56). Since this is limited and cumbersome, parallel transmit (pTx) technology

was introduced, which supplies multiple power amplifiers, thus allowing the user to easily manipulate the individual transmit amplitude and phase to generate an improved field distribution by software control.

Many applications have been studied using pTx technology. RF shimming is a technique that drives individual channels with tuneable RF phase and amplitude in order to optimize B_1 field by finding a minimized cost function see in Equation (2.5) (57).

$$B_1^+(\vec{x}) = \left| \sum_{k=1}^n V_k \cdot B_{1,k}^+(\vec{x}) \cdot e^{i(\phi_k(\vec{x}) - \Theta_k)} \right| \quad (2.5)$$

where V_k is the voltage amplitude, and $B_{1,k}^+$ is the measured single-channel RF field, ϕ_k is the relative phase maps, Θ_k is the relative phase offset, and k is the coil element

A tailored RF pulse can be introduced using a selectively excited spatial k-space trajectory(58,59). Although, this sequence requires a long scan time for use in clinical studies, many efforts have been put in to accelerating the scan time for practical usage.

Overall, pTx technology offers a promising solution to solving B_1^+ inhomogeneity at ultra-high field, but the safety of pTx applications must be more carefully investigated to prevent patient injury from excessive local RF heating.

At ultrahigh field ($\geq 7T$) the reduced wavelength results in B_1^+ field inhomogeneity due to the wavelength approaching the size scale of the object being scanned. This can result in complete signal cancelation in some regions, a problem that has been addressed using techniques such as Time Interleaved Acquisition of Modes (TIAMO) where images from two or more transmit states are acquired in an interleaved manner, facilitating imaging with full coverage of a volume (60).

2.4 MRI RF Safety: Specific Absorption Rate Assessment

MRI is an imaging technique that uses a non-ionizing RF electromagnetic field to scan biological tissue non-invasively, which is known to be less harmful compared to the imaging techniques using ionizing radiation, such as plain-film X-ray and X-ray Computed Tomography (CT). The MRI antenna arrays use RF electromagnetic wave, which is usually between 64.3 MHz and 400 MHz, depending on the main magnetic field strength. Although the RF wave could increase the temperature of the subject when in the RF transmit state. According to the international regulation IEC 60601-2-33, excessive RF energy is prohibited for patient protection. The maximum core and local tissue temperature is limited to 39 °C, and the rise of core temperature is limited to 0.5 °C (61). However, local body temperature is not trivial to monitor during an MRI scan. Therefore, estimation of temperature increases are usually assessed by pre-calculated computer simulations of biological tissues and also via experimental measurements of tissue-equivalent phantoms.

2.4.1 *Magnetic resonance imaging radio-frequency safety*

The International Electrotechnical Commission (IEC) has defined the requirements for basic safety and essential performance of magnetic resonance equipment for medical diagnosis. The limit of RF energy is defined by a maximum allowed temperature increases and specific absorption rate (SAR) (61). The source of RF energy is the applied RF transmission to generate a B_1 transmit field. However, the tissue temperature cannot trivially be measured in-vivo and it is instead limited using SAR which in turn is calculated using simulations of RF antennas. SAR is a direct way to assess RF exposure, but an indirect way to assess heating in the human body. It is widely used in MRI as well as in the cell phone industry. SAR is the power per unit mass deposited in the tissue and defined by Equation (2.6).

$$SAR = \frac{\sigma \|E\|^2}{2\rho} \quad (\text{W/kg}) \quad (2.6)$$

where σ is the electrical conductivity, E is the electric field, and ρ is the mass density.

According to regulations, SAR should be considered locally in any 10 g of tissue and globally over the exposed body mass. The average SAR over the exposed body mass is called global SAR. SAR is also averaged locally using specific mass averaging, usually for kernel sizes of 1 g or 10 g of tissue, this is called average local SAR.

In practice, the scanner determines the voltage (and hence energy) needed to produce a 90 or 180-degree flip angle during a calibration routine. The transmit voltage required for a specific sequence can then be estimated by adding together all the energies of the constituent RF pulses and dividing by pulse repetition time (TR). This power can then be converted to an look ahead estimate of global SAR using a model of the exposed body mass or similarly using EM simulations to estimate local SAR (62). On a single transmit channel system, the 10 s and 6 min SAR are calculated in real time using a power monitor fitted between the RF amplifier and coil which allows global and local SAR to be determined. If the real time system detects the SAR limits have been exceeded, the scanning is stopped.

The electric field present in the sample can be calculated by solving Maxwell's equations. Maxwell's curl equation can be written as Equation (2.8)

$$\begin{aligned} \frac{\partial B}{\partial t} &= -\nabla \times E, \\ \frac{\partial \epsilon E}{\partial t} &= -\sigma E + \frac{\nabla \times B}{\mu} \end{aligned} \quad (2.7)$$

where σ is electrical conductivity, E is electric field, t is time, ϵ is electrical permittivity, B is magnetic induction, μ is magnetic permeability.

Finite-difference time-domain (FDTD) analysis is a popular method for calculating EM fields by solving Maxwell's equations in the time domain (63). The Maxwell's curl equation (2.8) is discretised and solved with a computer in the FDTD method using a Yee Cell approach. In the FDTD method, the reference points for the electric (E) and magnetic (H) field components are staggered in the three directions in the Yee cell cube to increase the finite difference accuracy of the approximations, as seen in Figure 2.7.

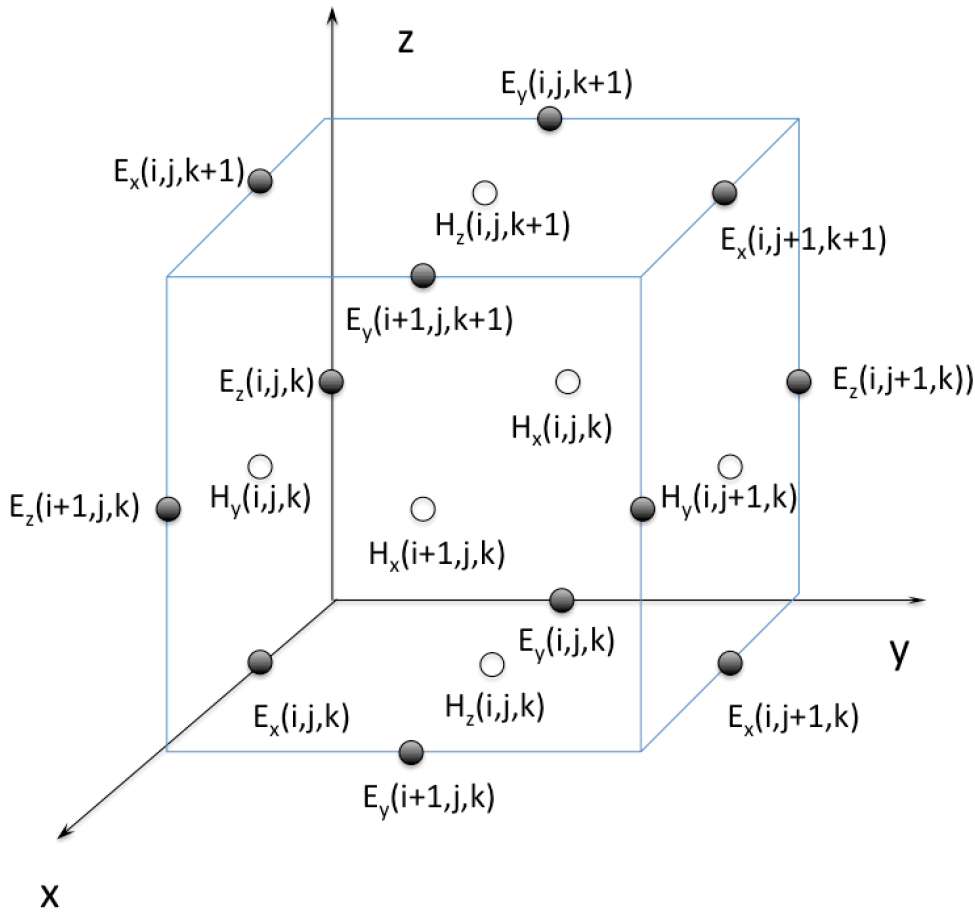


Figure 2.7: Diagram of a Yee cell cube, showing key positions: E-components are located in the middle of the edges, and the H-components are in the centres of the faces. From Collins et al 2006, reproduced with permission.

It has the benefit of having a relatively small amount of calculation time compared to the frequency-domain method. There are commercial software

implementations of EM solvers using the FDTD method, such as Sim4Life (ZMT, Switzerland), XFDTD (Remcom, USA), and HFSS (Ansys, USA). The frequency-domain method is also used to calculate EM fields. It requires longer computational time than the time-domain method, but it is less restrictive in its minimum gridding requirement. Examples of commercial software that calculate EM fields in the frequency domain are CST (CST GmbH, Germany) and FEM (Comsol, USA). SAR is not easy to estimate solely by E-fields, since it is also affected by electrical conductivity and relative permittivity of the sample as seen in Equation (2.6) (64). Therefore, a proper selection of voxel models with well-characterised dielectric properties is necessary in order to obtain a good estimation of SAR.

Human body models have been developed to enable estimation of electromagnetic (EM) field behaviours in biological tissues using simulations. One such model is HUGO, which was developed by the U.S. National Library of Medicine in 1986. Male and female cadavers were used to obtain transverse CT, MRI, and cryosection images as part of the Visible Human Project (65). Based on these data, three-dimensional segmented images were developed and these human body models, the male model of which is known as HUGO, were used to assess EM safety in the cell-phone industries and in MRI RF safety studies. The dielectric properties of tissue compartments play an important role in EM simulation, which was studied in 1996 by C. Gabriel (66). In that paper, the author studied the relative permittivity and electric conductivity of over 25 tissue types at frequencies between 1 MHz to 20 GHz using animal tissues at 20 and 37 degree Celsius. These properties were then used in human body models. Further studies and developments in human body models are ongoing, moving towards personalized models,posable models, and dedicated human nerve models, this is discussed in detail in Section 5.2 of Chapter 5.

2.4.2 RF safety in parallel transmission: *Q*-matrix and Virtual Observation

Points

The numerous RF configuration possibilities potentially results in numerous simulations being required to simulate RF fields for safety. To simplify this problem it was shown that SAR calculation can be simplified using a *Q*-matrix, introduced in 2012 by Ingmar Graeslin (67). Since some input parameters and weight-averaging used for SAR calculation are not RF shim relevant, using the *Q*-matrix methodology they can be pre-calculated once and then the transmit configuration applied. As such the *Q*-matrix contains non-time varying information, and is calculated at each pixel location in complex form, see in Equation (2.8). SAR correlation matrices for each voxel in the volume, Q_v , are pre-calculated by using the electric field vector, $\mathbf{E}(\mathbf{x})$, that is caused by a 1 Volt input on channel k for a given conductivity (σ_v) at voxel v . The superscript H transposes the complex conjugate.

$$Q(x) = \frac{1}{V} \int_V \frac{\sigma(x)}{2\rho(x)} \cdot \mathbf{E}^H(x) \cdot \mathbf{E}(x) dV \quad (2.8)$$

where V is the averaging volume, σ is the electrical conductivity, ρ is the mass density, $\mathbf{E}$ is the normalised electric field vector, and $\mathbf{x}$ is the location.

This formulation of the $\mathbf{Q}$ enables the spatial averaging (such as a 10 g average) to be pre-calculated and the spatial averaged SAR is determined by multiplication of $\mathbf{Q}$ and the complex transmit voltage. The complex-valued voltage waveform U of transmit channel k is used for the calculation of local SAR, $SAR(Q_v)$, at the voxel v in the volume.

$$SAR(Q_v) = \int_{\Delta t} \mathbf{U}^H(t) \cdot Q_v \cdot \mathbf{U}(t) dt \quad (2.9)$$

where Δt is the time interval, U is a voltage waveform, Q_v is the *Q*-matrix, and v is the voxel location

Note that the Q_v matrices generated include averaging over 10 cm^3 regions, corresponding to the 10g averaging standard for local SAR.

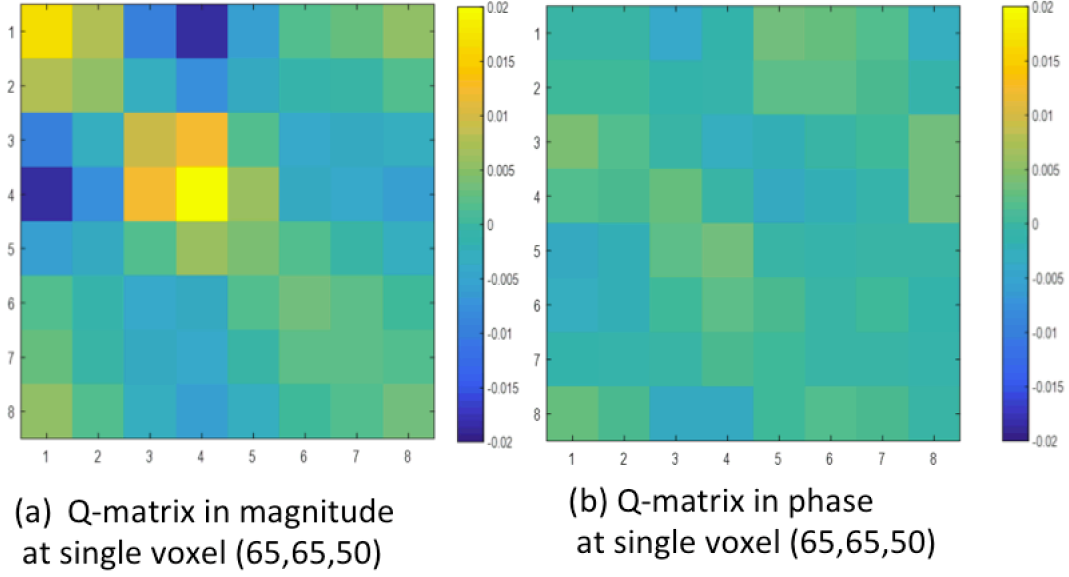


Figure 2.8: Example of Q-matrix of 8-channel coil, (a) magnitude, (b) phase

Figure 2.8 gives an example Q matrix calculated from the Duke Model. The diagonal elements of the Q matrix is the SAR that would be incident should only that channel be transmitting and the off-diagonal elements gives the complex interaction between two channels. Therefore Q can be viewed as a SAR correlation matrix.

Assessment of local SAR in parallel transmit is simplified using the Q matrix, still millions of simulated voxels locations need to be monitored. Eichfelder *et al.* introduced the concept of Virtual Observation Points (VOPs) to greatly reduce the size of this problem and to predict and control the maximum local SAR in pTx. In this approach, the number of monitored points can be greatly reduced using a controlled overestimation of local SAR.

All of the SAR correlation matrices are clustered into m sub-volumes, where each is represented by one matrix A_j (for each cluster j) that fulfils the conditions of Equations 2.7 and 2.8 for all matrices of S_v and all multichannel excitation voltages

U . In the work by Eichfelder *et al.* Q_v in Equation (2.9) is referred to as S_v below.

$$\int_{\Delta t} \mathbf{U}^H(t) \cdot S_v \cdot \mathbf{U}(t) dt \leq \int_{\Delta t} \mathbf{U}^H(t) \cdot A_j \cdot \mathbf{U}(t) dt \quad (2.10)$$

$$\max_{v=1, \dots, m} \int_{\Delta t} \mathbf{U}^H(t) \cdot S_v \cdot \mathbf{U}(t) dt \leq \max_{j=1, \dots, N} \int_{\Delta t} \mathbf{U}^H(t) \cdot A_j \cdot \mathbf{U}(t) dt \quad (2.11)$$

$$\mathbf{U}^H S_v \mathbf{U} \leq \mathbf{U}^H A_j \mathbf{U}, v \in \{1, \dots, m\}, j \in \{1, \dots, N\}$$

where Δt is the time interval, U is a voltage waveform, S_v is the matrix equivalent to the Q-matrix at voxel v , A_j are the Virtual Observation Points that dominate all elements for cluster j , and j is the cluster

Since the A_j represents a cluster, the local SAR for any S_v within the cluster will not exceed the local SAR predicted by A_j .

Equation (2.11) can be rewritten with $(A_j - S_v)$ as being positive semi-definite (psd), if the eigenvector of the Hermitian matrix $(A_j - S_v)$ is always real and non-negative, for all S_v of cluster j , or in other words $\lambda_{\min}(A_j - S_v) \geq 0$. In this condition A_j dominates S_v .

If there are some members of $\mathbf{A}$ that are dominated by others, a new set of matrices $\mathbf{A}'$ can be generated by clustering non-dominant matrices $\mathbf{B}$, with $\epsilon > 0$, as a stringent criterion to control the size of cluster.

$$\lambda_{\min}(\mathbf{B} - \mathbf{S}_v) \geq -\epsilon \quad (2.12)$$

where B are the non-dominant matrices, S_v is the matrix equivalent to the Q-matrix, and ϵ is the finite overshoot

New matrices $\mathbf{A}'_j, \{A_1, \dots, A_N\}$, can be rewritten as $\mathbf{A}'_j = \mathbf{B} + \mathbf{Z}$, to satisfy the conditions of Equations 2.8 and 2.9. Maximum overestimation now can be calculated as Equation (2.13)

$$\|Z\| = \lambda_{absmax}(Z) \quad (2.13)$$

where Z is the Hermitian psd matrix

The purpose of VOPs is to find a small number of matrices A_j and then use this subset of matrices to estimate peak SAR (A_j) reliably with overestimation ($<5\%$) but also without underestimation.

Many voxels in regions of low electric field can be neglected in local SAR estimation using VOPs, since clusters representing low E-field regions are likely to be dominated by those in high E-field regions. This results in reliable control of local SAR monitoring within a tailored area of interest and with rapid calculation – particularly useful for rapid RF pulse sequence design.

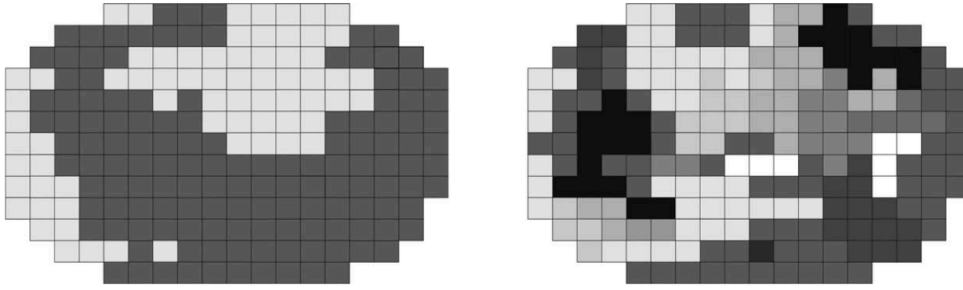


FIG. 2. 2D illustration of the clustering for a large (left) and a small (right) overestimation value for u with two (left) and 11 (right) clusters and thus two and 11 VOPs, respectively.

Figure 2.9: Example of VOP clustering, taken from Eichfelder *et al.* 2011.
Reproduced with permission

2.4.3 Limits of SAR calculation and future RF safety direction

With VOP compression a number of different EM models can be compressed together to control local SAR estimation for a population. This however can lead to an unwanted overestimation of SAR in a given individual, as the worst-case VOP solution is used. In addition, the EM model is generally only relevant to healthy volunteers or patients with a normal anatomy, which could lead to the underestimation of local SAR for subjects who have abnormal anatomy or pathology,

for example elderly subjects with large ventricles (4,68,69). Therefore, the desire for a personalised SAR model is increasing, which could in turn reduce SAR overestimation.

Although SAR is the method used to regulate RF safety, the results of thermal simulation and SAR do not always agree due to the complex thermal behaviour in biological tissues (70). Additional validation is therefore recommended to assure further safety in patients despite current regulation for MRI only regulates RF safety by SAR proxy. Recently, some researchers have extended RF safety into thermal dose simulation, which can prevent possible tissue damage that can occur even in the regime of low energy exposure (71).

3 Assessment of the Validity of Different RF Coil Simulations and Sensitivity Analyses

3.1 Introduction

In ultra-high-field MRI ($\geq 7\text{T}$), there are two specific needs for EM simulation: one is the estimation of transmit and receive magnetic field (B_1^+ and B_1^-) distributions and the other is the estimation of specific absorption rate (SAR) via electric (E) field simulation.

Several numerical techniques have been introduced to solve Maxwell's equations as full-wave solvers: namely the method of moments (MoMs) (72), Finite-difference time-domain (FDTD)(73), and finite element method (FEM) approaches. Among these, the FDTD approach is a popular method for calculating EM fields by solving Maxwell's equations in the time domain (63,73). This method not only allows calculation of B_1^+ fields in MRI, across arbitrary main magnetic field strengths, but also allows the calculation of SAR and SNR (74,75). These simulation studies have been further extended to allow thermoregulatory estimation in MRI (76,77), since physiological effects due to RF electromagnetic fields are known to induce RF heating in tissues (78,79). These thermal simulations also allow the application of Pennes bioheat equation (80) Such thermal simulations can potentially be used to satisfy regulatory requirements which include thermal limits for RF safety, alongside SAR (IEC 60601-3) (81).

Temperature measurement is a direct way to assure patient safety, and can be used to support the accuracy of simulation along with B_1^+ field measurement. While it is not trivial to monitor temperature changes in a patient, in Section 3.4.4 of this chapter three methods of monitoring phantom temperature changes resulting from RF heating are presented.

Since the results of the EM and thermal simulations are sensitive to the physical properties of the phantom, it is important to characterise these properties. Several phantom properties are needed for EM simulations, including density, dielectric properties (i.e. electrical conductivity and relative permittivity), and thermal properties (i.e. specific heat capacity, thermal diffusivity, and thermal conductivity). In Section 3.3 of this chapter we describe how our phantoms were constructed and how their physical properties were measured or determined.

Matching simulated and physical values (resistance and reactance) of lumped element is not trivial. In Section 3.4.2 three methods to deal with this are evaluated.

Simulation settings, including the position of the object, the choice of material properties, grid size and resolution affect the simulations and need to be carefully selected (4,82). By having a finer grid size in the EM simulation, more accurate results can be expected, whereas having a coarser grid size will speed up computational time. Also, a densely located simulation grid size could overload limited computer system capacity. In Section 3.5 of this chapter we evaluate the effects of changing the grid size on the results for a 7T pTx head coil.

3.2 RF coil used: 8-channel pTx head coil

A cylindrically shaped 8-channel transceiver coil (Affinity Imaging, Jülich, Germany, Diameter: 292mm, Length: 200mm) was used to image and heat phantoms in this Chapter using a 7T parallel transmission (pTx) MRI system (Siemens, Erlangen, Germany), as seen in Figure 3.1.

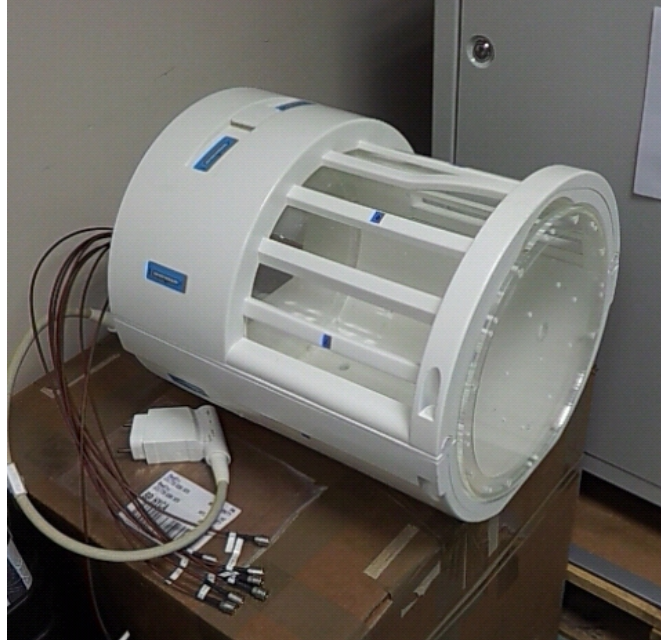


Figure 3.1: Picture of the 8-channel pTx head coil

The coil consists of eight rectangular elements, each formed from copper strips (lateral and longitudinal length of each element: 110 and 220 mm; 10 mm strip width). The eight elements are arranged around a 300 mm diameter cylindrical former without a shield. Each loop has 8 capacitors equally distributed around the copper strip, and two decoupling capacitors were connected between adjacent loops bridging the top and bottom capacitors in the longitudinal portions between the nearest neighbouring elements. Each loop is then connected to eight T/R switches to perform as a transceiver coil. An RF shield is not used in our 8-channel pTx coil.

3.3 MR phantom design for assessment of RF heating at 7 Tesla

3.3.1 Pork phantom

Pork and beef phantoms are a feasible option for RF heating assessment. It is cheap and easy to purchase at shops, and can be expected to be characteristic of human muscle (83). Despite its advantage, the size, shape, and quality of such phantoms are difficult to manage, since all products have different slaughter dates, fat proportions and sizes, as seen in Figure 3.2.

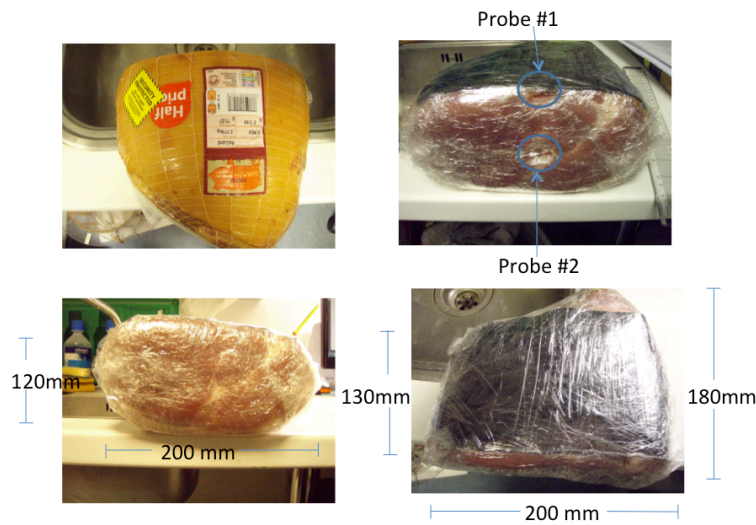


Figure 3.2: A pork gammon joint prepared for an RF heating test with top surface covered with a liquid crystal sheet, and position of fibre optic probes is indicated.

Minced pork is an alternative that can be easily shaped and replicated in simulation, as seen in Figure 3.3 where it was placed in a rectangular disk. The thermal properties of pork is reported as 2760 J/kg/°C, 0.66 kcal/kg/°C (84), and electrical properties of minced pork loin are reported as ϵ_r : 60, σ : 0.85 S/m at 300 MHz (83). In the phantom of Figure 3.3, shop purchased minced pork was used and placed in a rectangular cuboid container of $200 \times 180 \times 120 \text{ mm}^3$. The complications of using a meat phantom is that it does not keep for long, its properties can change during storage and that a large amount of minced pork is needed to assess the full volume of coil.

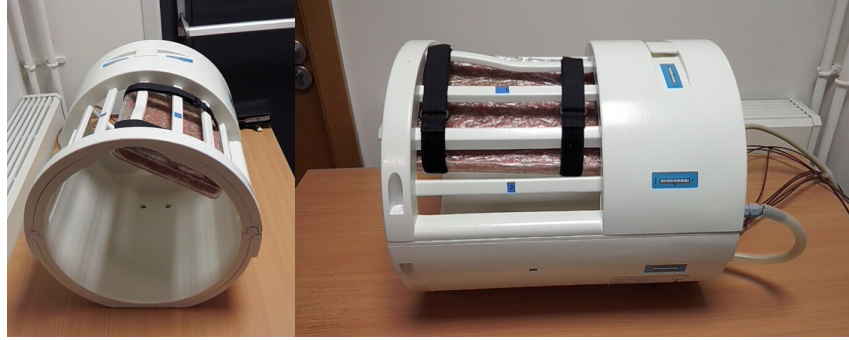


Figure 3.3: Picture of the pork phantom attached to a single element of the 8-channel pTx head coil

3.3.2 Agar-gel phantom

An agar-gel phantom can last longer than meat and its physical properties can be controlled for replication *in-silico*. A cylindrical acrylic (poly-methyl methacrylate, PMMA) container was fabricated (Advanced Fabrications Ltd, London, United Kingdom) with a diameter of 280 mm, height of 300 mm and shell thickness of 5 mm. This design that fitted tightly into the 8-channel pTx head coil (Figure 3.1) to assess the full volume of the coil, the phantom container is shown in Figure 3.4.

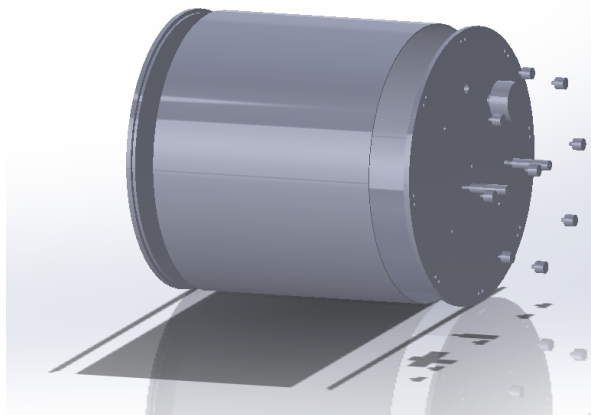


Figure 3.4: CAD drawing of the phantom container and the positions of the plastic straw guide

Twenty five 3 mm diameter of holes were made in the top endplate to guide temperature probes into positions of interest using plastic straws (top endplate was fabricated at IBME workshop, University of Oxford, United Kingdom).

Phantom production procedure

In order to assess the safety of scanning the human brain with 7T MRI, the average dielectric properties of grey matter and white matter at 297.2 MHz (ϵ_r : 51; σ : 0.57 S/m) were used to design a PRF-compatible MR phantom (85,86). Sodium chloride and polyethylene powder (Sigma-Aldrich, USA) are used to control conductivity and relative permittivity, and these are mixed with agarose and benzoic acid (85,87).

The phantom recipe contained the following proportions per Litre of de-ionized (DI) water: agar (20 g), permittivity was decreased by polyethylene powder (150 g), conductivity was increased by sodium chloride (4 g), and benzoic acid (30 g) was added as a preservative, with a total phantom volume of 16.8 Litres (85,87).

To mix the constituents the following procedure was adopted: firstly, all ingredients were gently mixed in 1 Litre laboratory glass bottles (DWK Life Sciences, Mainz, Germany) requiring the preparation of 18 bottles in total. All materials were heated using an autoclave with an average temperature of 160 °C to dissolve the ingredients, which providing homogeneous mixture of ingredients, also preventing the agarose being burnt near the heating source. All bottles were then poured into the plastic container, at which point the polyethylene powder, an insoluble ingredients, was added and evenly distributed and gently stirred during the cool down process. The mixture was stirred for 5 hours until the sample temperature dropped to 38 °C at which point agar starts to solidify. Any bubbles on the top were purged using a needle, as seen in Figure 3.5.

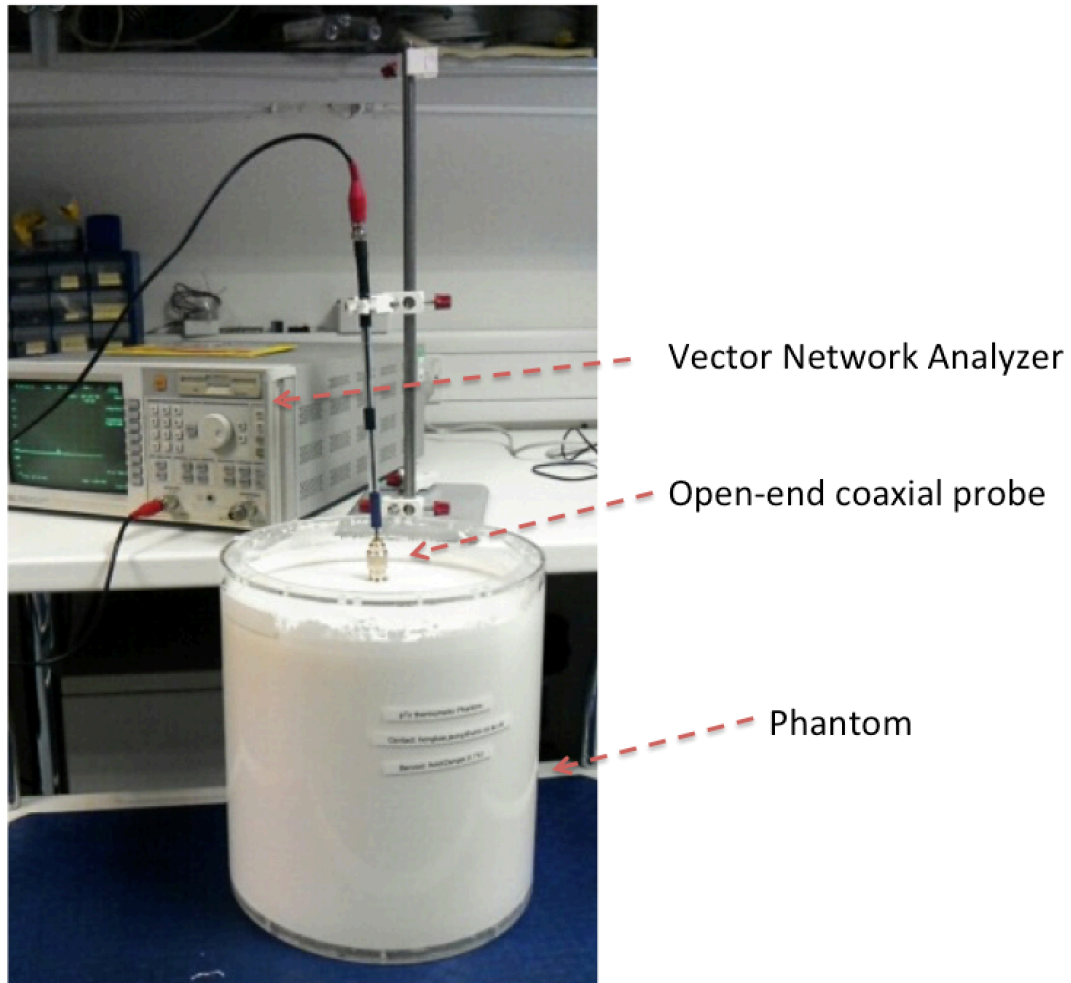


Figure 3.5: Picture of agarose phantom and measurement of its properties using an open-end coaxial probe. An alternative method using TX-151 and a magnetic stirrer will be described in Section 4.3.1 of Chapter 4.

Measurement of dielectric properties using an open-ended coaxial probe

The dielectric properties of biological tissues or phantoms are a key factor in determining the dissipation of electromagnetic energy. In particular, relative permittivity and conductivity must be known in order to calculate EM fields and SAR. The relative permittivity describes how much electrical energy can be stored in an electric field. Specifically, the relative permittivity is the ratio of the sample dielectric permittivity relative to the permittivity of a vacuum ($\epsilon_0 = 8.854 \times 10^{-12} \text{ F} \cdot \text{m}^{-1}$).

$$\epsilon = \epsilon_0 \epsilon_r \quad (3.1)$$

where ϵ_0 is the permittivity of a vacuum, and ϵ_r is the relative permittivity of the sample.

The relative permittivity is a complex quantity. The real part is the ability of the substance to store energy from an external electrical field. The imaginary part is a measure of how lossy the material is to an external electrical field. These are described in equation (3.2).

$$\frac{\epsilon}{\epsilon_0} = \epsilon_c = \epsilon'_r - j\epsilon''_r = \epsilon_r - j \frac{\sigma}{\omega \epsilon_0} \quad (3.2)$$

where ϵ_c is the complex permittivity, ϵ'_r is the real part of the permittivity, ϵ''_r is the imaginary part of the permittivity, σ is the electrical conductivity, ω is the angular frequency, and ϵ_0 is the permittivity of a vacuum

The dielectric properties of a material can be calculated by measuring the difference of the voltage standing wave ratio between distilled water and the material under test. Using the Debye equation, the complex permittivity of distilled water at 297.2 MHz is calculated and compared with an experimental measurement, thus acting as a calibration step. The values of the relevant parameters for distilled water are: $\epsilon_\infty = 4.6$, $\epsilon_r = 78.3$, and $\tau = 8.07 \text{ ps}$ in equation (3.3).

$$\varepsilon_c = \varepsilon'_r - j\varepsilon''_r = \varepsilon_\infty + \frac{\varepsilon_r + \varepsilon_\infty}{1 + j\omega\tau} \quad (3.3)$$

where ε'_r is the real part of the permittivity, ε''_r is imaginary part of the permittivity, ε_r is the relative permittivity of the sample, ε_∞ is the optical permittivity, ω is the angular frequency, and τ is the relaxation time.

The coaxial probe method is a relatively accessible method to measure complex permittivity, and is known as the best method for liquid and semi-solid (powder) materials, due to air gap influences (88). To measure the dielectric properties a measurement probe, a coaxial line, and a set of system calibration standards are needed. To measure the dielectric properties of the phantom in this thesis an N-type bulkhead connector was cut to have a flat surface with a round flange, as seen in Figure 3.6.

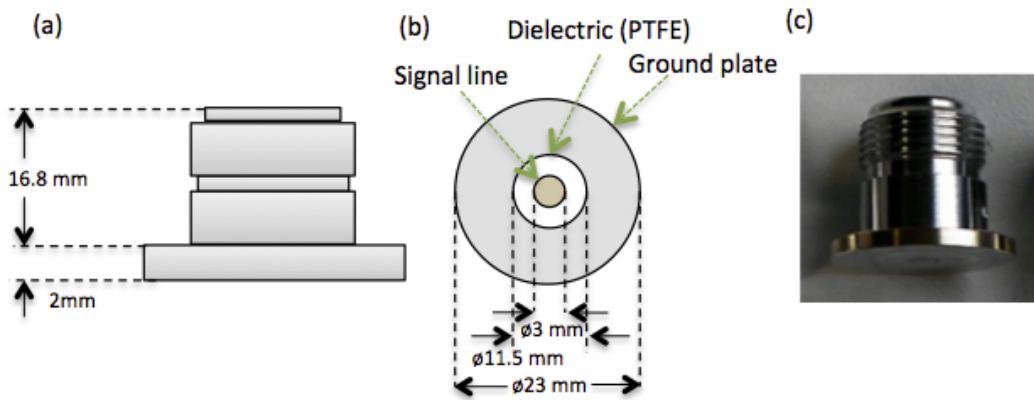


Figure 3.6: The measurement probe; (a) shows the dimensions from the left side; (b) shows the dimensions from a bottom view; (c) shows a picture of the measurement probe.

The central conductor of another N-type connector was then soldered onto a semi-rigid coaxial cable, either a plastic, or copper pipe were used to keep it as rigid as possible, as seen in Figure 3.7.

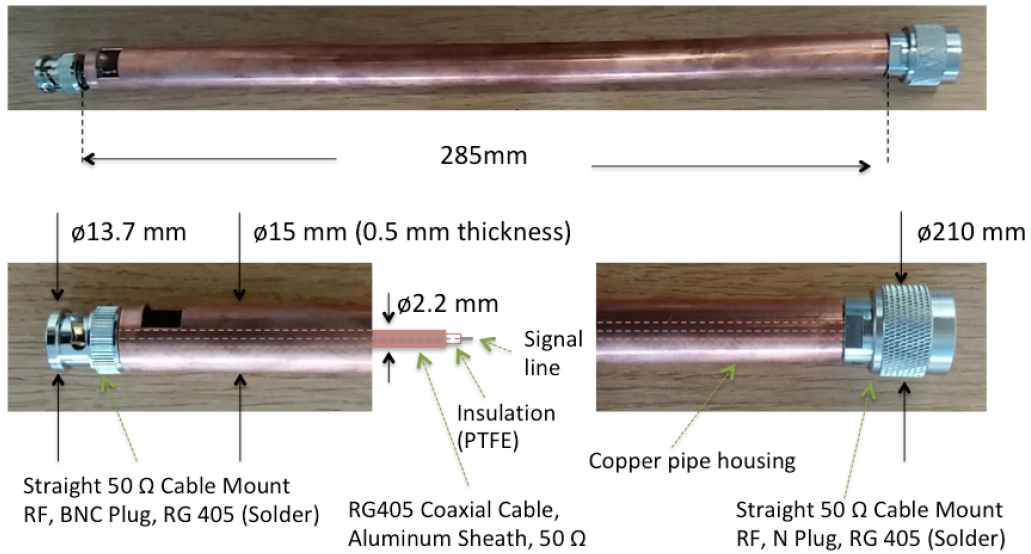


Figure 3.7: An open-ended coaxial probe covered with a copper pipe housing outside: supplying one side with N-type connector, another side with BNC-type connector.

An open-circuit and short-circuit calibration kit was made. For the ‘open-circuit’ probe a separate pair of identically cut N-type bulkhead connectors were connected facing each other; for the ‘short-circuit’ probe the signal and ground plate were connected with conductive material. An N-type 50-ohm load was also used for the system calibration, as seen in Figure 3.8.

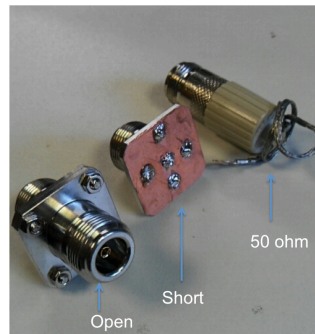


Figure 3.8: Calibration standards

To measure the complex permittivity, firstly the open-ended coaxial cable needs to be connected to the network analyser, allowing the port of the network analyser to be calibrated. The measurement probe is then placed on the surface of a sample of distilled water to measure the voltage reflection coefficient S_{11} . The complex form can

be converted into admittance (Y) using the Möibous transform as in Equation (3.4) where Y_0 is the characteristic admittance of 0.02 S, (i.e., 1/50 Ω), of the measurement probe:

$$Y = Y_0 \frac{1 - S_{11}}{1 + S_{11}} \quad (3.4)$$

where Y_0 is the admittance, and S_{11} is the reflection coefficient at the measurement probe.

This admittance can also be determined using the relative permittivity of the substance in conjunction with two, constants, C_0 and G_0 , shown in Equation (3.5) that are a function of the measurement probe. C_0 and G_0 can be computed using the pre-calculated complex permittivity of distilled water (89) via Eqn 3.5, where C_0 and G_0 can be isolated using the real and imaginary components of the admittance and known ϵ_r of distilled water:

$$Y = j\omega\epsilon_r C_0 + \sqrt{\epsilon_r^5} G_0 \quad (3.5)$$

where ϵ_r is the relative permittivity, and C_0 and G_0 are constants.

When solving the 5th order equation for C_0 and G_0 multiple answers can be found. The expected true value will have a positive C_0 and a negative G_0 , with an absolute value of the G_0 being smaller than C_0 .

We applied this method to saline water for accuracy verification and then applied the results to our phantom.

3.3.3 Results of phantom characterisation

For verification of the electrical properties measurement method, the dielectric properties of 0.3% saline water were measured and shown to have an accuracy that is within 2 % of the estimated theoretical values (Table 3.1). The dielectric properties of the phantom were measured as 55.66 and 0.52 S/m for relative permittivity and conductivity, respectively. A 9.1 % difference was found between theory and experiment for the relative permittivity, and a -8.7 % difference was found for conductivity, illustrating the importance of measuring these values.

Material	3% Saline		Phantom	
	ϵ_r	σ (S/m)	ϵ_r	σ (S/m)
Estimated value	77.98	0.60	51.00	0.57
Measured value	77.62	0.59	55.66	0.52
Difference	0.4 %	1.6 %	+ 9.1%	- 8.7%

Table 3.1: Results of the measured dielectric properties of the phantom

3.3.4 Discussion of phantom production

Agar phantom design for RF heating measurement was performed. We found a 10% difference for the relative permittivity and conductivity due to loss of water during boiling and stirring. Large amounts of water evaporation was observed when the phantom was heated with the autoclave, which may be caused a decrease in the permittivity. Excessive heating should be avoided to minimize water evaporation. The stirring time for solidifying was 4 hours until temperature cooled down to below 38 °C. TX-151 may need to be considered to increase viscosity and decrease the time for solidifying, providing lower losses from water evaporation (90). Key factors to prolong the lifetime of phantom are: avoiding water evaporation, a proper choice of preservative, and effective sealing of the end plates of the phantom.

3.4 Set-up of simulation environment, the assessment of lumped element simulation schemes

3.4.1 Introduction

The achieved and labelled values of reactive components in RF coils differ and as a result the predicted fields and performance of the coil differs from reality. In this section we evaluated and compared three methods that have been reported in the literature, including i) an ideal current-driven mode, ii) a method that simulates correct matching and tuning, and iii) a simulation with real capacitor/inductor values.

These methods were compared using the coil and phantom geometry described above. Three experiments were carried out to evaluate the three methods of setting lumped element values. The first compares an ideal current-driven mode to a simulated matched/tuned mode in a non-pTx CP configuration using simulations. The second experiment evaluated the use of a pork mince phantom setup for thermal validation and the third compares all three methods to phantom measurements made on a single pTx channel using an MR thermometry experiment. The three methods evaluated are:

Ideal current-driven mode: Collins *et al.* (91) demonstrated B_1^+ field behaviours and SAR at various frequencies using current sources to replace lumped elements and to the drive input ports. This assumes the coil impedance is matched to the feed impedance. In this case, the voltage reflection losses at the port and crosstalk between neighbouring elements are not considered. Nevertheless, they showed this method was able to predict the EM field behaviours in CP mode of an RF coil, and the resulting SAR. This is the fastest of the methods as only a single simulation is required. This setup is shown in Figure 3.9-a). For the ideal current simulations the

source is set to harmonic mode as a voltage source with a $50\ \Omega$ impedance in 100 periods simulation time, the delay period (which determines the phase) was set identically for all sources within a given element and a phase difference of $\pi/4$ between coil elements was introduced for CP mode.

Simulated matched/tuned mode: To adapt a simulation to achieve *in silico* tuning and matching is a time consuming iterative process. Several broadband simulations, which use a Gaussian pulse, are carried out. For each simulation the reflection coefficient (S_{11}) at the feed point of the coil is captured and plotted on a Smith chart and used to adapt lumped element values for subsequent iterations. Interaction between neighbouring elements (decoupling) can be adjusted in the same manner. This process is continued until the simulation reflects the measured reflection coefficients of the coil as determined on the bench with a network analyser. Seven capacitors are equally distributed around eight positions for each element (see Figure 3.9-b), with the eighth position used as the voltage source.

The capacitor values are optimized until $S_{11} < -5.0\text{dB}$ at 297.2 MHz without matching and decoupling. For each of the eight transmit elements, a voltage source is used at the feed ports. Once optimized values were determined at broadband simulation the simulation was finally run in harmonic simulation.

Although not carried out in this work due to not having access to the optimisation software tool MATCH (ZMT Medtech, Switzerland), the process of tuning and matching a simulation can be simplified by using co-circuit simulation (92,93). Co-circuit simulation runs multiple simulations where all lumped elements are replaced by feed ports in a similar way to the ideal current-driven mode, except that each feed port (lumped element) is simulated separately. The array of simulations can be retrospectively combined using circuit theory to find the combination of lumped

element values required to describe the target reflection and coupling. This can be further extended to optimise the phase of the coil response as well as its magnitude (94).

Simulation with ‘real’ physical capacitor values: Describing coil responses by finding optimised capacitor values to match the scattering matrix measurements, one study recommends using of the most similar capacitor values to those used in reality (95). This method is based on the fact that electrical behaviours in LC circuits could behave differently depending on the balanced or unbalanced condition of capacitor values in the LC circuit (96). In this sense, the authors propose that the field behaviours and RF heating coming from real capacitor values and their combination can be more realistically predicted. For this purpose the capacitor values were obtained from the manufacture and applied directly to the capacitors in the same manner as the optimised capacitor values were applied (Figure 3.13). Simulation using ‘real’ physical capacitor values was evaluated in terms of RF heating in Experiments 2 and 3.

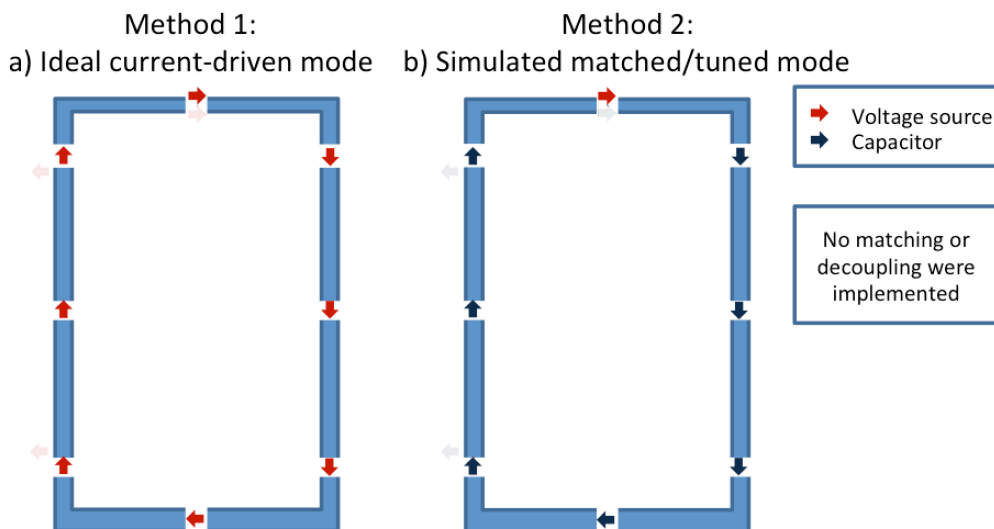


Figure 3.9: The position of capacitors and voltage sources in two popular simulation methods; a) Ideal current-driven mode, b) simulated matched/tuned model.

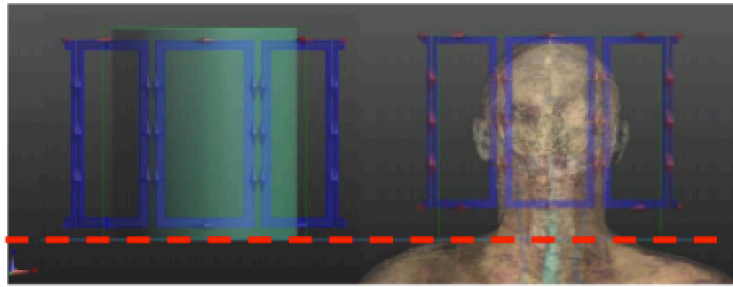


Figure 3.10: SAR average line of phantom and human model

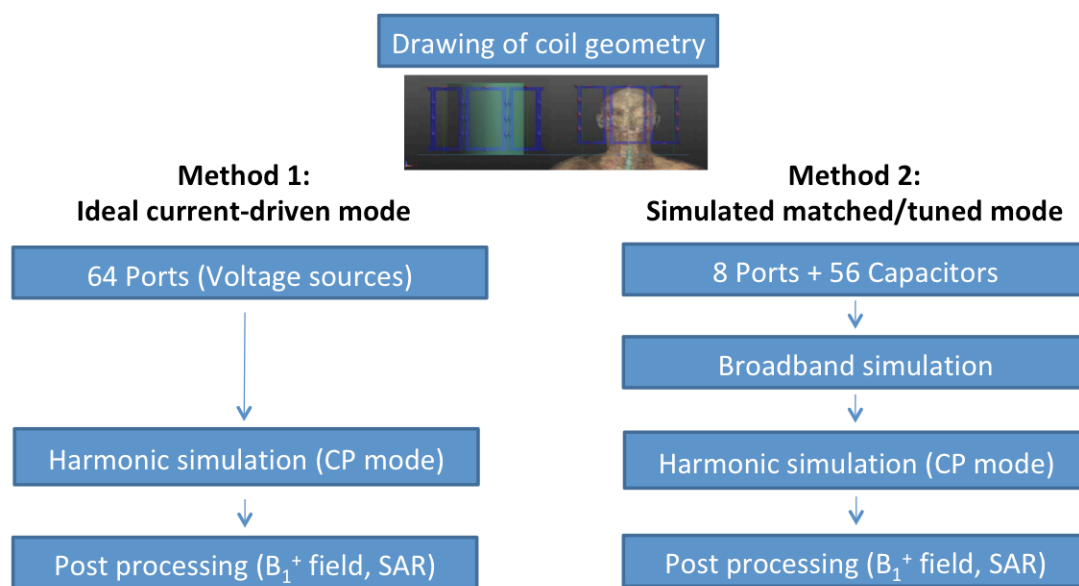


Figure 3.11: Diagram of the simulation process used for the two methods

3.4.2 Methods

Experiment 1: comparison in CP-mode of ideal current and simulated tuned/matched

To compare the difference between the ideal current and simulated tuned/matched methods, the B and E field were simulated in SEMCAD X for these two methods. For CP mode, each simulation was carried out with a of $\pi/4$ phase shift between each transmit element. This simulation method was applied to both the phantom described above and Duke v1.0 (97) from the IT'IS virtual family. The phantom was simulated with the expected (not measured) electrical conductivity, relative permittivity of brain (ϵ_r : 52, σ : 0.55 S/m), and density of 1042 kg/m³ as this is a conceptual simulation-only study. Duke was placed along the centre of the coil and aligned such that the top of his head was aligned with the top of the coil, as seen in Figure 3.10.

The B_1^+ field, SAR, and 10g averaged SAR (SAR_{10g}) were normalized to an input power that yielded a 2 μ T B_1^+ field at the centre of the coil, as described by Collins et al (75). Global SAR (SAR_{ave}) was calculated as the average normalized local SAR within the region of interest which was the full volume above the red line shown in Figure 3.10. The maximum 10g averaged SAR ($10gSAR_{max}$) was also found. This process was all carried out in MATLAB (The Mathworks, Natick, USA).

Experiment 2: Evaluation of real capacitor values using a pork mince phantom

SEMCAD X (Speag, Zürich, Switzerland) was used to calculate electric (E) fields and temperature changes for a single element that was modelled with real capacitor values. The pork phantom was modelled with electrical properties of relative permittivity ϵ_r : 60, conductivity σ : 0.85 S/m, density: 1037 kg/m³ and specific heat

capacity: 2760 J/kg/°C, all taken from a previous study at 300 MHz (98,99). A thermal simulation was carried out in SEMCADX. The initial temperature was set to the same temperature as the experiment (20 °C). A summary of this setup is shown in Figure 3.12.

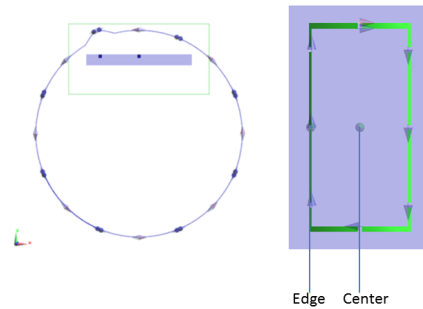


Figure 3.12: Schematic of the RF coil and the position of the fibre optic probes used in the phantom and in the simulation

A GRE pulse sequence was used to heat the pork phantom for a saturation of 1 min at a high power of 35 W average forward power at the coil plug on one channel, the TR/TE = 16.5/1 ms. Shop-purchased minced pork (fat content of 5%) contained in a rectangular case ($150 \times 256 \times 10 \text{ mm}^3$) was used as an experimental phantom, and liquid crystal sheets (Edmund, United Kingdom) were placed on top of the phantom to observe surface temperature changes. The phantom was placed 25 mm away from an arc-shaped single element of the coil. The initial temperature was controlled by putting the phantom in a water bath before the experiment and set to the baseline measurement temperature of the liquid crystal sheet (20 °C).

Two optic fibre temperature probes (Neoptix, Quebec, Canada), one located at the edge of the pork near the centre capacitor of the longitudinal copper strips and the other in the centre of the phantom, were used to measure temperature changes, as shown in Figure 3.12. The optic fibre probe has a resolution of 0.1 °C, and accuracy of ± 1 °C, and it has an 11 metre cable length to connect between the centre of bore and the control room of the 7 T MRI system.

The reflected power of each port was measured on the bench using a network analyser, in order to characterise the S-parameter matrix.

For the case of a short period of heating, heat conduction can be ignored, and thus the temperature rise with respect to time can be converted to SAR by multiplying by the specific heat capacity (100,101) as defined by Equation **Error! Reference source not found.** The expected temperature change over time from the simulation was calculated from the result of the SAR calculation using the thermal simulator of SEMCAD X.

$$SAR = c \frac{dT}{dt} \quad (3.6)$$

where c is the specific heat capacity, dT is the temperature change, dt is the time change.

Experiment 3: Comparison of all three simulation methods to experimental heating tests using proton resonance frequency thermometry

For this experiment Sim4Life (ZMT, Zürich, Switzerland) was used to solve Maxwell's equations in the time-domain, yielding E-field and SAR distributions. All simulation methods were evaluated at 297.2 MHz (7T) and were carried out on the phantom described above. The simulated matched/tuned method and 'real' capacitor value method were used, and additionally included the matching and decoupling capacitors as tuned values (former), and values reflecting the real capacitors (latter). This included two decoupling capacitors placed between each element and a matching capacitor parallel to the drive port.

For the ideal current-driven method, voltage sources were added in the position of the matching and decoupling capacitors, as seen in Figure 3.13.

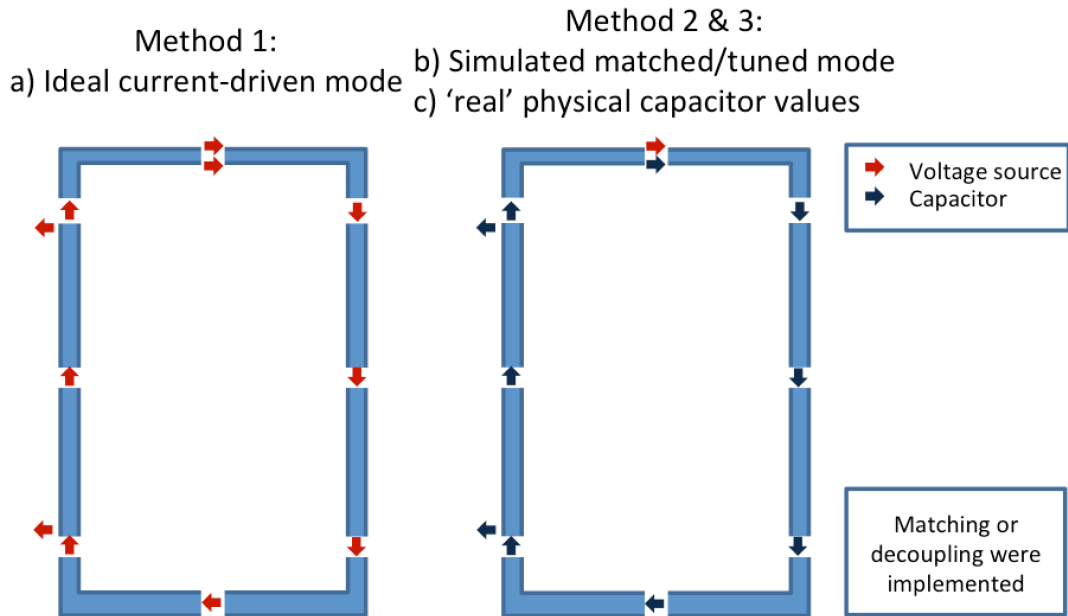


Figure 3.13: Circuit drawing showing the three different coil simulation methods, matching, and decoupling capacitors are added for RF heating simulation

For RF heating predictions the Sim4Life thermal simulation package's was used. This package uses a bio-heat equation to calculate thermal changes resulting from deposited RF energy. The thermal properties of the agar phantom were set from literature values, with heat capacity $C_p = 4200 \text{ J/kg/K}$, thermal conductivity $k = 0.498 \text{ W/m/}^\circ\text{C}$, and density $\rho = 1021 \text{ kg/m}^3$ (102). The properties of the acrylic container were set to $C_p = 1460 \text{ J/kg/K}$, $k = 0.19 \text{ W/m/K}$, $\rho = 1170 \text{ kg/m}^3$) were assigned from literature values (103) . The initial temperature of environment and phantom were both set to 20°C . The results of EM simulation were used as heating source, and it is normalised to conducted power, 20.39 W , after accounting for reflected voltage. The 'Mixed' boundary type was chosen. It is typically used at surfaces surrounded by air where the heat-loss is dependent on the temperature difference. The heat transfer coefficient of body is reported in the range between 4 and $7 \text{ W/m}^2/\text{K}$ (104), we set is as $6 \text{ W/m}^2/\text{K}$ from literature value of the head (105).

3.4.3 Results of lumped element simulation method experiments

Experiment 1: comparison in CP-mode of ideal current and simulated tuned/matched

The normalization factor (voltage scaling) required to achieve a $2 \mu\text{T } B_1^+$ field at the centre of the coil was 24.87 and 36.64 for the ideal current and tuned/matched methods respectively. The B_1^+ profile when simulating using ideal current and tuned and matched values agreed to within 2% of each other over the whole FOV. Figure 3.14 and Figure 3.15 show B_1^+ profiles and slices from the two methods, respectively. Table 3.2 reports the global SAR (SAR_{ave}), maximum 10 g SAR ($10\text{gSAR}_{\text{max}}$) and calculation times. The global SAR differed by -6.5% and $+3.7\%$ in the phantom and

human model respectively, and local SAR by -11.57 % and +3.13 %.

		Method 1: Ideal current	Method 2: Tuned/Matched	Differences
Phantom (Cylinder)	SAR _{avg} (W/kg)	1.43	1.53	6.56%
	10gSAR _{max} (W/kg)	1.95	2.20	11.57%
	Calculation time	4 min	11 min	7 min
Human Phantom (Duke, Virtual Family)	SAR _{avg} (W/kg)	1.73	1.66	-3.74%
	10gSAR _{max} (W/kg)	5.58	5.41	-3.13%
	Calculation time	7 min	22 min	15min

Table 3.2: Results of unaveraged local SAR and location of 10gSAR_{max} estimates of one iteration of tuning and matching

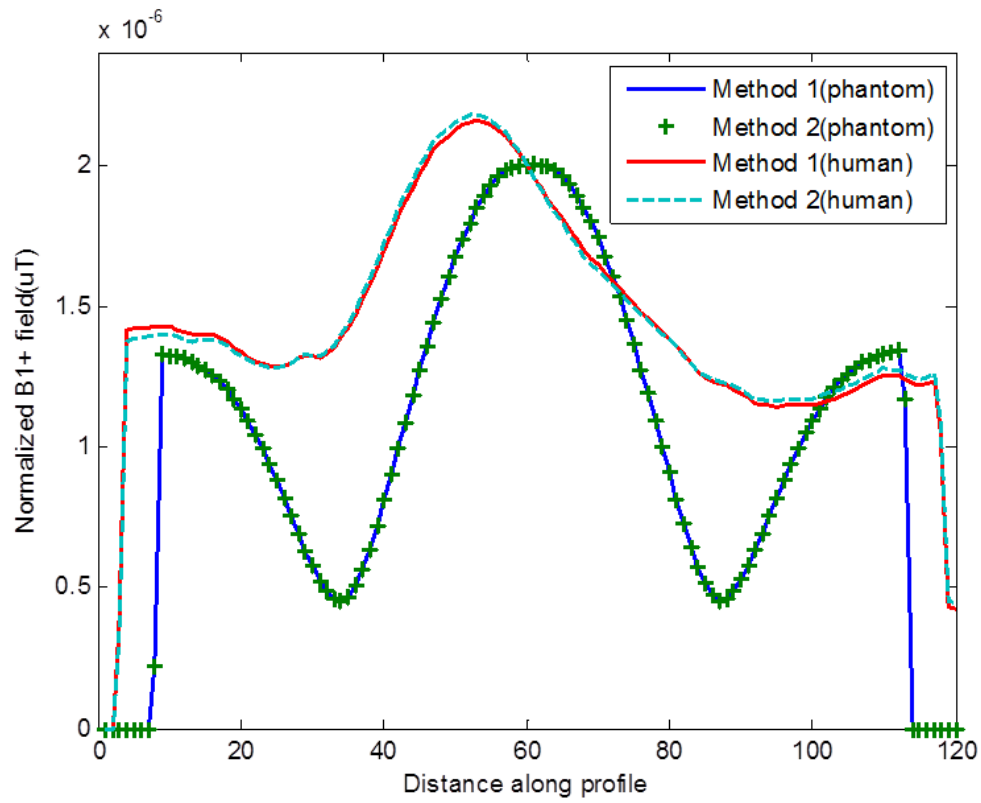


Figure 3.14: B₁ transmit field profile at coil centre

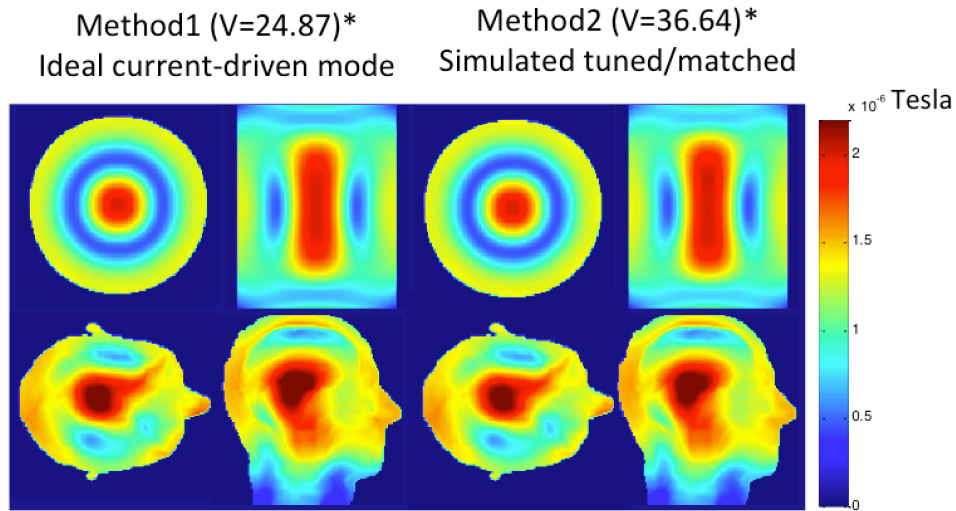


Figure 3.15: Normalised B_1 transmit estimated field distribution at the centre of the phantom and human head (B_1 transmit fields were normalised to $2\mu\text{T}$ at the coil centre. (*=Normalisation factor)

Figure 3.16 shows the global SAR and 10g maximum SAR estimates at the centre of the coil.

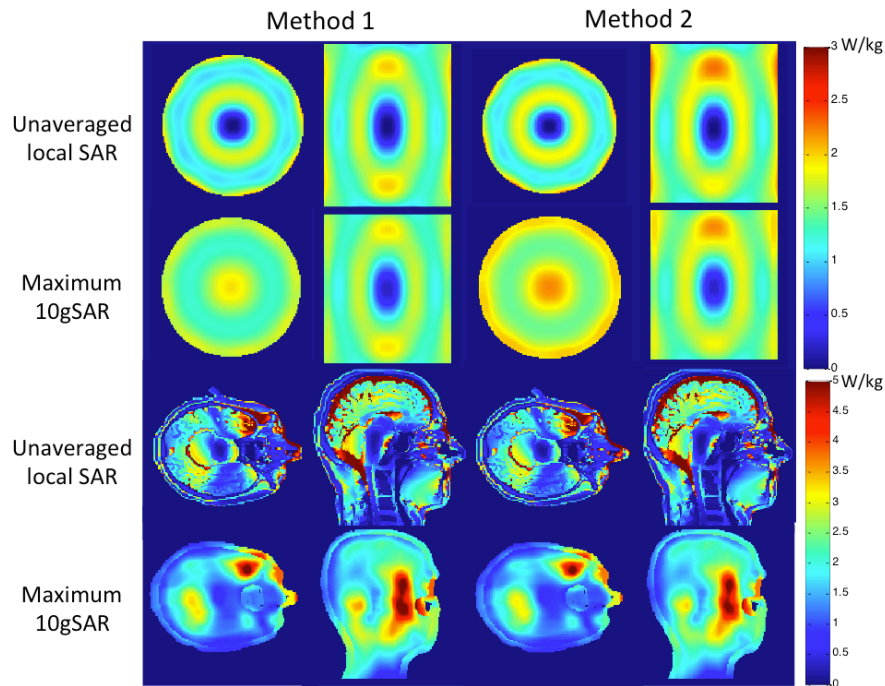


Figure 3.16: Results of un-averaged local SAR and location of $10\text{gSAR}_{\text{max}}$ estimates

Experiment 2: Evaluation of real capacitor values using a pork mince phantom

Thermal changes calculated from the 10g averaged SAR estimation are displayed in Figure 3.17.

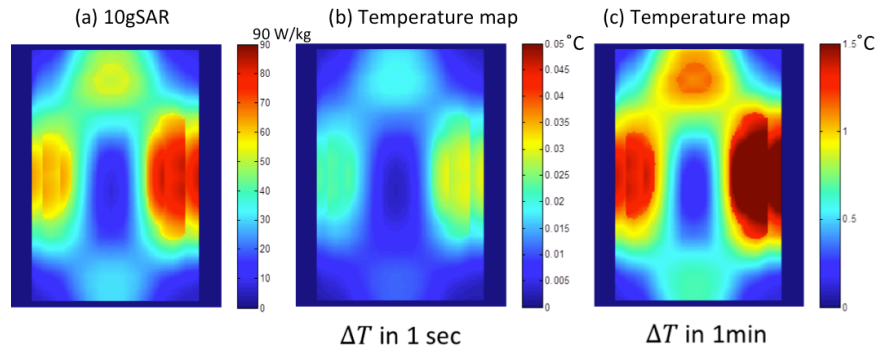


Figure 3.17: Simulated 10g SAR and thermal changes calculated using 10gSAR and the specific heat capacity

Similar surface temperature changes were observed both in the liquid crystal sheets and in the EM simulation, as seen in Figure 3.18.

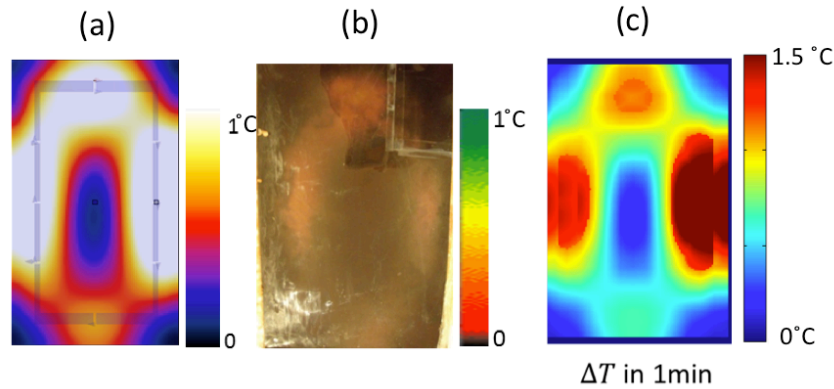


Figure 3.18: Thermal change calculated by: (a) thermal simulation, (b) observed by experiment using liquid crystal sheets, and (c) calculated using 10gSAR and the specific heat capacity

Surface profiles show that the temperature increased along the path of the copper strip, and is particularly concentrated close to the matching capacitor (source) and centre of the longitudinal copper strip, as seen in Figure 3.18(a).

Simulated and experimental temperature changes resulting from 60 seconds of heating are shown in Figure 3.19. The initial temperature of the experiment was, Experimentally, a 0.7 °C increase was found at the edge of the phantom in response to an input power of 35 W for 1 minute, while a 1.8 °C increase was predicted by the EM simulation. In the phantom centre the EM simulation predicted a 0.2 °C increase whilst the optic probe measured a 0.1 °C increase.

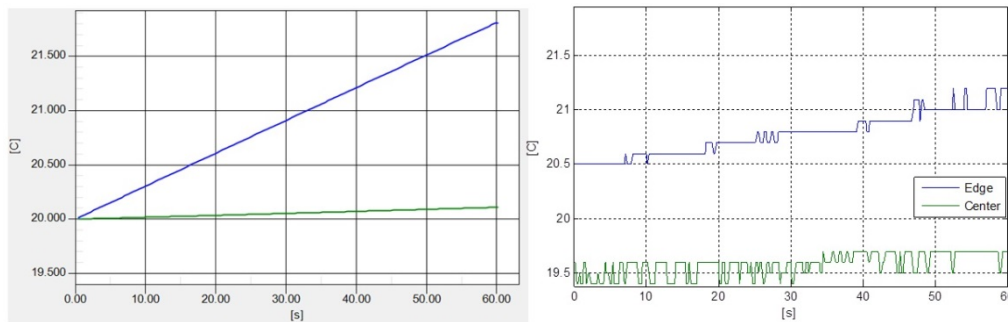


Figure 3.19: Results of simulated temperature at phantom (left) and measured temperature using fibre optic probe (right). (The initial temperatures at the centre and the edge of the pork phantom were not stabilised at 20 °C as in the simulation.)

Experiment 3: Comparison of lumped element simulation methods to measured thermal maps

For the idea current simulation, the predicted RF heating profile showed an ‘ideal’ pattern without evidence of coupling from adjacent coil elements, while the simulations with matched/tuned and real values demonstrated interference between neighbouring elements, pushing main heating patterns inward, as seen in Figure 3.20. The PRF demonstrated asymmetries in the thermal profile.

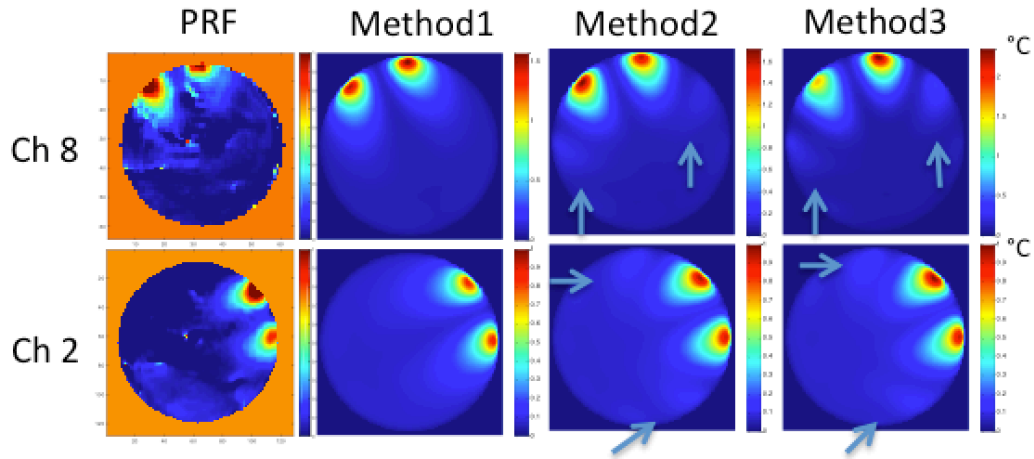


Figure 3.20: RF heating profiles (Power scaling factor: Ch8=26.8W, Ch2=14.5W);
Arrows pointing out couplings from adjacent element

A single-channel RF heating experiment gave a maximum temperature rise of 2.63 °C over a 5 min 20 sec heating period for Channel 8 measured by the fibre optic probe, see Figure 3.21.

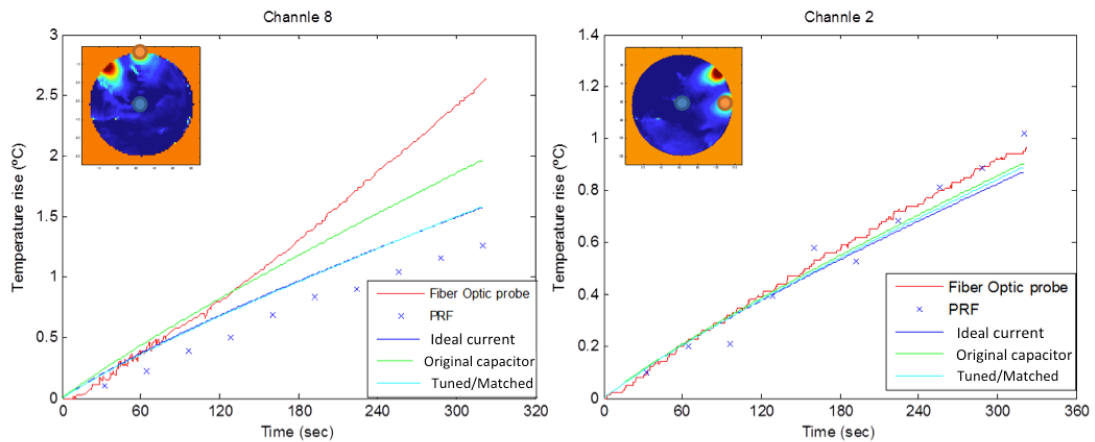


Figure 3.21: Measured and experimental temperature elevation at edge point

With PRF thermometry a maximum rise in temperature of 1.09 °C was observed at the edge of the phantom. The real-time fibre optic temperature measurement was compared with the PRF measurement and the 3 simulation methods, as shown in Table 3.3.

	Optic Fiber probe	PRF	Method1	Method2	Method3
Channel 8	2.63	1.14	1.56	0.83	2.30
Channel 2	0.97	1.02	0.86	0.88	0.90

Table 3.3: Temperature changes ($^{\circ}\text{C}$) at a monitoring point at the edge of the phantom

Method 3 showed the closest estimation of the measured heating profile in both Channels 8 and 2, with an accuracy that was within 15%. The three simulation methods showed different amounts of predicted heating, which are shown in comparison with the experimental PRF measurement in Figure 3.22.

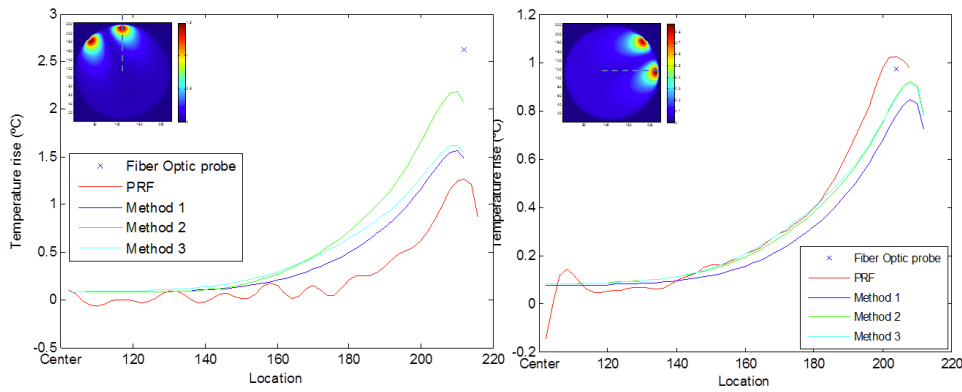


Figure 3.22: Temperature elevation in profile view

3.4.4 *Discussion of methods of simulating lumped elements*

In the CP mode phantom simulations, an 11.5% difference were found in the maximum 10g averaged SAR, with a smaller difference of only 3.1% observed in the human model simulation. It is possible that in the human model simulation there is a better agreement because the phantom is much closer to the capacitors and more sensitive to them. The calculation time was on average 66% faster for the ideal current method versus the matched/timed method, which for coil development is a significant saving in time. With respect to B_1^+ , the two methods agreed well, this is expected in the centre of the simulations because the comparison is inherently normalised to the central B_1^+ , however the profiles remained the same. In the matched/tuned method additional time is required for a broadband simulation to tune the coil for each target phantom and frequency, whereas in the ideal current method this is not required and as such is simpler to set up and faster to run while still providing an accurate depiction of the B_1^+ distribution and also a good estimation of the maximum SAR characteristics, although the SAR distribution was not well matched between the two methods. This indicates that for coil design purposes or when using a simple single channel transmit coil the ideal current method may be sufficient, but may not be sufficient to capture the subtleties of local SAR in pTx.

Further studies are needed to evaluate differences between the two methods when using other coil geometries, human models, at different frequencies, and to assess the effects of more realistic distributions of capacitors in tuned coils. In conclusion, the ideal current method is a feasible option for rapid evaluation of B_1 transmit field and SAR distributions in CP mode using parallel transmit coils.

RF heating test using pork phantom

RF heating profiles were assessed using a liquid crystal film and optic fibre measurements on an 8-channel coil and a minced pork phantom. Initial temperatures observed from two fibre optic probes were slightly different, 19.5 °C and 20.5 °C, which could be due to the residual inhomogeneity in temperatures, or offsets of the probes. The 30 minutes that the phantom was in a water bath may not have been sufficient, to achieve an evenly distributed temperature. There are substantial differences found between the predicted and actual temperature increases, most notably a -61% difference at the edge of the sample. However, the distribution and position of the maximum of the heating agreed well between simulations and liquid crystal sheets. Despite the easy access of pork phantoms that can be purchased from a shop it is difficult to control the quality of the phantom, and store it for repeated experiments due to the limited expiration date of the sample.

The limitation of using a liquid crystal sheet is that a quantifiable data analysis is not possible. In addition, the actual heating can be underestimated when the sheet for measurement is located between the heating source and the object. The quantifiable surface temperature measurement can be achieved by using an infrared thermal camera.

Some types of fibre optic probe, such as those used in GaAs semi-conductive (SC) systems, are sensitive to the main magnetic field (106). The product used in this thesis was a SC system; so an in-house calibration test was done to enable adjustment of the measured absolute temperature at the centre of the MRI scanner (at 7 Tesla field strength) to adjust it into absolute temperature in the control room. During this calibration process it was found that the presence of the main magnetic field does not affect measurement of relative temperature changes, so that the apparent measured

temperature can be easily corrected by subtraction of the relevant offset temperature caused by the main magnetic field.

Comparison of various simulation schemes with RF heating test

Differences between empirical and simulated results for RF heating were found in all methods. The ideal current model has the advantage of fast calculation times and is easy to implement in various coil geometries. Amongst the three simulation methods assessed, the simulation using realistic capacitor values was closest to the experimental measurements obtained during RF heating. The precise distribution of capacitors used in the coil design may generate different field behaviours and coil characteristics. However, this technique is difficult to adapt for use with certain commercial coils, since accurate coil geometry and capacitor values are usually not provided. Therefore, application and use of this technique is likely to be limited to in-house constructed RF coils, or coils for which full information is provided.

Care is needed to interpret the PRF results, since random uncertainties of PRF MR thermometry have been observed ranging from 0.3 °C to 1.4 °C (107). The discrepancy between the experimental and simulated heating patterns suggests that a more accurate model of the coil is required to have confidence in using the simulated RF heating pattern as a safety validation step. The results show dropout in regions due to poor transmit homogeneity. Further studies will be described in the next chapter, with improved PRF thermometry and reduced artefacts.

New advanced methods to tune and match RF coils should be investigated, one proposed solution is to match the simulated and measured scattering matrix when optimising a simulation. The method of optimising reflected power at each coil port was introduced by Kozlov, called Co-circuit simulation (92). Using this method, port

responses can be monitored by applying different combinations of LC components from pre-calculated multiport simulations, so that an optimum combination of capacitances (or inductances) can be chosen to minimize reflection from the port. In order to monitor and optimise the response from each coil element, multi-port broadband simulations are required by replacing all lumped elements into the port as well as the actual port at each element. This requires a huge amount of calculation time (e.g. for the 88 separate simulations that would be required in our coil) and space for data storage, but once a multi-port broadband simulation is completed it allows the user to optimise any coil element. Previous studies have focused on matching the measured scattering matrix on the bench to the simulation by means of S-parameters, but the introduction of advanced hardware, such as directional couplers (DICOs), allows one to measure reflection coefficients on-the-fly during the scan at the centre of the bore, which results in an increased confidence in the measurement and better reflects the true coil response in the actual experiment. Furthermore, this technique can be applied to optimize not only the magnitude, but also the phase of the scattering matrix (94). Reference 21 has shown that benefits of matching the reflection coefficient can be limited when only magnitude is used for matching. Matching to the scattering matrix may not be suitable for coils with many capacitors as used in this chapter, this is because it becomes an ill determined problem with more capacitances than scattering matrix parameters.

3.5 Effects of spatial resolution in EM simulation

In this section the effects of grid size on the EM simulations were considered (108). Previously, simulations with dense grids were not possible due to limits of system memory and computational capacities. Collins *et al* have reported that it is necessary to utilize a minimum of a $2 \times 2 \times 2 \text{ mm}^3$ isotropic voxel in order to simulate the anatomy of the head and neck region, and a minimum of $5 \times 5 \times 5 \text{ mm}^3$ isotropic voxel resolution for the rest of the body, demonstrated using birdcage coil (82). It is more complicated when specifying the grid resolution to represent RF coils active components, for example a coarse grid may result in discontinuities in electrical elements or their connections to lumped elements. This results in the electrical behaviour of the coil elements changing. A variable grid system can be used in Sim4Life. A variable grid allows users to have a spatially varying grid density, which is more efficient on computer memory, and a higher grid resolution near electrical elements and a low resolution for simple geometries or remote from the RF coil. The representation of the human models should also be considered, for example high resolution voxel models, such as MIDA (109), which have 115 tissue compartments described at $0.5 \times 0.5 \times 0.5 \text{ mm}^3$ resolution. To take full advantage of these high resolution models dense grids are required in simulation to account for small tissue compartments. In this section we evaluate the effect of grid resolution on the simulations.

3.5.1 Methods

The 8-channel pTx head coil described above was used in simulations that incorporated the cylindrical phantom. The phantom dielectric properties were the

expected values of an average brain (not measured values) of ϵ_r : 51, σ : 0.57 S/m. Scattering parameters were used to evaluate the required resolution to simulate the electrical behaviour of the RF coil by increasing the resolution until the scattering is no longer affected by an increase in resolution.

The phantom was modelled at the centre of the cylindrical 8-channel transceiver coil (diameter/length: 292/200 mm), with capacitor values of a real-life coil. A single element of the coil was simulated with 27 W input power. Specific absorption rate and S-parameters were calculated using six different grid sizes, chosen to span a range of resolutions from 150×150 to 400×400 over a field of view with dimension $350 \times 350 \text{ mm}^2$.

3.5.2 Results

Figure 3.23 shows the simulated reflection coefficients for the driven channel for the various grid resolutions. At higher grid resolutions the reflection coefficient converges to a frequency of 307 MHz.

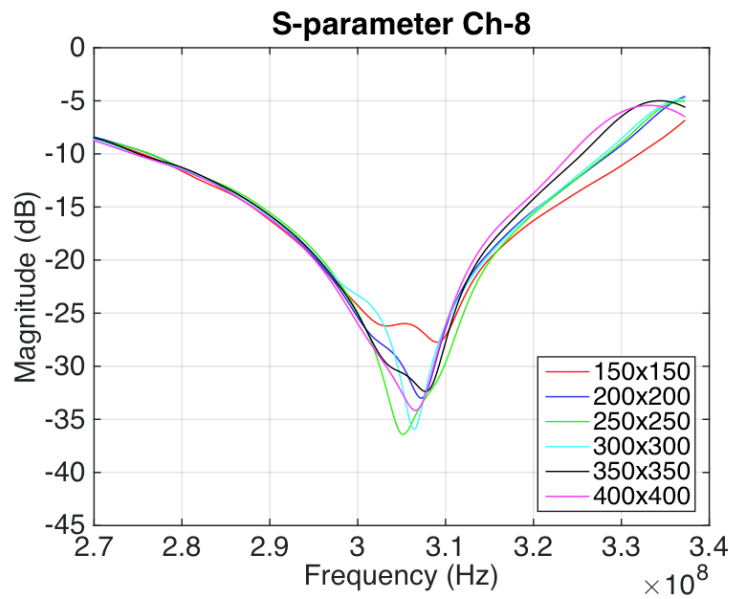


Figure 3.23: Reflection coefficient at different grid sizes for channel 8

Figure 3.24 shows the estimated heating and SAR deviations as a function of grid size, compared to a reference grid size of 400×400 .

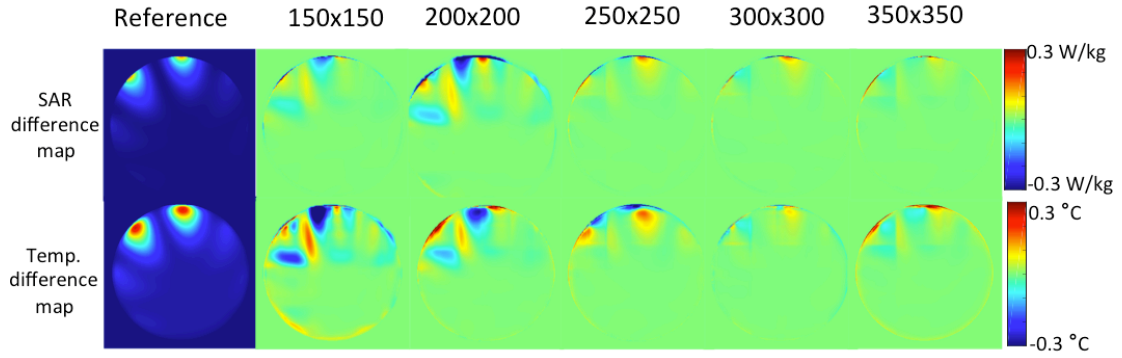


Figure 3.24: Global SAR and temperature difference compared to a 400×400 grid

The maximum temperature and global SAR values are reported in Table 3.4. We observed significant variations close to the boundaries for grid sizes of 150×150 and 250×250 , but these deviations stabilized for grid sizes larger than 250×250 .

Grid size (Cell)	150x150	200x200	250x250	300x300	350x350	400x400
Max. Temp. (°C)	2.09	2.21	2.08	2.11	2.12	2.12
Local Temp. (°C)	1.92	2.02	1.85	1.86	1.88	1.85
Max. SAR (W/kg)	1.49	1.63	1.48	1.49	1.49	1.53
S_{11} (Ch8) (dB)	-22.79	-22.89	-22.01	-23.00	-23.35	-22.29
Calculation time (HH:MM)						
Broadband	0:41	0:52	1:22	1:56	3:26	5:22
Harmonic	1:10	1:41	2:41	3:50	6:51	10:40

Table 3.4: Results of temperature elevation, SAR and S_{11} for different grid resolutions

3.5.3 Discussion on sensitivity of resolution in simulation

EM simulations were conducted over a range of grid sizes and the results compared. Simulations with larger grid sizes (higher grid densities) provided more consistent results, with deviations at the boundaries observed for smaller grid sizes (lower grid

densities). Further studies are needed to investigate the method to estimate optimal grid sizes under specific conditions and for different RF coils.

The simulation results with different resolutions showed uncertainties when an insufficient grid density is used due to limits of computing power, although, it has been shown that high-resolution computation is not necessary when the object is homogeneous, under which conditions the EM properties are captured well with a grid size of 250×250 . The minimum requirement for gridding is to provide sufficient resolution, especially for adequately describing the coil geometry. Further efforts to increase computation may not be necessary to go beyond 1 mm resolution in our coil for the case of a homogeneous phantom. This needs to be re-investigated in simulation for the case of different coil geometries and for different objects.

3.6 Effects of gradient coil presence as an RF shield in EM simulation

In this section we evaluate if the presence of an RF shield will affect the results of EM simulations of the RF coil described above. In practice, the gradient coil can serve as such an RF shield (41), and indeed many gradient coils incorporate an RF shield into their design and construction. However, a head transmit coil is relatively small compared to the gradient coil, so the effect of the gradient coil is often ignored in EM simulation. In this chapter, we assess the effect of including or excluding a gradient coil in the EM simulation to determine the sensitivity of the simulation to its presence.

3.6.1 Methods

Two simulations were run, one with and one without an RF shield. The dimensions of the shield were taken from our 7T scanner's SC 72 (Siemens, Erlangen, Germany) gradient coil with a length of 158 cm and diameter of 64 cm. This was simulated as a surface with perfect electric conductivity (PEC) material, as shown in Figure 3.25. We calculated B- and E-field distributions and temperature changes with and without the conductive surface present to establish if the gradient coil showed any effect as an RF shield (input power: 26.68 W, TA: 5 min 20 sec).

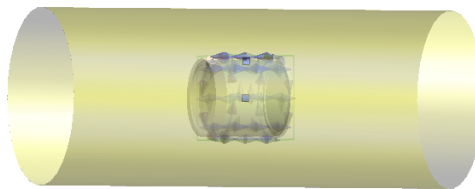


Figure 3.25: Simulation set up showing incorporation of the gradient coil as an RF shield (yellow), outside of the 8-channel head coil (blue)

3.6.2 Results

Figure 3.26 shows the effect on the B_1 transmit field and temperature changes depending on whether the gradient coil (acting as an RF shield) is included or not included in the simulation model.

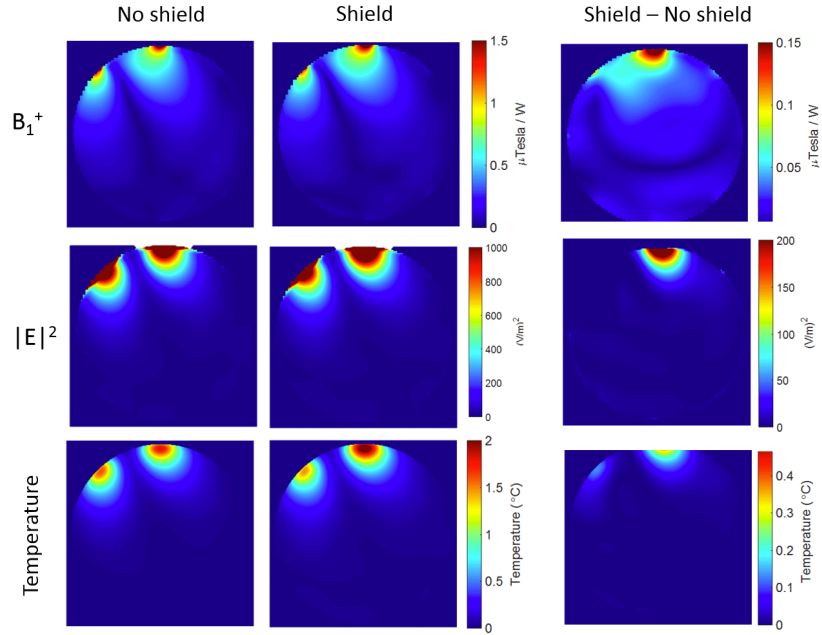


Figure 3.26: Results of B_1 transmit field and temperature changes depending on inclusion or non-inclusion of the presence of the gradient coil.

The edge temperature changes were compared in profile view between the results obtained when the gradient coil was present as an RF shield or not, in Figure 3.27.

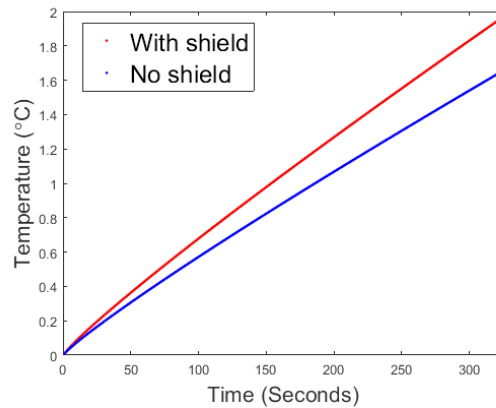


Figure 3.27: Results of edge temperature changes with and without gradient coil present and acting as an RF shield

3.6.3 Discussion of the use of a gradient coil RF shield in the EM simulation

The effect of the gradient coil acting as an RF shield was assessed. Regarding B_1 transmit field calculation, a difference in the maximum B_1 of 3.2% was found for whether the gradient coil was included in the model or not. Regarding RF heating simulation, a 0.31 °C temperature difference was found in our simulation (input power: 26.68 W, TA: 5min 20 sec). This could result in (conservative) over-estimation of RF heating compared with experimental results.

The presence of a gradient coil as an RF shield seemed to result in a higher amount of energy deposition, potentially due to the reflection of B_1 radiation, and the frequency shift resulting in different port response, but it has a limited effect on either B_1 transmit field, E-field distribution and RF heating, which can thus be ignored in our condition.

3.7 Summary Conclusion

This chapter presented a phantom design and electrical property characterisation process that was used to evaluate multiple initialization and setup conditions for EM simulations. We found that:

- The chosen phantom recipe controlled the electrical properties and closely mimicked those of human tissue (brain).
- Using an open-ended coaxial probe to measure the electrical proprieties demonstrated that the phantom's electrical properties were within 10% of the predicted values.
- Using measured electrical properties of the phantom in simulation significantly (9.1%) altered the predicted RF heating compared to using the

expected properties.

- Ideal current-driven simulations of loop elements significantly reduced the computation time compared to tuning and matching the simulation while providing a realistic prediction of B_1^+ , although this method poorly predicted the RF heating.
- Using realistic capacitor values in simulations provided the closest match to predicted RF heating. However, significant differences remained between simulation and measurement.
- A simulation grid size of $1 \times 1 \times 1 \text{ mm}^3$ or less around coil elements was found to minimize errors in RF heating prediction.
- Including an RF shield in the simulation increased the deposited RF energy, however the B_1^+ and E-field distribution was minimally affected.
- PRF RF heating measurements calibrated against a real fibre optic temperature change can be used to assess and validate different types of RF simulation, pTx methodologies for PRF are presented in the next chapter.

In conclusion choosing a proper simulation method and environmental set-up is important, as they affect the confident of thermal predictions.

4 RF Heating Assessment of a pTx Head Array Coil

4.1 Introduction

The use of pTx adds complexity to the estimation and monitoring of RF energy deposition (110,111) through difficulties in predicting safe levels for the local SAR. In particular, when using pTx the local SAR no longer has a simple linear relationship to input energy, but instead has a complex relationship dependent on the superposition of local E-fields, which can vary in time through an acquisition. Thus, electromagnetic (EM) simulations of each transmit channel are required to monitor in real time the expected local RF energy deposition (112).

In order to assess the validity of the electrical model of a simulation, measurements are required. Proton resonance frequency shift (PRF) thermometry is widely used in MRI RF safety studies, both in-vivo and in phantoms for validation and to monitor the temperature changes in certain conditions (113). PRF uses the modulation of the chemical shift of hydrogen when attached to oxygen due to temperature dependent electron shielding. By using the linear relationship between phase changes in the water resonance signal and temperature, thermal elevation can be accurately captured experimentally (Equation (4.1)).

$$\Delta T = \frac{\Delta\phi - \Delta\phi_{drift}}{\alpha\gamma B_0 TE} \quad (4.1)$$

where $\Delta\phi$ is the phase change in the water signal caused by the temperature change, $\Delta\phi_{drift}$ is a correction term for any background (non-temperature-related) phase drift, α is the proportionality constant in the linear temperature dependence of water protons, γ is the gyromagnetic ratio, B_0 is the main magnetic field, and TE is the echo time.

Although, the phase changes of a water image should be proportional to temperature change, there are non-temperature-related phase drift behaviours which need to be corrected to capture accurate temperature changes (102). This unwanted phase drift can be complex, for example due to static field changes caused by heating of passive shim material that is incorporated into the gradient coil, so an appropriate method is required to correct this phase drift. The use of fibre optic probes is an example of a non-magnetic device used to monitor absolute temperature changes. It can be implemented to monitor temperature changes at multiple observation points and to correct non-RF-heating related phase drift (106). Use of an oil phantom has also been suggested for phase drift correction, since the phase changes of protons in oil are independent from temperature changes (3). Likewise, a B_0 field probe can be used for capturing phase drift by observing phase changes in a set of Fluorine (^{19}F) samples (114)(115). This has led to several recipes being proposed to produce tissue-equivalent phantoms for MR safety studies. For example, Ito et al. proposed a method to mimic tissue properties by mixing polyethylene powder to decrease permittivity, sodium chloride to increase conductivity and agarose to solidify the phantom (90).

Simulating an EM field in software allows many parameters to be configured, including geometric properties, coil capacitor values and simulation spatial resolution, all of which can alter the result of the simulation (4,116,117). In the case of pTx any deviation of the simulation from reality is compounded by the interaction of multiple channels (which is hard to fully model in simulations) and injects uncertainty into SAR prediction, which can require the adoption of prohibitively restrictive limits in order to ensure safety. To gain confidence in the validity of such simulations, measurement of the B_1 transmit and E-fields are required. B_1 transmit fields can be measured easily via MRI techniques, however E-fields cannot be

measured with standard MR equipment. An alternative is to map the thermal effect (heating) of these fields on the sample as a surrogate (ultimately, in fact, the safety parameter of most direct safety relevance). Although impractical to achieve in the case of *in-vivo* imaging, heating effects can be measured in representative phantoms for each element of a transmit array and for different transmit configurations.

For power deposition durations much shorter than the relevant time constants for thermal conductivity of a phantom, SAR and temperature increase are related by heat capacity. As such, temperature monitoring offers an elegant way to validate EM simulations. The thermal behaviour in reality differs from SAR due to thermal conduction, perfusion, and boundary conditions (76,77). Therefore to validate EM simulations using temperature measurements a phantom with known electrical and thermal properties is needed. This phantom should be able to assess the full volume of the coil and have similar electrical properties to human tissue. Numerous phantom recipes have been introduced (87,90,118,119) along with methods to characterize their electrical properties (120).

A popular way to measure temperature changes throughout a phantom is via an MRI phase sensitive method that uses proton-resonance frequency shift (PRF) (1,102,121). The resonance frequency of water changes with temperature and as a result is reflected in the phase of the image, with a greater effect for a longer echo time. However, a confound to PRF measurement is the possibility of extraneous influences on the main magnetic field, in particular induced magnetic field changes arising from gradient coil heating/cooling. Methods to monitor such unwanted field drifts include using oil-filled samples as fiducial markers that have a negligible thermal PRF response, however such markers can add complexity to the phantom design and EM simulations. Hardware solutions include using B_0 field cameras or a

number of thermal probes (4 or more) to capture spatial gradients of absolute temperature changes (114,122,123). However, such hardware may not be easily available to many research groups.

As described in Section 2.3 of Chapter 2, the TIAMO technique can be used at ultra-high-field ($\geq 7\text{T}$), in order to facilitate full imaging coverage of the volume with minimum loss from signal cancelation (60). Additionally, it is desirable to induce heating with a different transmit configuration to that used for imaging and enable flexibility in evaluating heating of different pTx configurations or channels.

In this chapter we assess via EM simulation the impact of electrical and thermal phantom properties on measurement error and present the methods used to measure these properties. A multi-echo PRF technique is used to assess a pTx coil, in which multiple echo times are adopted for increased accuracy and to reduce measurement-to-measurement instability, along with a TIAMO image acquisition to reduce B_1 transmit dropout. To address gradient-heating-induced field changes, a stabilization pre-scan method is evaluated.

4.2 RF coil used: 8-channel pTx dipole array

A 7T Magnetom human MRI scanner (Siemens Healthineers, Erlangen, Germany) was used in conjunction with an 8 channel transmit/receive dipole coil array (MR Coils BV, Zaltbommel, The Netherlands) as shown in Figure 4.1 (42).

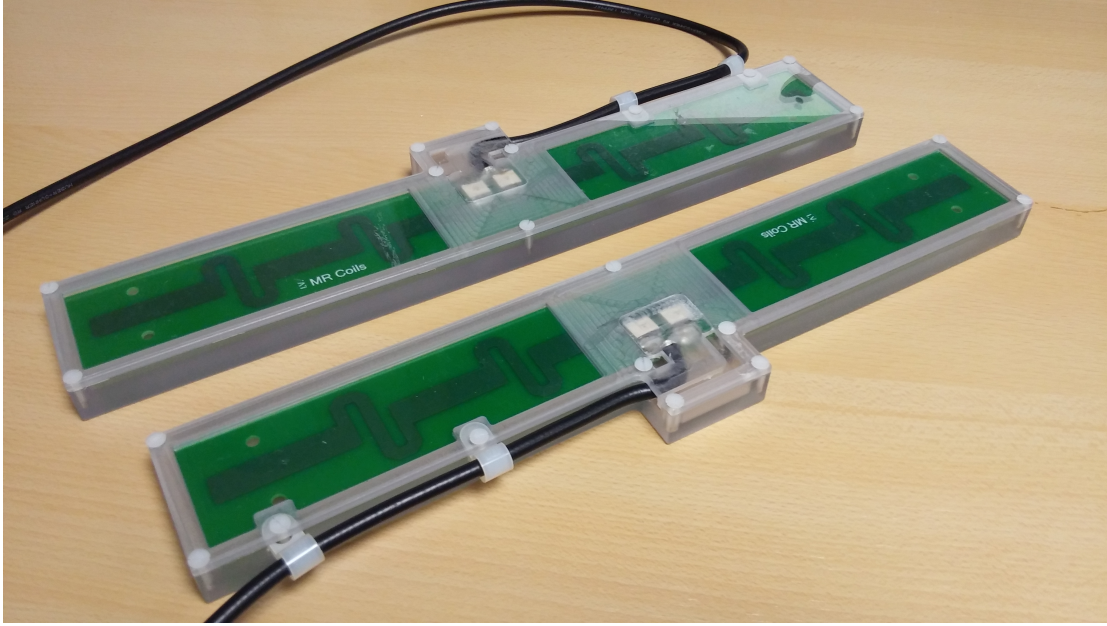


Figure 4.1: Fractionated dipole elements with 20 mm PMMA spacer and covers

The fractionated dipole antenna was introduced in 2016 by Raaijmakers et al. and is popular for body imaging at 7T. The dipole is inductively shortened using meander structures and reduces the SAR by 41 % to 63 % compared to alternative high field coils. It provides a large longitudinal field-of-view (42). Drawings of meander structures, PCB, and dielectric pad were provided by Dr. Matthew Restivo to facilitate EM modelling along with their material properties, then PMMA housing and matching capacitors were added on the top of original drawings.

4.3 Methods

4.3.1 MR phantom design of RF heating at 7 Tesla

Agar-gel phantom version 2: Alternative phantom production procedure

The production of an Agar-gel phantom using an autoclave presented difficulties including uncontrolled water loss, and a long production time as discussed in Chapter 3. In this section an alternative procedure to produce a large volume agarose phantom is described. In our alternative procedure, a hot plate was used instead of an autoclave, as this allowed a lower heating temperature of 121°C. A setting compound TX-151 (similar to corn starch) was also added to increase the viscosity and reduce the setting time. The phantom container described in Chapter 3 (diameter 280 mm, height 300 mm, and thickness 5 mm) was used. The phantom recipe contained the following proportions per Litre of de-ionized (DI) water: agar (20 g), polyethylene powder (150 g), sodium chloride (4 g), TX-151 (68 g, Oil Center Research International, Lafayette, LA, USA), and Benzoic Acid (30 g), with a total phantom volume of 16.8 Litres (85). This recipe targeted the average electrical properties of brain white matter and grey matter at 297.2 MHz (ϵ_r : 51; σ : 0.57 S/m). The following procedure was adopted: firstly, the DI water was boiled on a hot plate and mixed with sodium chloride (Sigma-Aldrich, United States) and benzoic acid (Fisher Scientific, UK) using a magnetic stirrer. Agar powder (Sigma-Aldrich, United States) was mixed in until the colour of the solution became transparent. The temperature of the hot plate was maintained below 300 C° to avoid burning the agarose with continuous stirring near the heat source. When the water started boiling (bubble formation) the heat source was turned off and TX-151 (Oil Research Company, United States) was added by sprinkling gradually while quickly stirring. The solution was filtered using

a strainer to remove undissolved TX-151 and added into the phantom container along with the polyethylene powder (Sigma-Aldrich, United States) which is an insoluble ingredient and is mixed until it is evenly distributed. Any bubbles on the top were purged using a hypodermic needle.

Determining the thermal and dielectric properties

In order to reproduce the properties of the phantom *in silico* the dielectric and thermal properties (specific heat capacity, thermal diffusivity, thermal conductivity, and heat transfer coefficient) needed to be characterized. In the case of the electrical parameters, the dielectric properties of the phantom were measured with an open-ended coaxial probe and network analyser as previously described in Section 3.3.2, and saline water was used for verification of the measurement (89).

The specific heat capacity of the phantom was estimated using the weighted mass and specific heat capacity of each component in kcal/kg/°C [TX-150 (equivalent to TX-151): 0.3; polyethylene powder 0.52; H₂O: 1; NaCl: 0.217; Benzoic acid 0.288; Agar 0.382] (124–126). Thermal diffusivity of the phantom, K , was measured using a laser flash system LFA 427 (NETZSCH-Gerätebau GmbH, Germany), averaged five times across four different samples ($K=0.126 \text{ cm}^2/\text{s}$). This value is then used to calculate thermal conductivity (κ), via measurements of density (ρ) and specific heat capacity (C_p) where:

$$K = \frac{\kappa}{\rho \cdot C_p} \quad (4.2)$$

and κ is thermal conductivity, ρ is mass density, C_p is specific heat capacity.

The heat transfer coefficient determines the thermal coupling of the phantom to its environment. This was calculated by storing the phantom in a room controlled to 23 °C for 3 days and then subsequently placing the phantom in the scanner room, which

was maintained at a controlled temperature of 18.6 °C. The temperature of the phantom was then monitored using a 2-channel fibre optic probe (Neoptix, Canada) for 47 hours, one probe placed at the edge of the phantom and the other at the centre. The observed temperature changes were then compared to matched simulations in Sim4Life (see below) in which various heat transfer coefficients were assessed.

4.3.2 *Electro-magnetic simulation*

EM simulations were performed in Sim4Life (ZMT Medtech, Zürich, Switzerland). The setup included a model of the 8-channel transmit/receive dipole array(42) placed symmetrically around the cylindrical phantom described above. The coils do not have tuning capacitors, and the matching capacitor values were chosen from the real coil values. A model of the gradient coil was not included as an RF shield in this simulation. The electrical and thermal properties of the phantom contents were set to the values measured using the protocol described above and the shell of the phantom (5 mm thick PMMA) was set to ϵ_r : 3.2, σ : 10^{-9} S/m in the simulation. The grid size was $241 \times 247 \times 363$, with the maximum grid cell size, and the resolution was $1 \times 1 \times 1$ mm³ for the RF coil and allowed to adjust automatically in the software for the phantom. B_1 transmit fields were extracted and normalized to an input voltage of 1 V. The EM simulations were subsequently used as inputs to the thermal simulation tool provided in Sim4Life, and a target power at the source location was normalized to 6.56 W average conducted power (the value ultimately achieved at the coil location in practice) for 21 minutes duration. The heating maps calculated in the plastic container (outer 5 mm layer) were excluded in post-processing. A point virtual sensor was placed at the same location as the position of the fibre optic probe that was used experimentally. A mixed boundary condition was used with a heat transfer coefficient of 2.5 W/m²/K and a value of 18.6 °C used for the external temperature.

A sensitivity analysis of the thermal simulation was performed by adjusting each parameter of the dielectric and thermal properties (i.e. electrical conductivity, relative permittivity, density, specific heat capacity, thermal conductivity, and the heat transfer coefficient) by a $\pm 10\%$ difference.

4.3.3 Pulse sequence to evaluate pTx RF heating using proton resonance frequency shift

A pulse sequence was programmed to deposit RF energy on a specified channel and measure via PRF imaging the resultant heating using all channels. For this purpose a multi-echo 3D spoiled gradient echo (me-GRE) was adapted by adding a channel-specific, 10 kHz off-resonance Fermi RF pulse was used to consolidate RF heating efficiently without generating artefacts in signal acquisition, with a duration of 0.9 ms, prior to the RF image excitation and calibrated to deposit 10 W average power to the coil plug, as seen in Figure 4.2.

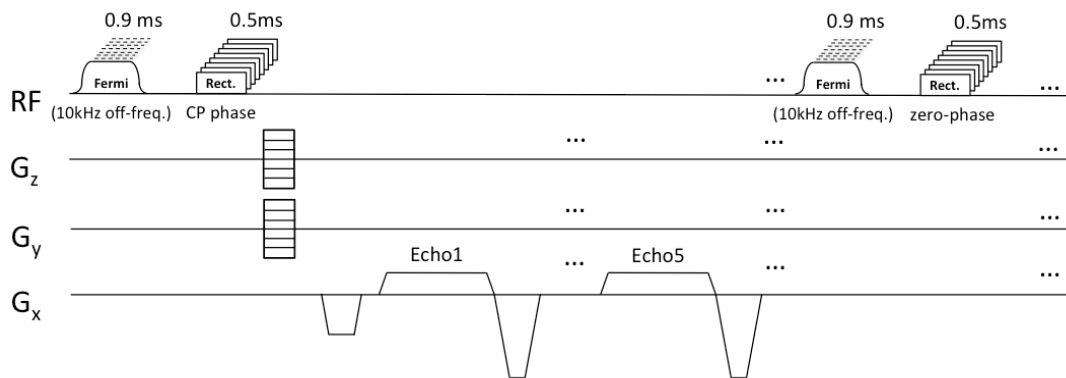


Figure 4.2: 3D GRE sequence diagram for PRF MR thermometry

In order to achieve adequate volume coverage, the me-GRE was set to acquire images in two transmit configurations, in an interleaved manner according to the TIAMO (60) regime. The image matrix size was set to $64 \times 64 \times 30$, with a field of

view of $300 \times 300 \times 300 \text{ mm}^3$, and an elliptical k-space coverage. The protocol resolution was $4.7 \times 4.7 \times 10 \text{ mm}^3$, TR = 14 ms, and TEs of 1.44 ms, 3.62 ms, 5.5 ms, 7.38 ms and 9.26 ms, excitation pulse voltage: 8.8 V (flip angle: 10°), and temporal resolution: 41 s. Each heating experiment was performed by applying a 0.9 ms heating pulse at 10 kHz off resonance on the chosen transmit channel prior to all excitation pulses to achieve an average absorbed power of 6.56 W, accounting for reflection, cable losses, and T/R switch losses. 30 image repetitions were acquired (total heating duration 21 min) after stabilisation of gradient-induced heating (see stabilisation protocol described below). The imaging excitation pulse contributed 0.07 W to the deposited RF energy per channel.

To evaluate the B_0 stability a one hour scan (86 measurements) without heating was acquired while monitoring the absolute temperature using a two-channel fibre optic probe (Neoptix, Quebec City, Canada). The PRF heating maps were reconstructed as below and first-order (X, Y, and Z) temperature gradients and bulk (spatially invariant) drift in temperature were calculated at each time point. The results from this stabilisation experiment were used to determine the number of heating-free scans necessary to establish thermal measurement stability (i.e., no remaining artifactual spatially evolving temperature distribution) before the main heating experiment could be performed.

4.3.4 Thermometry image reconstruction

The reconstruction of GRE phase images for multichannel coils at high field initially presented with Gibbs ringing, where ripples are seen particularly in the phase of the image near sharp boundaries. This is worse at high field due to the higher SNR and is pronounced in low resolution images. Therefore, we adapted two strategies to reduce these artefacts. Firstly, the edge of k-space is filtered with a Hann window function

$$w = 0.5 \times (1 - \cos(\pi \times \frac{n}{N})) \quad (4.3)$$

where n , N are constants used to decide the ratio of the window

The edge of the Hann window was determined by manually adjusting the ratio of n to N , with the outermost $n=30$ points chosen along with a value of $N=30$. Over-filtering could degrade spatial resolution, thus care must be taken in the selection of a value. The k-space data were then zero-padded to double the apparent resolution to $128 \times 128 \times 60$ and fast Fourier transformed to form images.

The second challenge is the combination of phase information from different channels and transmit (TIAMO) configurations. Multi-channel magnitude data can be easily combined using a sum-of-squares (SoS) method, but this does not apply to phase sensitive imaging. Therefore, in this case a singular value decomposition (SVD)-based receive combination method was implemented that finds an optimal combination for all receiver channels and measurements for a single voxel (127). This method calculates one optimal receive coil combination that preserves the relative phase and amplitude relationship between multiple images or measurements by finding the maximum singular value and vector at each point.

Following this, two different reconstructions were carried out, the first taking only the circularly polarised (CP, first TIAMO) mode transmit configuration images, and the second taking both TIAMO transmit modes (including one with zero transmit phase on all elements) by concatenating them in the receive dimension, giving 2×8 receive coil images which were combined using singular-value decomposition (SVD) using all the time points and echoes (127). The first echo of each measurement ($TE=1.44$ ms) was used to phase all subsequent echoes, this is expected to remove measurement-to-measurement instabilities of the transmit/receive chain. According to the results of the B_0 drift stabilisation experiment (see below) the 20th repetition of

the stabilization scan was used as a phase reference, and temperature maps were calculated using Equation (4.1), where $\alpha = -0.01$ ppm/°C, $\omega = 297.2$ MHz, $\gamma = 42.576$ MHz/T and $\Delta\phi_{drift}$ is derived from the fibre optic probe at the centre of the phantom (107)(1). The temperature maps from the second to the fifth echoes were combined by weighting them according to the product of their respective echo times and image intensities.

B_1 transmit maps in units of Hz/V were measured using a pre-saturation B_1 mapping method (Siemens-WIP543, TR/TE: 10 s / 1.97 ms) which acquires two turbo-flash images where the second image has a channel-specific non-selective saturation RF pulse applied prior to the readout train.

To calibrate heating in absolute units the B_1 transmit maps were calibrated according to the voltage delivered to the coil. Also, cable losses (including those within the T/R switch) were calculated on the bench as -1 dB, and the reflected power from mis-match was measured using the scanner's DICOs using a channel-multiplexed measurement, as in reference (128).

Two fibre optic probes were positioned, one in the centre of the phantom, and another 30 mm from the inner edge of the phantom. The 8-channel dipole array was placed equally around the phantom, as seen in Figure 4.3.

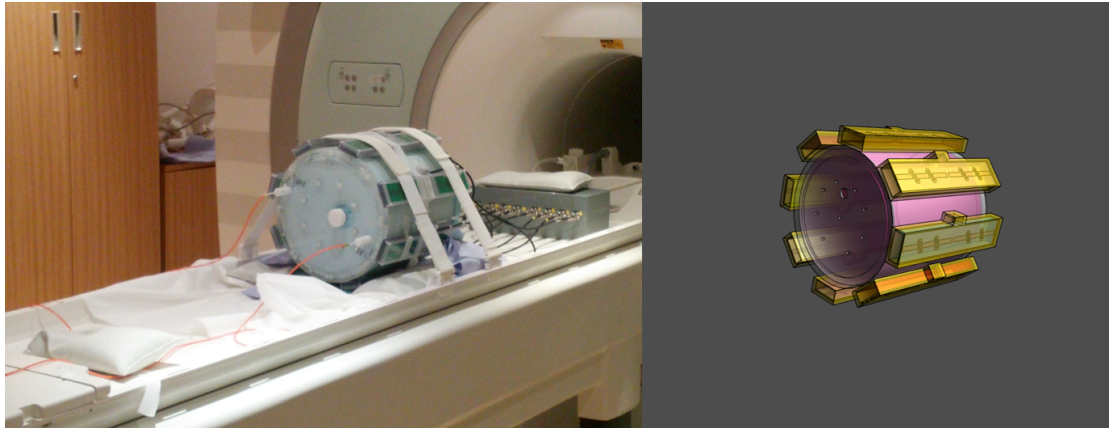


Figure 4.3: Experimental set-up, showing the phantom, coil, and fibre optic probes (left) and the model of the 8-element dipole array (right).

After heating experiments on each element the phantom was left to cool down for at least 3 hours before testing the neighbouring element.

4.4 Results

The measured, calculated and targeted characteristics of the phantom are listed in Table 4.1. For verification of the electrical measurements, the dielectric properties of 51.3 mM saline water were also measured, showing a measurement accuracy of within 1.6 %. The dielectric properties of the phantom were measured as $\epsilon_r=47.76$ and $\sigma=0.62$ S/m for relative permittivity and conductivity, respectively. Agreement to within 10% was found between the target and measured values for relative permittivity and conductivity, as seen in Table 4.1.

Material	51.3mM Saline		Phantom	
	ϵ_r	σ (S/m)	ϵ_r	σ (S/m)
Estimated value	77.98	0.60	51.00	0.57
Measured value	77.62	0.59	47.76	0.62
Percent error	0.4%	1.6 %	-6.4 %	+8.7 %

Table 4.1: Measured and target dielectric properties

The spatial gradient of apparent temperature change due to gradient coil heating is plotted against scan duration for the no-RF-heating stability evaluation scan, as seen in Figure 4.4.

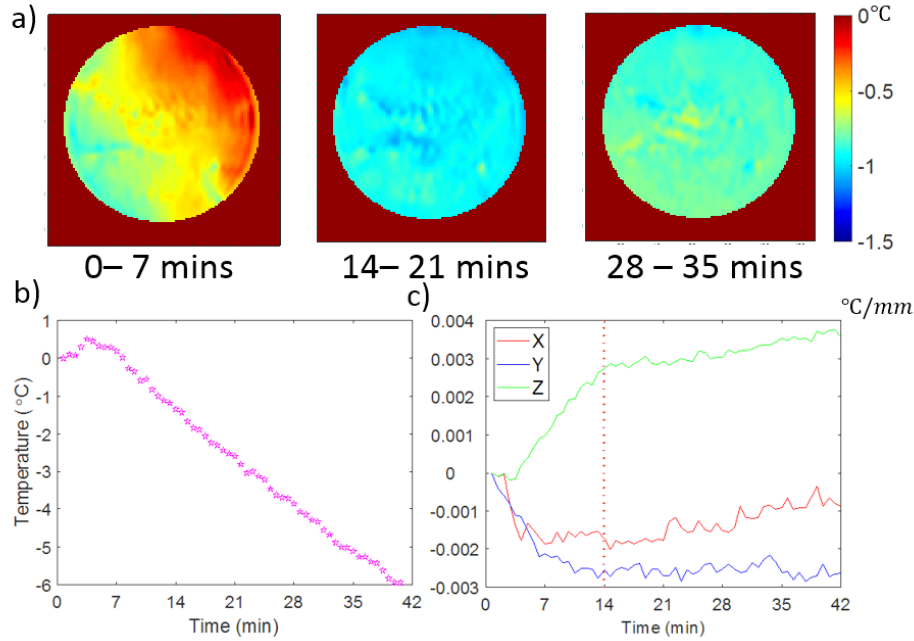


Figure 4.4: For the case of the no-RF heating experiment: a) shows temperature drift maps over various 7-minute intervals: 0-7 mins, 14-21 mins, and 28-35 mins. b) shows the average (spatially independent) apparent temperature drift over phantom. c) shows 1st order fitting in X,Y, and Z of the variation in apparent temperature drift over repetitions.

The spatial gradients in the temperature maps stop evolving after 14 minutes of scanning, however the average (spatially independent) temperature offset continues to increase throughout the scan. A stabilization period of 20 repetitions (= 13 min, 58 s) with a 0 V heating pulse on all channels was determined as a sufficient period to achieve negligible remaining spatially-dependent gradient heating effects, based on this calibration scan.

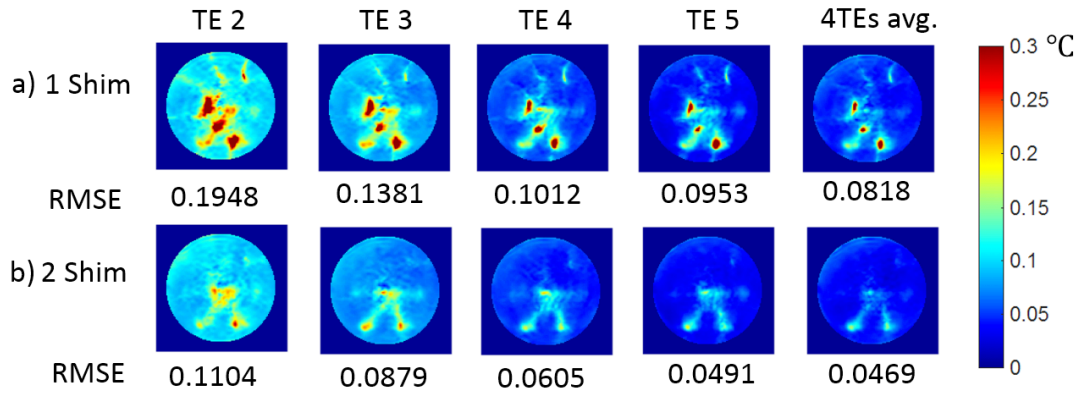


Figure 4.5: Standard deviation of PRF difference map in degree Celsius over each repetition in the centre slice of the phantom. a) shows the results of a single shim (CP mode) acquisition, b) shows results of a 2-RF-shim acquisition.

Figure 4.5 shows the temporal standard deviation of the PRF temperature measurements in a central slice over the remainder of the no-RF-heating scan, shown calculated with and without combination of the echo times, and transmit states. The average and peak standard deviation reduced from 0.062 to 0.044, and from 2.507 to 0.160 °C respectively by combining the two transmit states. The average standard deviation reduced from 0.108 to 0.045 °C for echoes 2 to 5, which was further lowered to 0.044 °C when combining the 4 echoes. The peak standard deviation reduced from 0.289 to 0.188 °C for echoes 2 to 5 and was further lowered to 0.160 °C when combining the 4 echoes. This trend is confirmed when looking at the temperature maps plotted as a histogram in Figure 4.6.

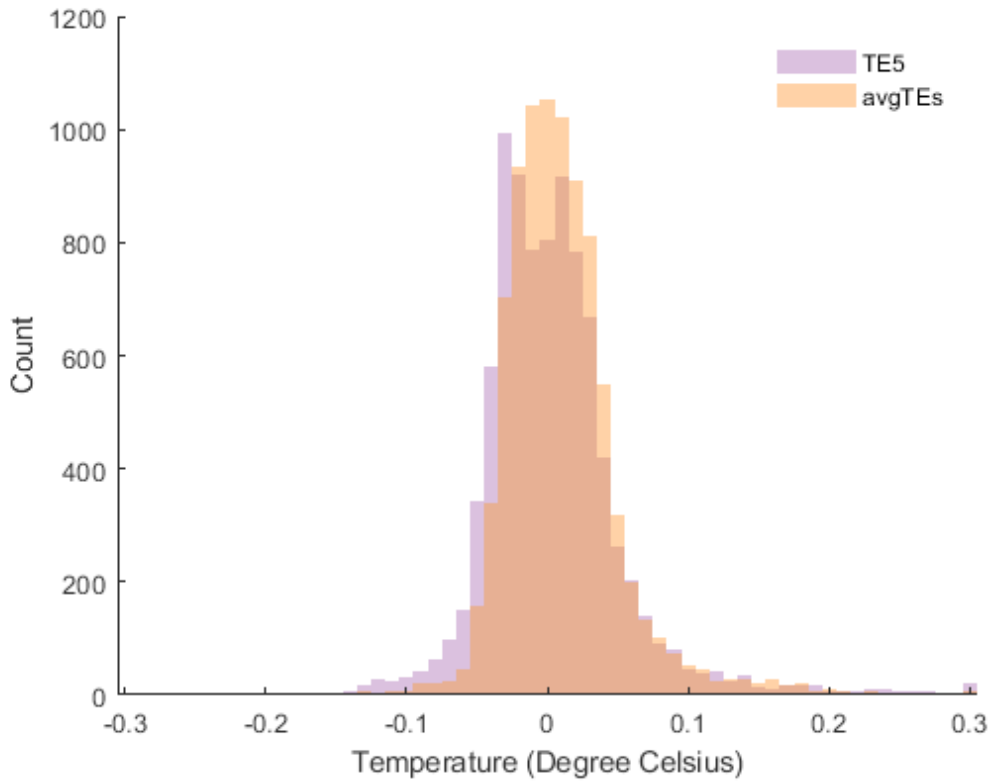


Figure 4.6: Histogram of temperature deviations taken from a PRF map with one repetition (41s) for the case of a 2-RF-shim acquisition, both for a single TE (TE5) and for the average across all TEs (avgTEs).

Figure 4.7 shows the measured B_1 transmit maps for all channels, and Figure 4.8 shows the measured PRF temperature maps when heating each of the 8 channels in turn. The measured B_1 transmit field and measured temperature maps are compared to the simulations in Figure 4.9, along with a comparison with the temperature measured with the fibre optic probes and the temperature rise at the probe locations as predicted by the thermal simulation. A residual field drift gradient is evident which produces up to a 0.25 °C error at the edge of the phantom.

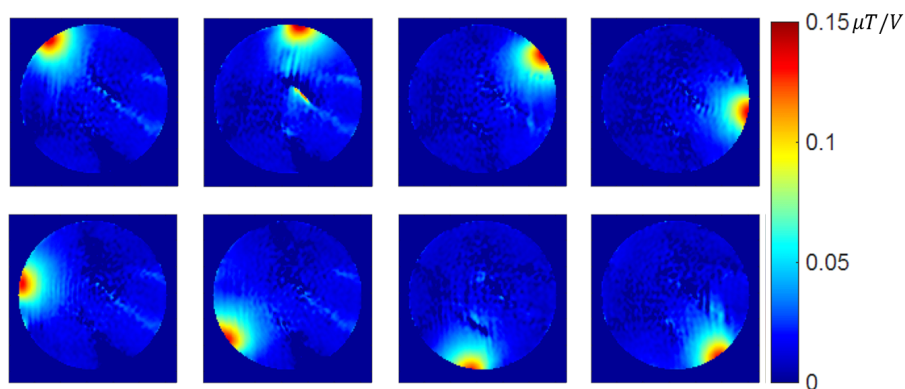


Figure 4.7: Individual B_1 transmit fields measured for each channel.

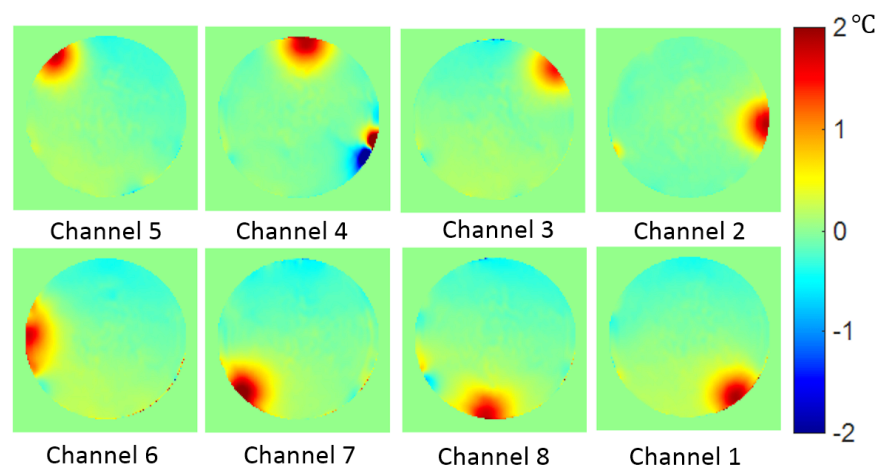


Figure 4.8: Measured PRF thermometry in each channel for the central slice. For transmit channels as labelled in the figure.

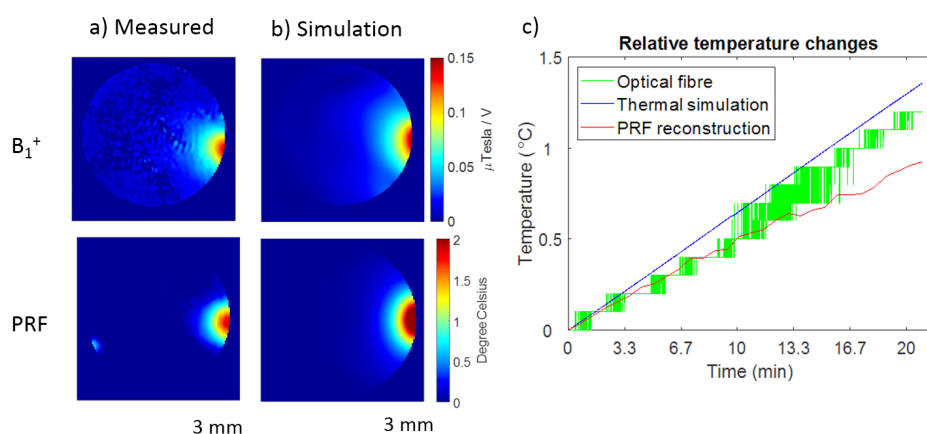


Figure 4.9: Results showing the B_1 transmit field and temperature map of channel 2.

a) shows the measured B_1 transmit field and PRF, and b) shows the results of simulation. c) shows the relative temperature changes at the edge of the phantom, as measured by the fibre optic probe, simulation, and PRF (using a 4 voxel ROI).

The effectiveness of phasing the data with the first echo is compared in Figure 4.10 for the heating profile from Channel 4 where an artefact is evident remote from the heating source. In this figure a reconstruction with and without phasing using the first echo are compared, where a visually smoother heating profile is achieved when using the first echo to phase the data.

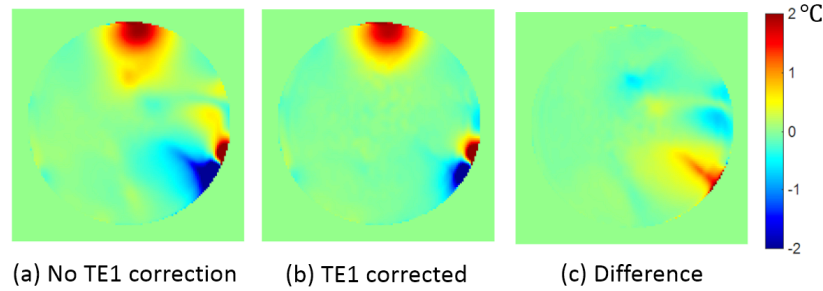


Figure 4.10: Combined echo evaluation of the effectiveness of phasing the data with the first echo

The sensitivity of the simulation to uncertainty in various material properties is compared in Table 4.2, showing temperature changes at the edge of the phantom at the end of the simulation time (i.e., after 21 minutes). It is evident from Table 4.2 that the density and specific heat capacity of the phantom are the two most sensitive parameters to characterise accurately.

Results (°C)	Difference	Dielectric properties		Density	Thermal properties		
		ϵ_r	σ (S/m)	ρ (kg/m ³)	Cp (J/kg/°C)	k (W/m/°C)	Heat transfer coefficient (W/m ² /°C)
1.34	-10 %	1.32 (-1.84%)	1.32 (-1.82%)	1.49 (11.06 %)	1.49 (10.76 %)	1.34 (0.07 %)	1.34 (0.00 %)
	+10 %	1.37 (2.17 %)	1.37 (2.83%)	1.23 (-8.66 %)	1.22 (-8.96 %)	1.34 (-0.20 %)	1.34 (-0.01 %)
Average brain ^{27,35,36} (Muscle) ³⁶		51.00 (58.24)	0.57 (0.77)	1043 (1090)	3647 (3421)	0.52 (0.49)	-
Measured value (calculated)		47.76	0.62	(1022.22)	(3776.3*)	(0.4864)	(2.5**)

Table 4.2: Sensitivity of the simulation estimated by observing temperature changes at the location of the edge sensor at a time point of 21 minutes of heating, by changing each parameter by 10%. (* calculated by mass fraction, ** calculated from experiment)

Figure 4.11 shows the results from the cooling down experiment and from simulation.

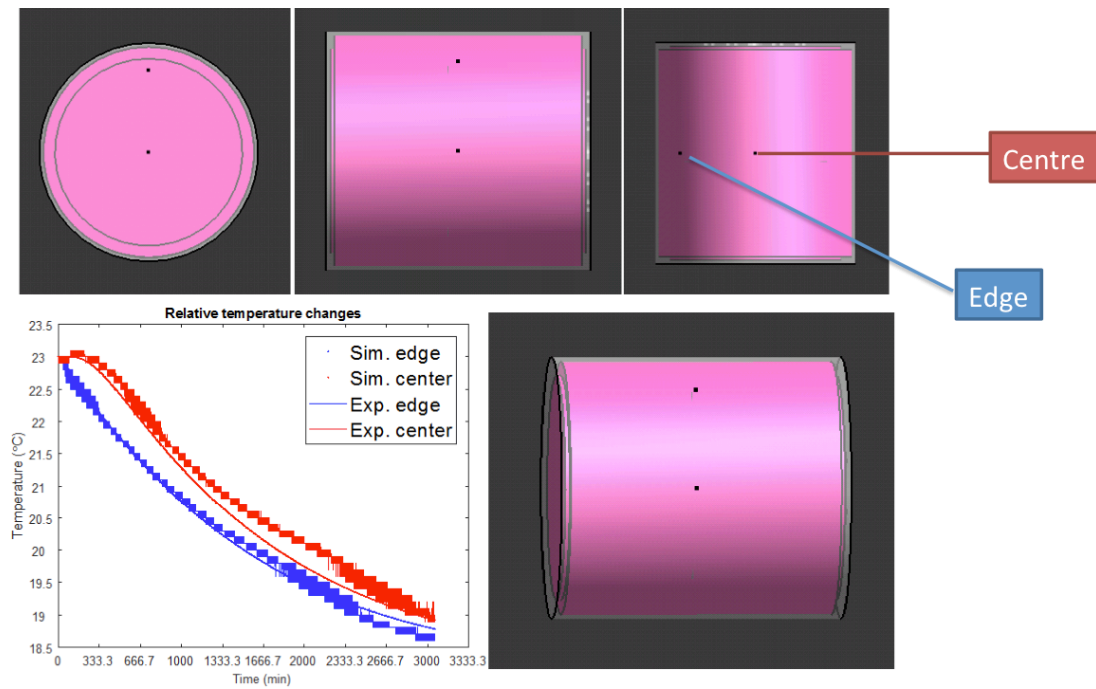


Figure 4.11: Results from the cooling experiment to determine the heat transfer coefficient (thermal coupling of phantom to environment) and the same from the Sim4Life simulation (Position of sensors are coloured as red(Centre) and blue(edge))

4.5 Discussion

In this study a procedure is proposed for RF safety phantom characterization, along with a pulse sequence to measure channel-specific RF-induced heating using PRF thermometry.

In a sensitivity analysis of the simulation, the phantom's density and specific heat capacity are shown to have the greatest impact on the heating, with a 10 % change in these parameters causing the heating results to vary by 10 % in the simulation.

The physical properties of a proposed safety phantom are also described. The density of the phantom is likely to change slightly over time due to water evaporation. As such, this value should be recalculated periodically using updated weight and volume measurements. The specific heat capacity was calculated via a

mass fraction estimation of the component ingredients (124), which was compared with average brain and muscle properties reported in the literature (86,129).

Characterising the thermal conductivity and heat transfer coefficient was shown in the heating experiment to be not as critical as might be expected, since the heating duration is short and the induced temperature rise is small. Errors in these values by 10% appear to change the predicted resulting temperature rise by less than 0.2% in the simulation. However this error will increase with a greater rate or longer duration of energy deposition. Although small, accumulation of these uncertainties could result in a larger error, indicating that efforts should be made to estimate these parameters as well as possible.

The importance of the pre-heating stabilization scans is shown in Figure 4.3, which minimized any evolving B_0 field gradient drifts without requiring additional hardware. In our system, spatial field variation was stabilized and reached a steady state in 14 minutes. The time requirements for stabilizing the gradient coil may be different on other scanners, as they will depend on the amount of passive shim steel used during magnet installation, so phase drift calibration should be done for each scanner and PRF protocol individually. The advantage of mitigating field drifts in this way is that additional oil compartments or arrays of temperature probes do not need to be used for PRF map correction, although a single (spatially invariant) drift correction may still be needed, as was the case for our system. While field drifts were mitigated in the no-heating experiment, some residual drifts are evident in the heating maps of Figure 4.11 indicating that a longer stabilization scan period should be used in the future.

Despite thorough phantom characterization, a discrepancy remains between

simulation, PRF and fibre optic probe measurements, as seen in Figure 4.12. Further work is required to understand the origin of these discrepancies. These could be a result of an apparent discontinuity in the fibre optic probe result at around 13 minutes (see Figure 4.9) or may be from an error in the PRF calibration constant α or the accuracy of PRF thermometry.

Our proposed PRF measurement sequence uses two transmit states, which provide enhanced coverage of the phantom by reducing error in regions where otherwise there would have been a B_1 transmit void. By using a weighted average of multiple TEs a reduction in the variance of the calculated temperature was found, compared to using a single echo time, particularly in regions of lower signal. Higher accuracy means potentially less time needed to measure heating, which improves the accuracy of thermometry.

Phasing the multi-echo measurements using the first echo removes some artifactual temperature changes remote from the heating location and provides smoother heating profiles. Such phase changes could originate from changes in transmit or receive paths, for example where a single pTx amplifier minimally drifts causing a small phase change in regions affected by its transmit sensitivity and that of other channels. Although this method has removed much of the artifact, some artifact remains. This residual artifact could be explained by a change in a susceptibility boundary at the edge of the phantom, such as a single coil element physically shifting.

A dipole transmit array has a relatively simple geometry compared to other pTx coils. This means that it is relatively straightforward to optimise in simulation. However, more consideration would be needed for other coil arrays, such as matching the in-situ complex S-parameter values, decoupling circuitry, and capacitor

values used in reality (94,130).

Temperature measurements allow us to indirectly estimate the effects of E-fields without specialized hardware. However, to do so requires accurate measurement of thermal properties, something which direct E-field measurements do not require. Since such E-field probes are limited to a few specialised sites thermal measurements provide a viable alternative. The method proposed in this study can be extended to evaluate any transmit state, which may be useful to demonstrate that the complex interaction of transmit channels is adequately simulated.

Overall, the proposed pTx thermometry methods were successful, providing good coverage of the phantom and enabling characterization of each individual channel. The simulated temperatures aligned well with the experimental values and the PRF measurements aligned well with those of the fibre optic probe.

4.6 Summary Conclusion

We have presented: (1) an MR thermometry PRF technique that has been adapted for the RF heating evaluation of pTx coils; and (2) a sensitivity analysis of electrical and thermal simulation properties.

The sensitivity analysis demonstrated that errors in heat capacity and density had the greatest impact on thermal predictions, followed by the electrical properties, while the thermal conductivity and heat transfer coefficient had a minimal effect on the results.

The pTx based MR thermometry methods have demonstrated that:

- A gradient stabilisation period of 14 minutes mitigates the B_0 field gradient drifts, however residual spatially invariant frequency drifts remain that were tracked using a single fibre optic probe in a region with no expected heating.

- The TIAMO acquisition strategy provided full phantom coverage without ‘drop out’ regions.
- A weighted averaging of four echo times increased the measurement accuracy compared to using a single echo time, particularly in the low signal regions.
- There are still remaining discrepancies between the simulation and the experimental results. Further studies are needed to understand the source of these discrepancies.

5 Personalized Voxel Models using Non-linear Registration

5.1 Introduction

The importance of RF safety has been discussed in previous chapters. Ensuring RF safety in MRI relies on a pre-calculation of SAR using a biological whole-body voxel model. Historically these voxel models have been simple compartment models and more recently have been extended to more complex and realistic whole-body human voxel models such as HUGO (The Visible Human Project, NIH)(65). These realistic models enable a more accurate understanding of RF energy deposition. However, this approach does not account for inter-subject variability such as body size, shape, gender and build, as such a safety margin is added to account for potential variability and prevent exceeding the threshold for RF energy deposition. For this reason we investigate using warping to produce personalized voxel models and evaluate the simulations produced with respect to RF safety. Different tissue compartments have different dielectric properties and as a result if they are positioned differently in the simulation to reality the SAR prediction will be inaccurate. Jin *et al.* have assessed the effects of morphometric differences on SAR calculations in CP mode using non-linear registration (131). In their study, a non-rigid registration algorithm was used to register the voxel model with subject-specific MR images, which demonstrated the possibility of predicting the location of the worst-case 1g SAR value in a single-channel transmit 7T application over different subject morphometries and safety margins for human application. Garrec *et al.* have shown that a safety margin of 1.5 to account for inter-subject variability in MRI RF safety assessment to guarantee a <1% chance of exceeding the corresponding SAR limit (132).

The need for simulation using personalised models is increased in pTx systems. This is because SAR in pTx is calculated from multiple simulations (one for each transmit element) and the uncertainty from each is accumulated when combining the simulations. This makes it difficult to ensure RF safety in a population without using conservative safety margins. Registration methods allow a well-characterised voxel model to be warped into a subject's morphometry. The hypothesis is that by warping a well-characterised voxel model into the subject's morphometry, a personalised voxel model can be calculated and used in RF safety simulations that do not require large safety margins. While not assessed in this work, such personalised approaches have the potential to be used in complex situations such as large vessel disease or cancers, which could deviate substantially from a standard model.

Image registration is the process of overlaying multiple image data sets in the same spatial coordinate frame, enabling direct comparison between data sets of signal intensities, contrasts, functional activation, and other information. Typically it can be used in intra-subject studies, such as multimodality or longitudinal studies, and also inter-subject studies to get statistical meaning of the results obtained from a large pool of subjects.

This chapter introduces publicly available human voxel models then describes how to warp these models heads to a target T1 weighted image.

In this chapter, a method to personalise SAR modelling by non-linear registration of a high-resolution reference voxel model into a target (subject-specific) head morphometry will be introduced. Accuracy of personalising models for EM simulations in such a way is assessed by registering one model into another.

5.2 Review of publicly available voxel models

In this section a review of the various voxel models for EM simulation is presented.

Visible Human Project

In 1994, the Visible Human Project was launched by the U. S. National Library of Medicine (NLM, NIH), which provides three-dimensional anatomical details of a human male body (1994), and a human female body (1995). Based on this original Visible Human data, a well-known whole-body voxel model for EM simulation was introduced in 1998, known as HUGO. It is a model of a 38-year-old male, and has 5 mm³ isotropic-voxel resolution of the entire body. It was later revised by the University of Texas at Austin in 2010, and the most recent version (v2.6) provides 1 mm³ isotropic-voxel resolution, known as AustinMAN (133,134). A Visible Woman, comprising a voxel model from a 59-year-old female, was also originally provided with 5mm³ isotropic-voxel resolution. This was later revised by NEVA Electromagnetics, LLC and made available as the VHP-Female (v2.2 in 2015), which provides 26 categories of tissue compartment (184 individual parts) in a mesh structure format by Makrov et al., shown in Figure 5.1 (135). This model was further revised by the University of Texas at Austin as AustinWoman v2.6 with 1mm³ isotropic-voxel resolution (2018).

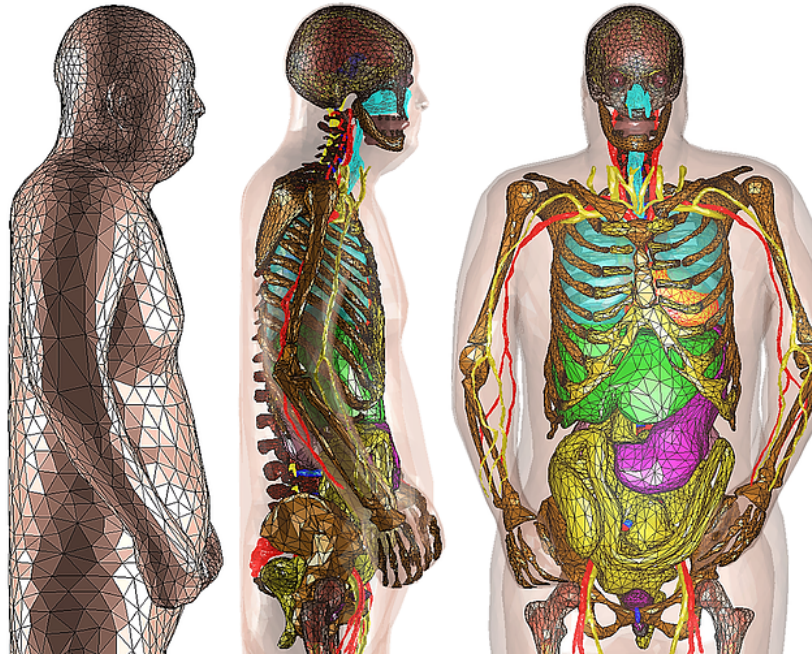


Figure 5.1: Example of VHP-Female model developed by NEVA Electromagnetics, LLC, taken from website www.nevaelectromagnetics.com/vhp-female-2-2. Included with permission

Virtual Population (IT'IS Foundation)

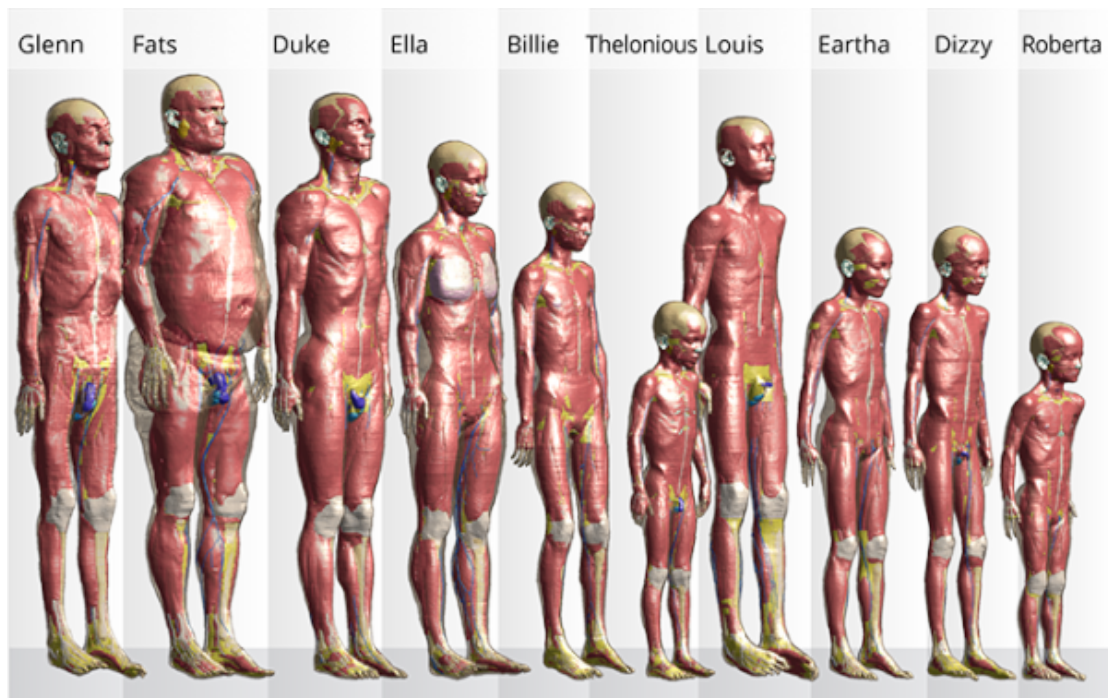


Figure 5.2: Picture of the Virtual Population, taken from website <https://itis.swiss/virtual-population>. Included with permission

Figure 5.2 shows the popular voxel model family called the Virtual Population (97). Each member has been named after a popular jazz musician: Duke Ellington, Fats Waller, Glenn Miller, Ella Fitzgerald, and so on. Duke is a male voxel model which was first introduced in 2010 by the IT'IS Foundation (Zurich, Switzerland). It is based on a 34-year-old male and had 77 tissue types in the whole-body in version 1.0. The latest version of Duke, v3.1, has 305 categories of tissue compartment with mesh structures, and models of various BMI (22, 26, 30) were recently introduced as a ViP3 Morphed to cover a wider population. Unlike versions 1.0 and 3.0, v2.0 only provides a limited number of tissue compartments for other simulation platforms than Sim4Life (ZMT Medtech, Switzerland).

Regional Human Model - MIDA

MIDA is a head-only high resolution ($0.5 \times 0.5 \times 0.5 \text{ mm}^3$) 29 year-old female head-only model. MIDA, was introduced in 2014 following a collaboration between the U.S. Food and Drug Administration (FDA) and IT'IS. It is called the Multimodal Imaging-based Detailed Anatomical model of the Human Head and Neck, in short MIDA (109). A number of different image modalities were used in its creation: structural T1- and T2-weighted MR images, a specific T2-weighted MRI sequence with high nerve contrast, magnetic resonance angiography (MRA), and diffusion tensor imaging (DTI), which provides details of anatomical structures to segment 115 different tissue compartments in the head and neck region. It is provided in both a surface model format (CAD) and a voxelized image format (.nii and .raw).

European models: Norman and Naomi

The Norman and Naomi models were developed as a European voxel model by the UK Health Protection Agency in 1996 (136). Norman is a 23-year-old male model, and has 37 tissue compartments. A female model, NAOMI, was introduced in 2005 (137), consisting of a 23-year-old female model with 41 types of tissue compartment. Both models were updated in 2005 with $2 \times 2 \times 2 \text{ mm}^3$ isotropic-voxel resolution, but no further updates to the model have been provided.

Asian models: Taro, Hanako, Chinese, and Yoon-sun

Models with Asian ethnic background were first introduced in 2004 by NICT (138). Taro and Hanako are Japanese voxel models, both providing 51 types of tissue compartments and $2 \times 2 \times 2 \text{ mm}^3$ isotropic-voxel resolution. Volunteers for imaging were chosen using the average height and weight of the Japanese population, aged between 18 and 30 years old. Taro and Hanako are both 22 years old, comprising a male and female model, respectively, and shown in Figure 5.3.

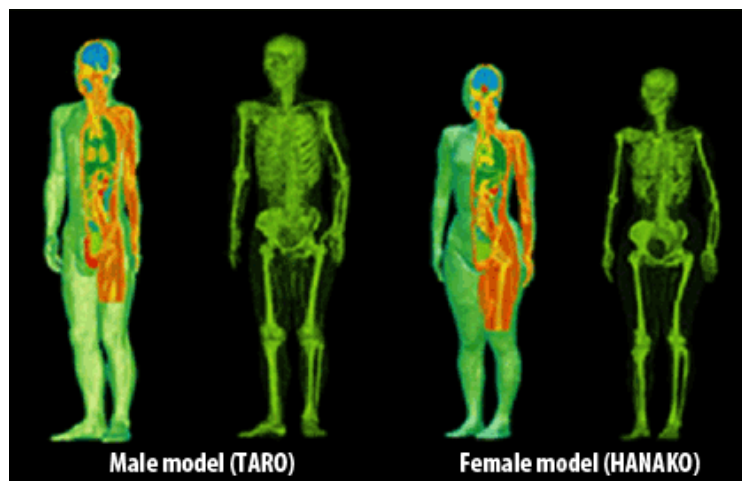


Figure 5.3: Taro (left) and Hanako (right) voxel model, taken from website emc.nict.go.kr/bio/model/. Included with permission

Recently, Chinese male and female models (139) were introduced in 2011 with $1 \times 1 \times 1 \text{ mm}^3$ isotropic-voxel resolution, and more recently a 26-year-old Korean female model, Yoon-sun, was introduced in 2018 by the Swiss-Korean collaborative NEUROMAN project, a collaboration between IT'IS and the Visible Korean team. It provides 322 tissue compartments, including detailed peripheral nerves and small structures using data obtained by the Visible Korean project in 2005 (140).

Table 5.1 compares the specifications of these 12 models in terms of resolution, number of tissue compartments, and publication date. In this chapter, three types of voxel models are used, namely Duke, Ella, and MIDA.

	Visible Human		Virtual Family		Head only Model	European Models		Japanese Models		Chinese Visible Human		Visible Korean Human
	HUGO; VIP-MAN (Austin Man)	VHP-Female (Austin Woman)	Duke (v3.0)	Ella (v3.0)	MIDA	NORMAN	NAOMI	TARO	HANAKO	CVH male	CVH female	Yoon-sun
Sex	Male	Female	Male	Female	Female	Male	Female	Male	Female	Male	Male	Female
Age	38	59	34	26	29	23	23	22	22	35	22	26
Resolution	3.6mm^3 (1mm^3)	5mm^3 (1mm^3)	0.5mm^3	0.5mm^3	0.5mm^3	2mm^3	2mm^3	2mm^3	2mm^3	1mm^3	1mm^3	$0.1 \times 0.1 \times 0.2 \text{ mm}^3$
Number of compartments	40 (64)	29 (58)	77 (305)	76 (305)	115	37	41	51	51	90	87	322
Release date (Latest update)	2000 (2018)	2015 (2018)	2012 (2014)	2012 (2014)	2012 (2014)	1996 (2005)	2005	2004	2004	2011	2011	2018
Developer	NLM (TAMU)	NEVA (TAMU)	IT'IS	IT'IS	IT'IS, FDA	HPA	HPA	NICT	NICT	CAICT	CAICT	IT'IS, VK project

Table 5.1: Specification of 12 existing virtual-human voxel models

5.3 Image Registration Process

5.3.1 Tool for Registration

FMRIB Software Library (FSL)

There are many software packages available for image registration, such as NiftyReg (141), Insight Segmentation and Registration Toolkit (ITK) (142), MIA (143), elastix (144), and ANTs (145). Also, other registration tools are also available in MATLAB (Mathworks, USA). A further package, FSL, includes a suite of registration tools for MRI data analysis. It is used particularly in analysis of functional MRI, structural MRI, and Diffusion Tensor Imaging in the brain (146–148). FSL provides tools for easy implementation of registration and statistical data analysis.

Brain Extraction tool (BET)

The brain extraction tool (BET) in FSL is used when excluding non-brain structures from MR images (149). This tool segments brain structures from non-brain structures, which are usually not considered in neuroimaging studies. Extracting non-brain structures is the preparation stage of the registration. Brain extraction is required in our intended protocol, which operates on T1-weighted images of the subjects. Brain extraction can be easily done on voxel models by applying zero contrast on non-brain compartments, as seen in Figure 5.4.

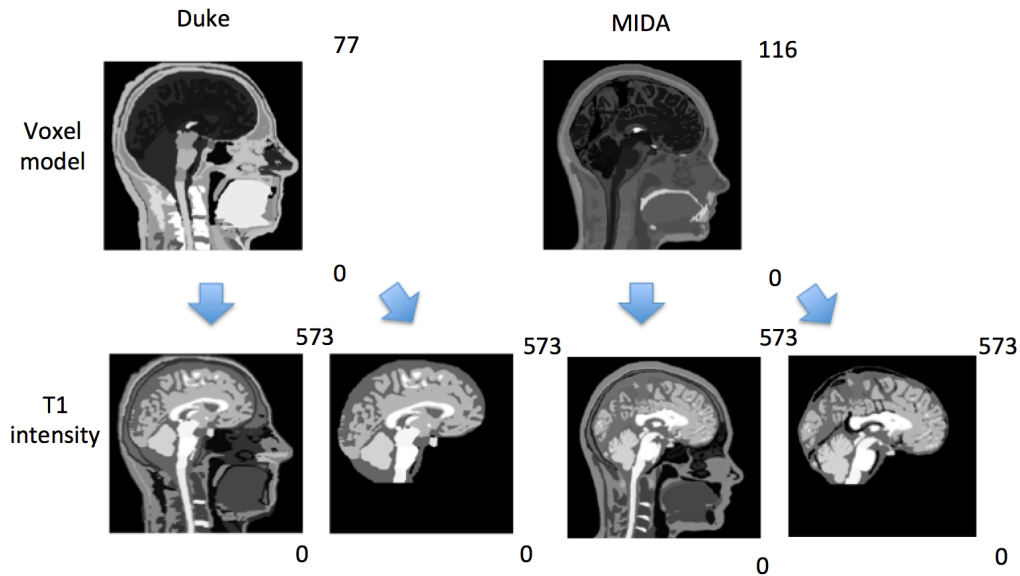


Figure 5.4: Process of brain extraction by applying zeroes to non-brain structures

FMRIB Linear Registration Tool (FLIRT) and FMRIB non-linear registration tool (FNIRT)

FSL provides tools for linear and non-linear registration, which are called FMRIB's Linear Image Registration Tool (FLIRT) and FMRIB's Nonlinear Image Registration Tool (FNIRT), respectively (150). FLIRT provides automated processing of linear registration for MR images using affine matrices including scaling, rotations, translations, and skew.

Linear registration is a simple and fast registration method to calculate three-dimensional translation, rotation, scale, and skew information between two datasets in a way that minimizes the cost function of their differences, as seen in Figure 5.5. The tool finds the transformation that minimises a cost function when translating and rotating one image into another. As FLIRT provides a rigid transformation, this facilitates a linear registration. The FLIRT tool is often used after extracting the non-brain structures, which may contain susceptibility artefacts near air/tissue interfaces or are not of interest in neurological studies. This tool is typically used to match a brain to image templates in standard space (e.g. MNI) for inter-subject studies.

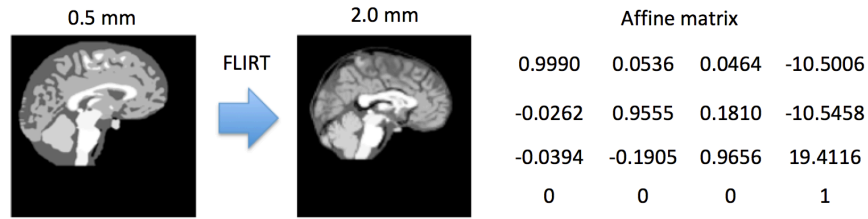


Figure 5.5: Process of linear registration (left) and result of affine matrix (right)

FNIRT is a tool for non-linear registration of MR images (151). In our case of personalised models, registration using affine matrices (as in the linear registration method described above) is not sufficient due to the more complex variations beyond the brain. Non-linear registration also involves a process of finding a transformation that registers two images together while minimizing the cost function - usually used for same-image-modality registration, such as T1-weighted MR contrast images. Non-linear registration uses an unlimited number of degrees-of-freedom, which requires lengthy calculation. Therefore the results of the linear registration can be used as a starting point for non-linear registration, this speeds up the FNIRT registration which has many more spatially localised degrees-of-freedom compared to the linear registration. It is recommended to use this process on under-sampled data of the reference voxel model, so that the warping process can maximise efficiency for registration in the overall structures rather than becoming confounded by its details. FNIRT calculates field warping coefficients which are vectors for each voxel that depict how they need to displace to minimise the registration cost function.

In addition, FNIRT uses multiple stages of under-sampled data, progressing from overall registration to details. In order to achieve a smooth non-linear registration, multiple registrations with down-sampled images are used in FNIRT. In this way, the registration prioritises the registration of overall structures, and detailed tissue compartments will introduce less bias to the process, so typically used to match a brain to image templates in standard space (e.g. MNI) for intra-subject studies.

‘fnirtfileutils’

The ‘fnirtfileutils’ tool converts warping vectors into a warping field matrix in a given matrix size and resolution. The warping field matrix contains the required numbers used for translation in units of mm in each axis.

Inverse warp (‘invwarp’)

When two images of differing quality of definition are registered, the registration should be performed to warp the lower quality image into the high quality image. For this purpose an ‘invwarp’ tool is provided in FSL which finds inverse vector information. This then become a twostep process where first the warping field is found using low-quality data as input and high-quality data as reference. Then the inverse warping field is applied to the high quality data to bring it into the lower quality image space.

Applying warp (‘applywarp’)

Once the warping field has been generated, the ‘applywarp’ tool is used. Three inputs are given to this tool: (i) the reference image which is used to provide image size and contrast, (ii) the input image to be warped, and (iii) the warping field. Based on the warping field, ‘applywarp’ correctly locates the corresponding image intensities from the reference data.

5.3.2 Terminology used in registration***Down-sampling (sub-sampling) for smoothness***

In order to maintain the presence of genuine tissue structures, a certain degree of smoothness is required in the registration process which otherwise may shrink or

expand anatomy to non-anatomical proportions. This smoothness constraint can be controlled in a couple of ways. First, using fewer degrees-of-freedom prevents sharp movement of image voxels. Smoothness can also be achieved by using low warp resolution, which results in having fewer degrees-of-freedom. Using more regularisation is likewise helpful in making a smoother warped image.

Down-sampling of target voxels was performed using the ‘applywarp’ function. Down-sampling was performed smoothly by choosing an adequate level of intermediary super-sampling (integer level: 4) and a spline interpolation method with minimal loss of information in the input image, as seen in Figure 5.6.

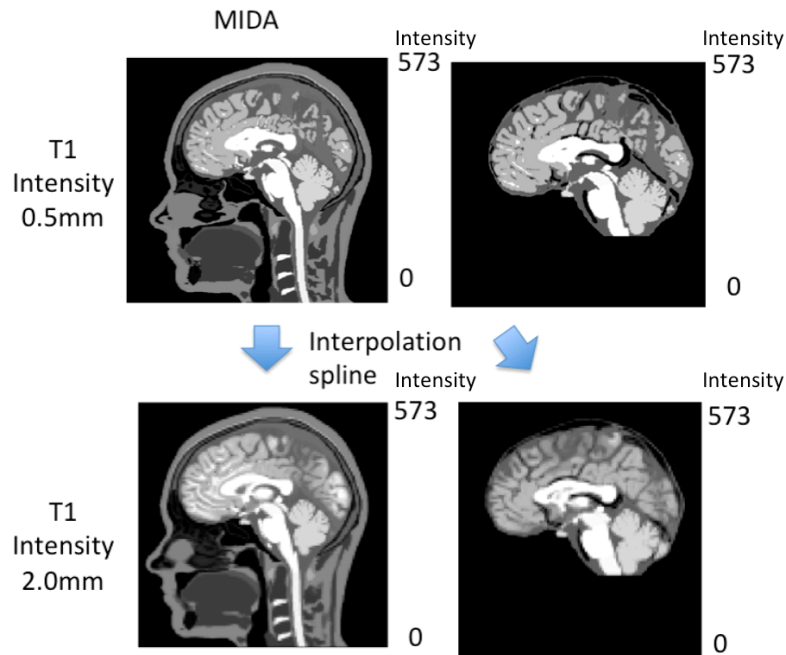


Figure 5.6: Down-sampling of reference model (MIDA) from 0.5 mm³ to 2 mm³ for smoothness of registration

Interpolation

The process of registration requires resampling an image onto a new image grid. This process of moving from the sampled grid to a new grid means that voxels do not map directly from one grid to the other and therefore require estimation of data values for the new grid locations. This estimation is called interpolation. Interpolation is a

method of constructing a new data grid by using a set of known data points. There are a couple of approaches to estimate and calculate data in the new grid.

Nearest neighbour sampling determines the voxel value given a point location. Alternative linear interpolation between two or more points could refine the values. Typically trilinear interpolation is used for volumetric datasets. However, linear interpolation results in a blurring effect that produces intermediate values that are not beneficial where discrete voxel values are required, such as in EM models.

B-spline fitting provides a weighted estimation where a polynomial spline function is created to provide a continuous smooth curve that passes through a given a set of control points, allowing the new voxel value to be estimated. The B-spline parameters can be adjusted to influence the shape of the curve generated.

Cost function

A cost function (or loss function) is used to measure the effectiveness of an image transformation (e.g., FLIRT) against its intended use (e.g., image registration). It represents the variance between the estimated image and the desired image – and as such the optimization algorithm attempts to minimize it. The cost function will vary depending on the application, such as quantifying the similarity between two images or by making a comparison of their intensity values.

5.3.3 Registration of voxel models

Overall process

Our proposed method is to use MR images to produce personalized electromagnetic models using non-linear warping between the image data from the subject in the scanner, and a well characterized electromagnetic model. To evaluate this

methodology we warped one EM model into another, where simulations for both a warped model and actual model can be undertaken. For our initial studies we used the Duke model as a representative subject in the scanner, since comparisons can then be made between the high-resolution model (MIDA) warped into Duke space, and the ‘ground truth’ of simulating Duke itself.

In this section, the MIDA, Duke and Ella models are used. The proposed registration method used in this thesis only registers the head and partial neck of the subject, as this is the information expected to be easily observed in the scanner. EM simulations of the head should be carried out with a body to load the RF coil. If a body is not used, over-estimation of RF heating and energy deposition can occur (4,152–154). For this reason this work adds a body model to the warped head models. Another reason to add a body model is to avoid confounding EM boundary effects that would occur if only a head model were used in the simulations.

Finally, a cross validation was carried out using the Ella model, which we expect to be more similar to our reference model MIDA (since both are based on female subjects of similar size), although in this case the registration will potentially have less benefit (109).

Chosen voxel models for application

MIDA was chosen as the standard model due to its high resolution in the brain. Two models were chosen to represent subjects in the scanner, Duke and Ella as described above. All of these models are both defined as a voxel models and surface models. In a voxel model, each voxel represents a specific tissue compartment. In a surface model each anatomical structure is defined by a CAD model containing a collection

of surface triangles as defined by vertices. The advantage of using a surface (CAD) model over a voxel model is that stricter integrity can be retained up until the EM simulation performs the process of adding depth to an image using a set of cross-sectional images known as ‘voxelization’. Conceptually, warping the surface-based model helps to preserve retention of tissue compartment definition without the potential risk of losing boundaries due to a limited grid resolution.

For our target, subject-specific model, Duke was used to represent the underlying subject in the MRI scanner. Duke is based on a 34-year-old male model and has 44 tissue types in the head and neck region as seen in Figure 5.7.

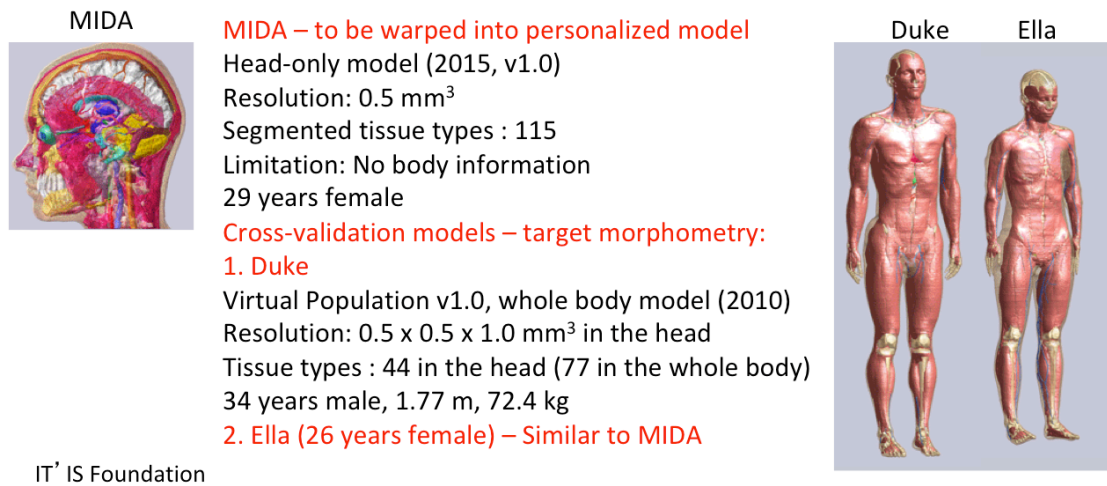


Figure 5.7: Comparison of three voxel models used in registration

Generation of synthetic T1 intensities

For subjects in the scanner (and the models used in evaluation), a set of T1-weighted images is used that are then registered to those for our reference model MIDA. As the underlying MRI images used to produce the MIDA are not available to us, MIDA T1-weighted images were synthesized. To synthesis T1 weighted images, an MPRAGE sequence was run at 3T (TR/TE 2380/3.96 ms, TI= 1200 ms, FA=8°, Siemens Prisma), and used to determine reference contrast intensities for the different

tissue compartments. MIDA's tissue-indices from the EM model, with corresponding tissue compartments, were replaced with the reference T1-weighted intensities. This process was repeated for Duke and Ella. Figure 5.8 shows this process for MIDA.

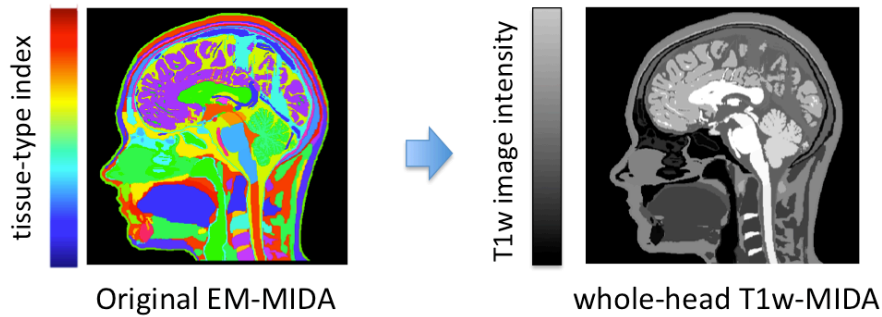


Figure 5.8: Generating a synthetic T1-image

One problem that needed to be addressed was a discrepancy between the number of compartments that existed in MIDA versus the number of compartments that existed in Duke and Ella. Several dedicated tissue compartments that existed in Duke and Ella were further segmented in MIDA, and thus were grouped and simplified and assigned the contrast of corresponding tissue compartments in Duke and Ella. (e.g. the cerebellum white matter and cerebellum grey matter in MIDA were replaced with the contrast of the cerebellum in Duke). The contrasts of tissue compartments grouped in the same tissue type are assigned the same contrast, as seen in Table 5.2.

Grouped Tissue type	Sample model (Duke)	Sample model (Ella)	Reference model (MIDA)
Muscle	Muscle	Muscle	30 types of Muscle compartments
Grey matter	Grey Matter	Grey Mater	Amygdala, Caudate Nucleus, Globus Pallidus, Mammillary Body, Nucleus Accumbens, Putamen, Substantia Nigra
Skull	Skull cortical, Skull cancellous	Skull cortical, Skull cancellous	Skull Diploé Skull Inner table Skull Outer table
Cerebellum	Cerebellum	Cerebellum	Cerebellum White Matter, Cerebellum Grey Matter
White matter	White matter	White matter	White matter, Cerebral Peduncle

Cartilage	Cartilage	Cartilage	Cartilage, Nasal Septum, Ear Auricular Cartilage
CSF	CSF	CSF	CSF, Ventricles Ear Cochlea, Ear Semicircular Canals

Table 5.2: Groups of tissue compartment used for registration and evaluation

Registration process

To facilitate the initialization of a non-linear registration, a linear registration is carried out on the brain. Non-brain structures and tissues below the brainstem were extracted by applying zeroes to non-brain compartments, in order to generate brain-only data as shown in Figure 5.4. (In the case of using a T1-weighted image from the subject, this could be done using the FSL BET tool (149) as described above.)

Down-sampling was carried out using ‘applywarp’. The images were down-sampled to a resolution of $2 \times 2 \times 2 \text{ mm}^3$ by using ‘superlevel’ as 4. The remaining options were passed via command line, as seen in the Appendix. (a simple header file is generated using the ‘fslcreatehd’ command, which specifies dimensions, a target resolution used for the reference image, and the 4×4 identity matrix (eye.mat) used for pre-transformation (-premat) as seen in the Appendix).

Registration of the voxel model was carried out using a two-step procedure, first a linear registration followed by a non-linear registration. The linear registration was done using brain-only data with FMRIB’s Linear Registration Tool (FLIRT) in FMRIB’s Software Library (FSL) (146). The linear registration provided an affine matrix which describes 12 variables to define scale, rotation, translation, and skew.

The non-linear registration was done using the full T1 weighted image volume with both brain and non-brain structures. FMRIB’s non-linear registration tool (FNIRT) was initialized with the affine transform and determined the warping fields, as seen in Figure 5.9.

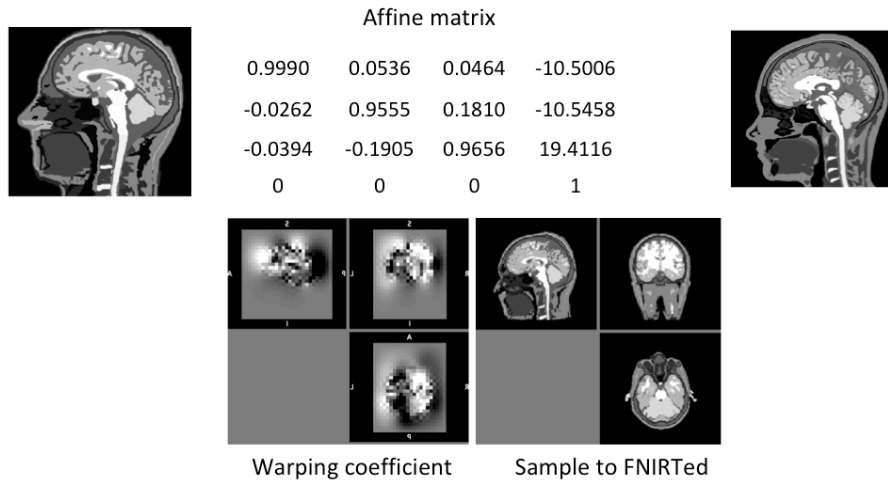


Figure 5.9: Process of non-linear registration using synthesised head and neck models and affine matrix, producing warping coefficients and a warped model

It is useful to prepare a configuration file which specifies the command line options in advance, and parameters are stated inside of brackets in the Appendix: where default values of the implicit masking and reference mask are replaced with zeroes. The remaining options were passed via command line, as seen in the Appendix Figure S1.1.

The output from FNIRT is a warping field that describes how voxels of the subject are to be shifted to create an image that resembles MIDA. This is a field that can be thought of as being in MIDA space, where each voxel is an arrow pointing to where that voxel came from in the subject's image.

Warping of voxel models

To form a voxel tissue compartment model the inverse of the warping field is required to define where each voxel in our subject space came from in MIDA space, in this way MIDA can be recreated in the subject space. This is achieved using the 'invwarp' tool to calculate the inverse warping field. This allows the reference MIDA voxel model to be warped into a subject-specific voxel model, as seen in Figure 5.10.

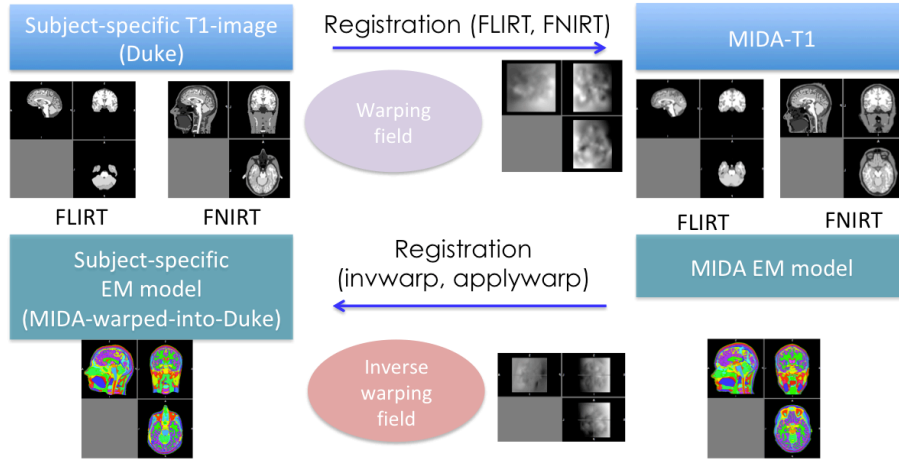


Figure 5.10: Diagram of the two-step warping process used for the voxel-based model

Warping of surface-based CAD models

Surface-based (i.e. CAD) models contain the coordinates of vertices in the reference image space. The warping of a surface-based model into a target model does not require calculation of an inverse warping field, because the forward warp field is used as a look-up table based on voxel coordinates and used to identify where they must go to warp into the subject. Thus, the vertices of the surface model are directly warped via translation without calculating an inverse warping field, as shown in Figure 5.11.

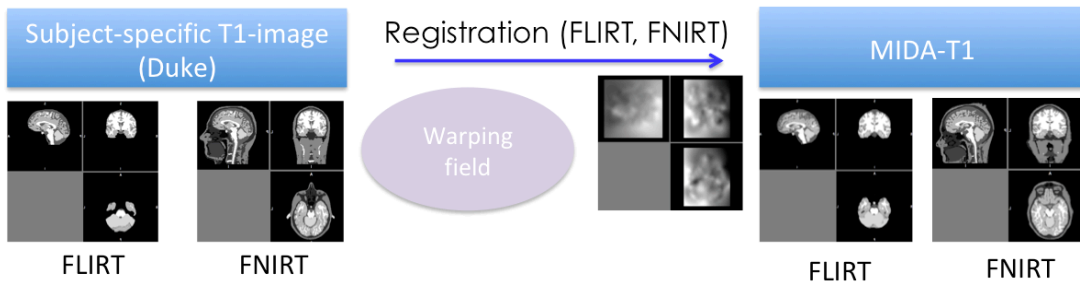


Figure 5.11: Warping process for surface-based models (CAD)

The surface-based warping process for the data shown in this thesis was done via MATLAB, using the warping field calculated by FNIRT. The reference surface-

based MIDA model, was loaded and registered to the same location in space as the warped voxel-based MIDA model that resulted from the above non-linear registration step. To accomplish this, an affine matrix (scaling, rotation, and translation) was found to register the voxel-based and surface-based models of MIDA using the minimum and maximum location of vertices in x,y,z . The warping coefficient was then converted into a warping field at each voxel, which indicates the amount of translation required for each vertex at its corresponding three-dimensional coordinate. A detailed explanation of each step used, and the required commands to complete the process, is provided in the Appendix.

5.4 Methods for evaluation of registration

In this section the model registration and warping is evaluated prior to simulations using a tissue compartment comparison and after simulation by comparing the fields and resultant dielectric properties.

5.4.1 Voxel-by-voxel comparison of various models

The composition of the three models by voxel compartment volume is shown in Table 5.3 with the total volume of each tissue presented in order of proportional volume, from largest to smallest. Warped tissue compartment models were compared by subtraction of voxel models to identify where the compartments matched. The number of correctly identified tissue voxels was counted and displayed as a percentage of the total number of voxels.

Tissue type	Sample model (Duke)	Sample model (Ella)	Reference model (MIDA)
Muscle	21.9%	19.05%	15.15%
Grey matter	12.6%	16.67%	11.70%
Skull	11.0%	12.98%	8.89%
Fat, SAT	9.7%	11.04%	14.04%
White matter	10.9%	9.94%	11.81%
CSF	5.2%	9.62%	4.71%
Skin	5.8%	6.76%	2.64%
Cerebellum	3.1%	3.52%	3.15%
Dura	2.57%	2.50%	2.01%
Air	1.51%	1.57%	2.10%

Table 5.3: The percentage volume of each major tissue compartment in the three voxel models

Since the reference voxel model, MIDA, has the higher number of tissue compartments, groups of tissues were compared against Duke based on similar tissue properties. For example, the cerebellum is regarded as one tissue compartment in Duke, but it was further separated as cerebellum grey matter and cerebellum white matter in the reference voxel model MIDA. These were therefore considered as a

single compartment, cerebellum, in the registration process and the evaluation process. The following are specific tissue types grouped for comparison in registration between the sample (Duke) and reference (MIDA) models.

5.4.2 Calculation of difference maps of physical properties, dielectric properties, E-fields

The accuracy of SAR prediction is a function of its dependent parameters, namely density, conductivity, and E-fields. The relative permittivity value indirectly affects SAR by changing the E-field calculation. Thus, by evaluating the differences in these input parameters, the expected effect of warping on SAR can be evaluated. The differences in conductivity and density maps were calculated from simple electromagnetic simulations of a one channel dipole coil, shown in Figure 5.12.

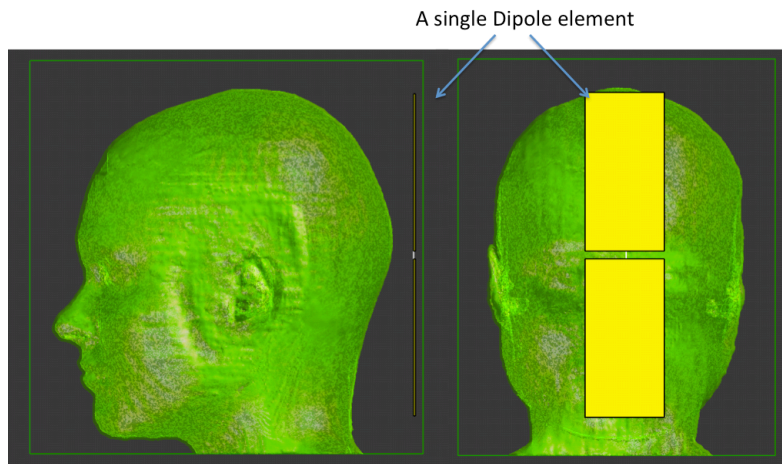


Figure 5.12: Simulation set-up to calculate dielectric properties map using a single dipole element

The conductivity map was calculated as the current density divided by the E-field, and the density map was calculated as the electric loss density divided by the specific absorption rate (SAR). This can also be achieved by replacing the tissue indices to density, and conductivity of each tissue. The total head weight is calculated using the

density map and compared to assess overall changes before and after the warping.

The mean squared-difference in the calculated E-fields was compared using the E-fields produced with 1 W input power using the 8-channel dipole elements used in Chapter 4. The squared E-field is proportional to the SAR, so the sum-of squares of E-field difference was calculated, shown in Equation (5.1).

$$\Delta E^2 = \sum |\mathbf{E}_1 - \mathbf{E}_2|^2 \quad (5.1)$$

The root-sum-of-squares of the E-field difference was also calculated.

5.4.3 *Mass calculation*

As mass is an integral part of the SAR calculation, the mass of the three different models was calculated using density maps multiplied by the resolution of the image from each head model. Through comparison of overall mass changes, one can get a sense of how much global difference exists before and after warping, and observe whether this difference was reduced in the warping process.

5.5 Results

5.5.1 Voxel-by-voxel comparison of various models

The first data column of Table 5.4 shows the percentage by volume of tissues in the Duke head model, the second data column shows the percentage of correctly identified voxels if no warping is done, and the third data column shows the percentage of correctly identified voxels when MIDA is warped into Duke (a model that will be denoted as MIKE).

Tissue types	Total volume in Duke head model (%)	Percentage of correctly identified voxel	
		MIDA to Duke (%)	Warped MIDA to Duke (%)
Muscle	21.9	34.1	44.2
Grey Matter%	12.6	35.0	54.5
Skull	11.0	15.9	45.2
White Matter	10.9	47.6	75.7
SAT	9.7	22.8	31.1
Skin	5.8	8.2	12.5
CSF	5.2	10.2	45.7
Cerebellum	3.1	71.0	89.0

Table 5.4: Specific tissue matching scores for directly comparing MIDA and Duke, versus comparing MIDA-warped-into-Duke (MIKE) and Duke (*Grey matter, Amygdala, Caudate Nucleus, Globus Pallidus, Mammillary body, Nucleus Accumbens, Putamen, Substantia Nigra are grouped as Grey matter)

Table 5.5 shows the specific tissue matching scores for directly comparing MIDA and Ella, versus comparing MIDA-warped-into-Ella (MELLA) and Ella.

Tissue types	Total volume in Ella head model (%)	Percentage of correctly identified voxel	
		MIDA to Ella (%)	MELLA to Ella (%)
Muscle	19.05	44.48	47.40
Grey Matter*	16.64	37.79	60.72
Skull	12.99	21.89	44.01
Fat	11.04	14.05	53.12
White Matter	9.94	57.57	80.58
Skin	6.76	10.57	57.84
CSF	6.10	14.87	51.32
Cerebellum	3.52	64.67	93.59
Dura	2.50	6.83	24.67
Air	1.57	28.47	51.41
Spinal cord	0.20	31.22	82.76

Table 5.5: Specific tissue matching scores for directly comparing MIDA and Ella, versus comparing MIDA-warped-into-Ella (MELLA) and Ella (* Grey matter, Amygdala, Caudate Nucleus, Globus Pallidus, Mammillary body, Nucleus Accumbens, Putamen, Substantia Nigra are grouped as Grey matter)

Results of voxel-based warping were also compared between MIDA and Duke, and Duke, versus MIDA-warped-into-Duke (Figure 5.13), MIDA and Ella, versus MIDA-warped-into-Ella (MELLA) and Ella, shown in Figure 5.14

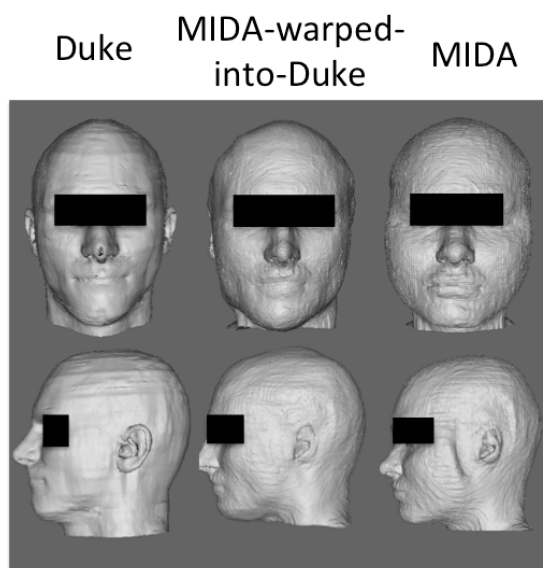


Figure 5.13: Results of voxel-based warping of MIDA, Duke, and MIDA-warped-into-Duke (MIKE)

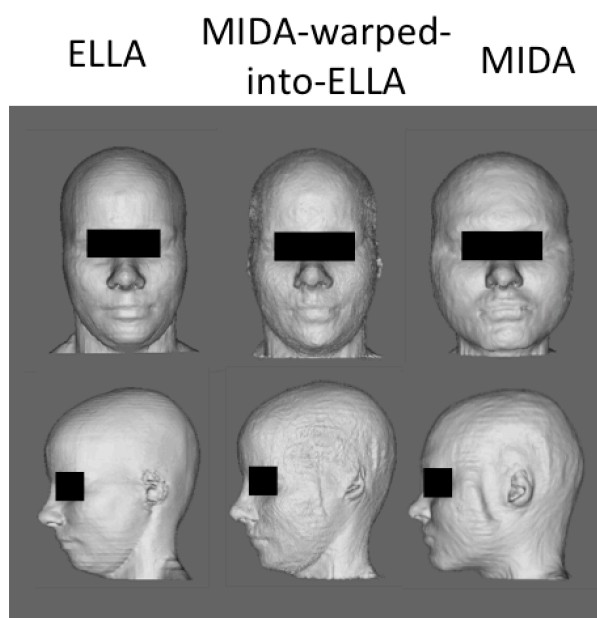


Figure 5.14: Results of voxel-based warping of MIDA, Ella, and MIDA-warped-into-Ella (MELLA)

5.5.2 Calculation of difference maps in input data for SAR calculation

The absolute difference of conductivity and density is compared between Duke, MIDA, and MIDA-warped-into-Duke (MIKE) in Figure 5.15. The mean conductivity difference was reduced from 0.407 S/m to 0.347 S/m when MIDA was warped into Duke space, a 14.74 % improvement compared to the average conductivity of Duke 0.5267 S/m. In the case of the density differences, the mean difference was reduced from 401.55 kg/m³ to 179.77 kg/m³.

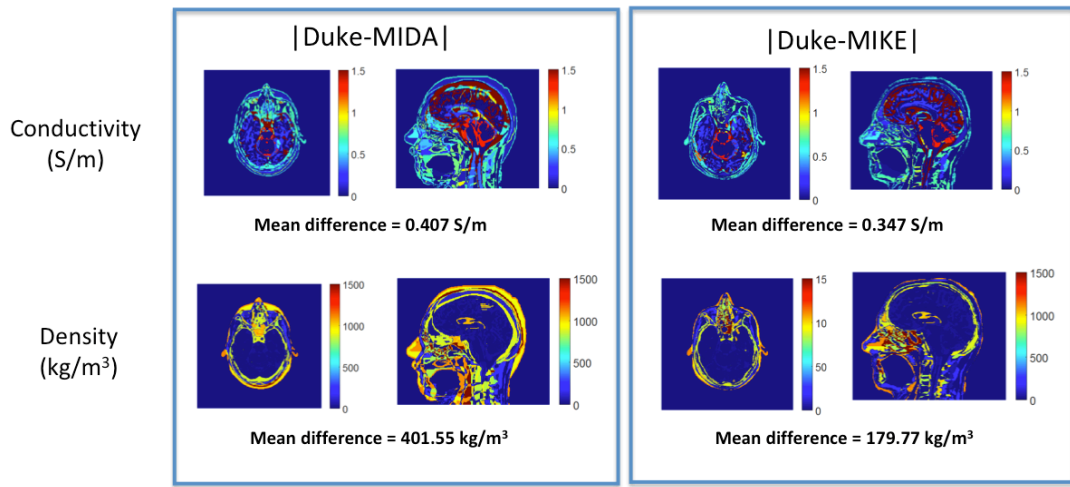


Figure 5.15: The fidelity of voxel EM properties for Duke: Conductivity and density differences

Figure 5.16 shows the difference of conductivity and density between Ella, MIDA-warped-into-Ella (MELLA), and MIDA. It can be seen that the effect of warping is to reduce the mean conductivity difference from 0.396 to 0.377 S/m, a 4.80 % improvement compared to the average conductivity of Ella 0.63 S/m. In the case of the density differences, the mean difference was reduced from 376.36 to 310.37 kg/m³ after warping MIDA into Ella space.

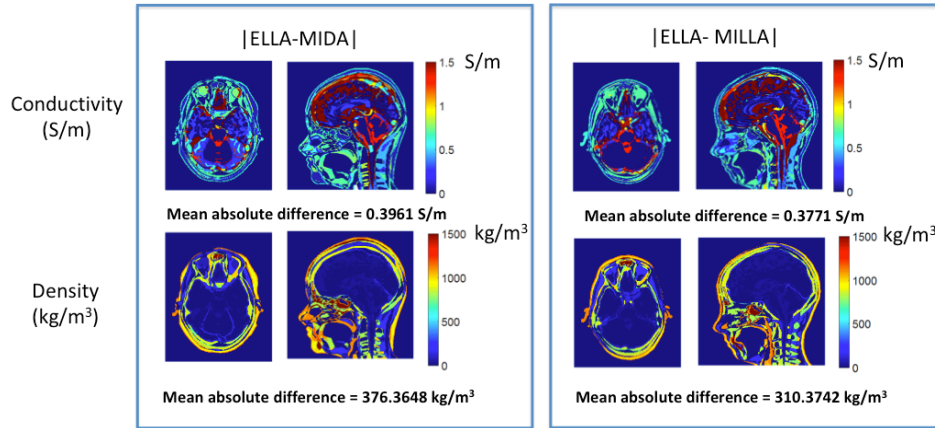


Figure 5.16: The fidelity of voxel EM properties for Ella: Conductivity and density differences

The mean squared difference of E-fields was also compared between Duke, MIDA, and MIDA-warped-into-Duke (MIKE), and are shown in Figure 5.17.

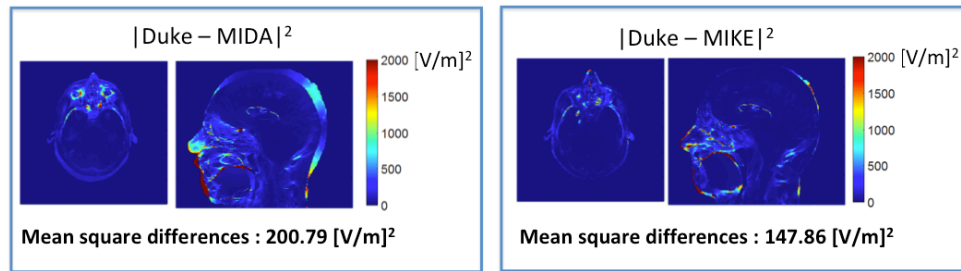


Figure 5.17: The fidelity of voxel EM properties: Mean squared differences of E-field between Duke, MIDA and Duke-warped-into-MIDA (MIKE), compared only in those areas that are shared by the two models

Finally, the squared E-field difference was also compared between Ella, MIDA-warped-into-Ella (MELLA), and MIDA, as shown in Figure 5.18.

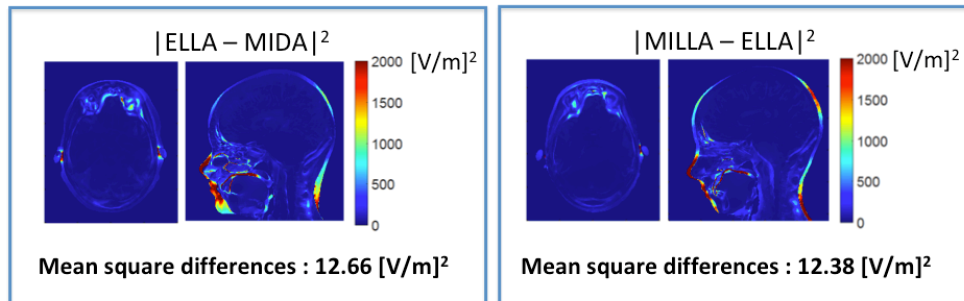


Figure 5.18: The fidelity of voxel EM properties: Mean squared differences of E-field between MIDA-warped-into-Ella (MELLA), Ella, and MIDA), compared only in those areas that are shared by the two models

Mass comparison calculation

The results of density mapping were compared among the three models (both before and after warping of MIDA into Duke space) along with comparison of the total head mass, shown in Figure 5.19.

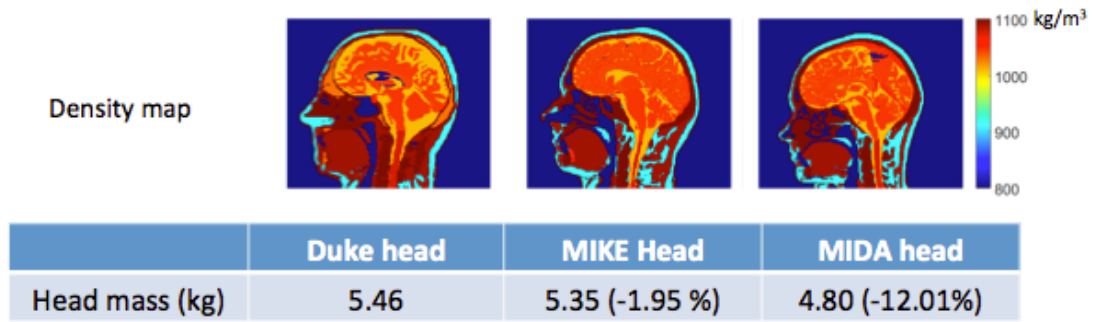


Figure 5.19: The fidelity of EM properties: Density and mass for MIDA-warped-into-Duke (MIKE), Duke, and MIDA

The mass difference of Ella and MIDA-warped-into-Ella (MELLA), and MIDA is also compared in Figure 5.20.

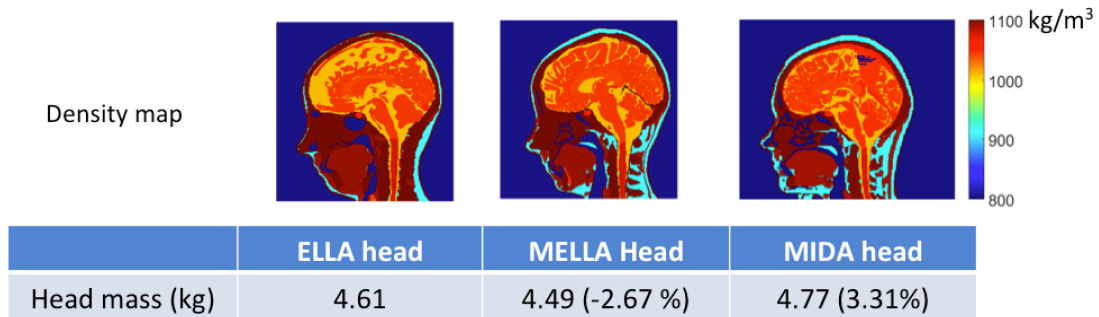


Figure 5.20: The fidelity of EM properties: Density and mass for MIDA-warped-into-Ella (MELLA), Ella, and MIDA

Voxel-based registration vs. CAD-based registration

Figure 5.20 shows the results of CAD-based registration and voxel-based registration of MIDA-warped-into-Duke. It can be seen that the results of the voxel-based registration lead to a staircase effect at the edge of the model due to the process of converting 2D slices into a mesh, whereas the CAD-based registration has smooth curvature as can be seen in Figure 5.21. The staircase effect could also occur in the case of the CAD-based model when the CAD-based model is voxelized, but the effect can be minimised by choosing a densely defined grid.

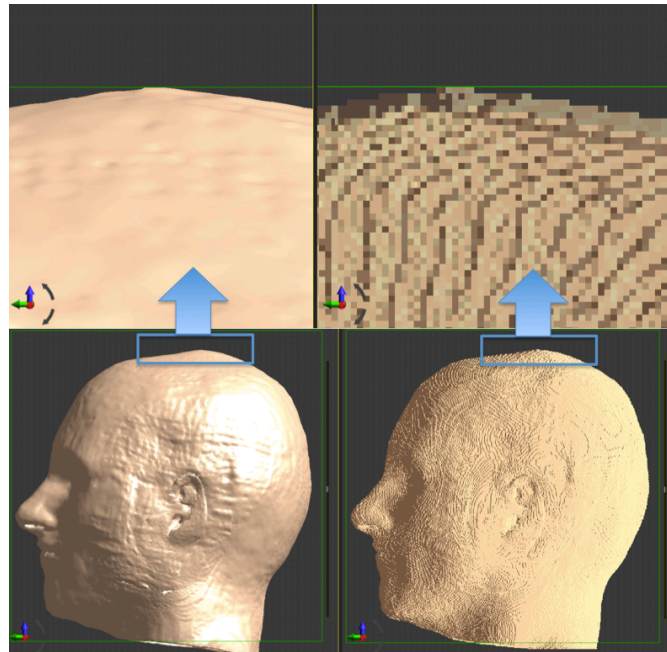


Figure 5.21: View of the surface-based model (left) and the voxel-based model (right) loaded into Sim4Life; i) top row: magnified image at the edge of the model, ii) Bottom row: entire head image.

Figure 5.22 shows the differences in dielectric properties between the CAD-based-MIDA and voxel-based-MIDA models using four different grid resolutions within the region of the MIDA head model.

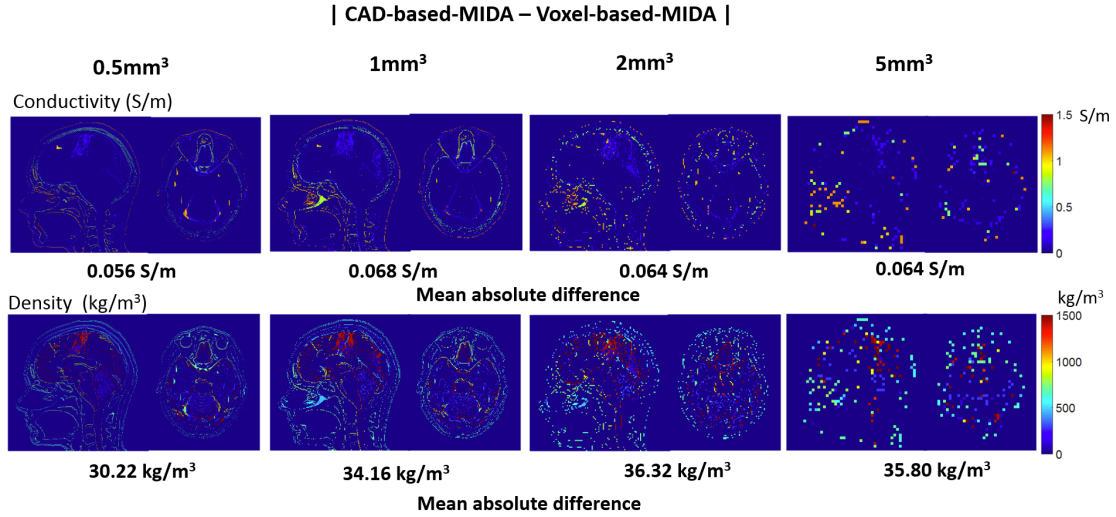


Figure 5.22: Differences in dielectric properties between CAD-based-MIDA and Voxel-based-MIDA for the case of four grid resolutions ($0.5 \times 0.5 \times 0.5 \text{ mm}^3$, $1.0 \times 1.0 \times 1.0 \text{ mm}^3$, $2.0 \times 2.0 \times 2.0 \text{ mm}^3$, and $5.0 \times 5.0 \times 5.0 \text{ mm}^3$).

It can be seen from Fig. 5.21 that differences between the two models are decreased from 0.064 S/m (conductivity) and 35.80 kg/m^3 (density) to 0.056 S/m and 30.22 kg/m^3 when the grid size is reduced from $5 \times 5 \times 5 \text{ mm}^3$ to $0.5 \times 0.5 \times 0.5 \text{ mm}^3$. Differences in dielectric properties between $2 \times 2 \times 2 \text{ mm}^3$ and $5 \times 5 \times 5 \text{ mm}^3$ resolution were small, since the results derived from voxel-based-MIDA at a $5 \times 5 \times 5 \text{ mm}^3$ grid size have a smaller number of sample points by a factor of 15.6 compared with the case of a $2 \times 2 \times 2 \text{ mm}^3$ resolution, which may lack sufficient samples needed for meaningful data comparison.

In addition to the improvement seen at the edge of the reconstruction, the CAD-based registration has the benefit of reduced import time into Sim4Life. The time required to import 115 tissue compartments was only 10 seconds when importing the CAD-based-MIDA model, since the tissue compartments in the CAD format are already converted into a mesh. This compares to 25 minutes needed to import the voxel-based MIDA model into our workstation, due to the mesh conversion process needed for each tissue compartment (Matrix size: $380 \times 450 \times 450$, Resolution: $0.5 \times$

$0.5 \times 0.5 \text{ mm}^3$). Also, registration using the CAD-based-model does not require the process of applying an inverse warping field, which takes $1 \sim 2$ hours in our computing system, and thus minimizes the uncertainties in warping coming from calculation of the inverse field.

Final warping results of the CAD-based-MIDA model into Ella and Duke space are displayed in Figure 5.23, followed by three original surface-based models of Ella, MIDA, and Duke in Figure 5.24.

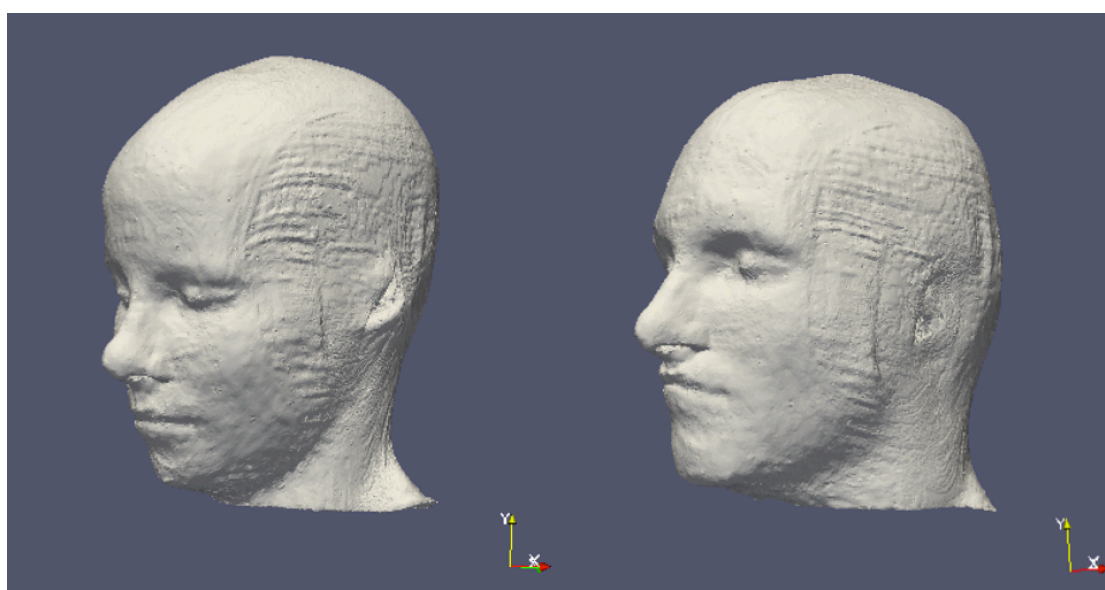


Figure 5.23: Results of the registration of surface-based models of MIDA into Ella (left) and MIDA into Duke (right) space.

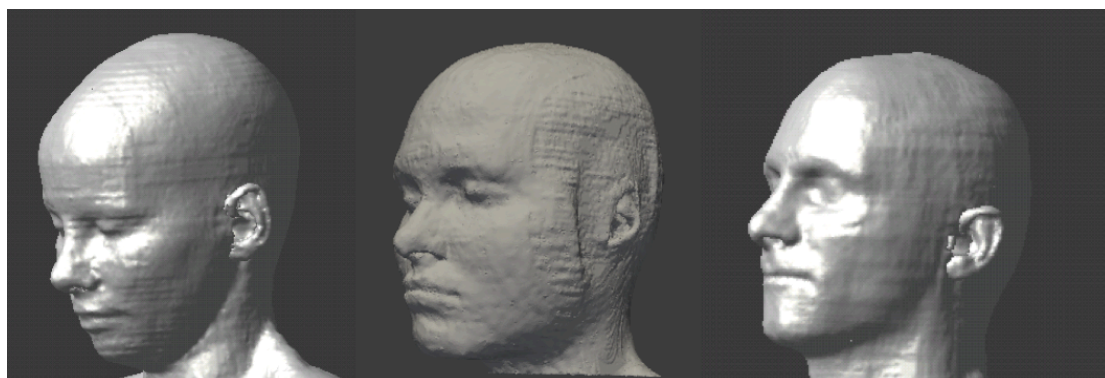


Figure 5.24: View of surface-based models: Ella (left), MIDA (centre), and Duke (right)

5.6 Discussion

Automated warping of models requires much less effort than manual segmentation. Manual segmentation requires an even larger amount of time and effort for a greater number of tissues in the segmentation. The proposed warping based method allows the use of existing high-resolution voxel models that can offer a way to avoid the significant efforts of segmentation.

As described in Section 5.2, various voxel models are available for EM simulation. The voxel model used as the reference for warping must be carefully chosen. Some models were developed many years ago, and have had no further update. The quality of these models, in terms of resolution and variety of tissue compartments, could be inadequate for the purposes of this study.

A proposed method of designing personalised SAR models is described and is realized via non-linear registration of synthetic T1-weighted MR images. By utilizing warping, the size and shape of the MRI subject can be accurately described in the simulation. The effects of warping were compared in terms of the input parameters - density, electrical conductivity, and E-field – required for SAR calculation.

The overall matching scores were improved after warping, and highlighted tissue types showing the great improvement in matching percentages, but there were no tissue compartments that achieved a 100% overlap after warping. A greater improvement was seen in Duke (albeit not a fantastic improvement), and less of an improvement in Ella. This could be because Ella is more similar to MIDA to begin with.

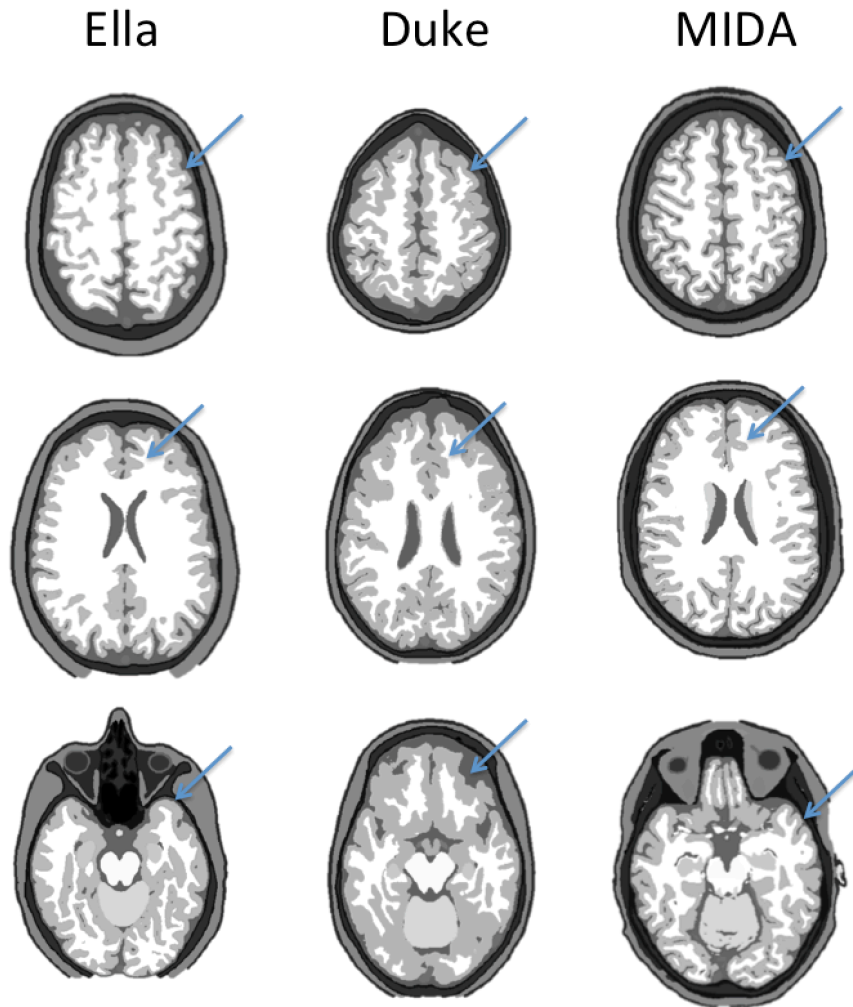


Figure 5.25: Axial view of synthetic T1 contrast images of Ella (left), Duke (middle), and MIDA (right)

Remaining differences are mainly found in two regions: brain regions of white matter and grey matter, and non-brain structures near the nasal cavity. Registering brain sulci is not trivial. The thickness of grey matter and brain sulci in Duke and Ella are not as realistic as those depicted in MIDA, which limits the registration of fine details in the brain, as seen in Figure 5.25. One option is to perform higher resolution registration to forcefully register fine structure, however this warping could degrade the quality of overall registration. The registration failed to capture differences in structures near the nasal cavity, we expect this was caused by a low quality segmentation of Duke and Ella in this region, as seen in Figure 5.26.

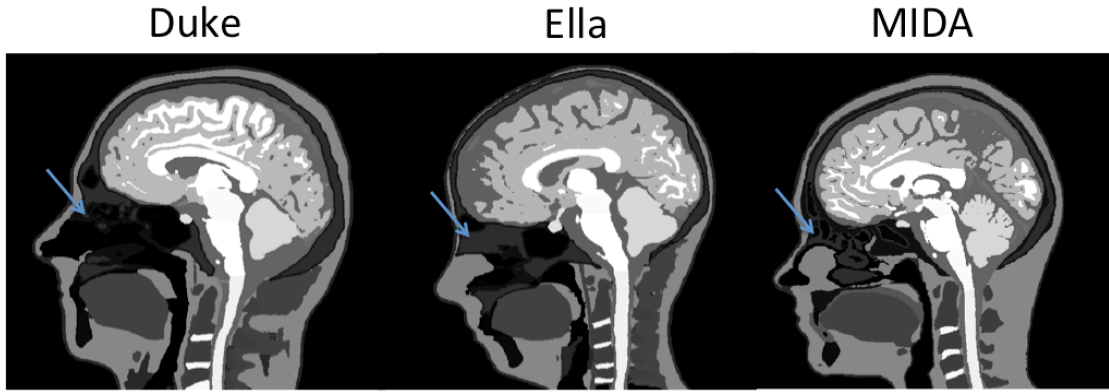


Figure 5.26: Sagittal view of the three models (arrows point to the nasal cavity where registration does not work well)

Several tissue compartments segmented in MIDA near the nasal cavity via support of multiple image modalities were often segmented as muscle in Duke and Ella. These subtleties in different model segmentations limit our intended application, since T1-weighted images generally do not support information on these complex structures found in MIDA. The effects of mis-matched SAR registration near the nasal cavity need to be further studied with two SAR averaging schemes assessing how mass averaging is done at the boundary where tissue meets air.

One potential approach to improve non-linear registration could be averaging warping fields calculated from two different directions: 1) Duke to MIDA as described in Section 5.4, and 2) inverse warping field after registration of MIDA into Duke. In such way it may be that potential errors from registration of fine structure can be cancelled, and overall registration can be improved.

The conductivity and density agreement improved after warping. The difference in mean conductivity between Duke and MIDA was reduced from 0.407 to 0.347 S/m when we warped MIDA into Duke space, and in the case of Ella was reduced from 0.396 to 0.377 S/m when we warped MIDA into Ella space. This translates to a 14.47 % and 4.78% reduction in overestimation of SAR in a conceptual calculation.

Mean squared differences of E-fields were compared using E-fields normalised

with 1 W input power of an 8-channel dipole element. As the square of the E-field is proportional to SAR, this results in a map showing where the greatest differences are expected. The difference in mass between Duke and MIDA was reduced from -12.01 % to -1.95 % when we warped MIDA into Duke space, and in the case of Ella was reduced from 3.31% to -2.61% when we warped MIDA into Ella space. This conceptually translates to a 10.06 % and 5.92 % under or overestimation of SAR.

The process of registering a voxel-based model and surface-based model was described. Conceptually, warping surface-based models is preferable as complex geometries can be retained up until the final voxelization in the simulation environment. This is expected to have a minimum loss of information through multiple voxelization steps or where grid resolution is not sufficient. Also, warping the surface-based model is one step simpler and faster in time than warping the voxel-based model, since it does not require the formation of an inverse warping field which is time consuming, often taking longer than 1 hour to calculate.

5.7 Summary Conclusion

We evaluated the hypothesis that non-linear warping of an electromagnetic model allows improved approximation of tissue compartments. This hypothesis was tested by warping one synthetic model (MIDA) into other target synthetic models (Duke or Ella). What we found was:

- The tissue compartments of white matter, skin, spinal cord, and cerebellum had the greatest improvement in alignment using this process. Grey matter, CSF and air had marginal improvements, while the process struggled to replicate the compartments of dura, skull and muscle.
- We demonstrated that warping a surface-based (CAD) model offered better

retention of information compared to warping a voxel-based model. This was because it ensured contiguous, smooth, biologically realistic tissue boundaries with a reduction in information loss similar to that of a high resolution warp ($0.5 \times 0.5 \times 0.5 \text{ mm}^3$).

- Use of surface-based (CAD) non-linear warping reduced the processing time by 1-2 hours by removing the inverse warping field calculation from the process.

There are innate differences between the description of tissue compartments in the two represented models, Duke (or Ella) and MIDA, which will likely cause effects that cannot be corrected via matching of morphometric differences. This and its effect on pTx SAR prediction will be investigated in Chapter 6.

6 Practical Utility of the Personalized Voxel Model

6.1 Introduction

As described in Chapter 5, various standard EM voxel models (e.g. HUGO, Duke, and Ella) have been used in RF safety simulation by adding an agreed safety margin, since they do not perfectly represent morphometric differences across the population. Due to these remaining uncertainties there exists the need for better personalised voxel models that are more suited to the subject in the scanner and that allow us to operate the scanner closer to the true SAR limit.

A handful of methods have been proposed to achieve personalised modelling (131,155–157), including finding personalised electrical properties via measured B_1^+ maps or segmented morphometric images. Segmented images have also been used to aid subject-specific registration to the NORMAN model, with this approach being applied to setting the power limits of a volume transmit coil (136).

There have been several approaches taken so far in the literature to develop a personalised voxel model: image segmentation (69), electrical properties mapping (156,158,159), and non-linear registration (131). Image segmentation with the underlying MRI of the subject is the most commonly used method to characterise and model the required dielectric properties. A T1-weighted MPRAGE sequence can be used to segment several brain structures, such as grey matter, white matter, skull, muscle, etc. However, CSF and bone-air interfaces are difficult to segment due to the short echo time and lack of observable magnetic susceptibility effect for this sequence (160), meaning that additional scans, such as T2-weighted image contrast (161) and MR angiography (162), are required to segment further tissue compartments. In regard to this, multimodality images are helpful to identify each

tissue compartment correctly in segmentation-based methods, which can require significant resources to scan and process the data.

Electrical properties tomography (EPT) has also been suggested to characterise the dielectric properties of subjects (156). By analysing the B_1^+ field in each of the three principal directions, dielectric properties – specifically electrical conductivity, and relative permittivity – can, in theory, be calculated from experimental data. The main advantage of this method is its capability of capturing dielectric properties during the scanning session itself, which can directly represent the underlying subject in the scanner. A validation study using a phantom was able to capture several dielectric properties, but there remain technical challenges for this method. Acquiring in-vivo data is not a trivial procedure due to patient motion and physiological noise. The quality of the B_1 transmit field acquisition will determine the implicit assumption of dielectric property characterisation. In addition, high-energy RF deposition is required to capture a good quality B_1^+ field in three dimensions, and adds to the scanning time. Furthermore, the complexity of different tissue compartments in the brain is difficult to separate out using only a flip angle mapping method, potentially resulting in the tissue property maps being considerably simplified in the brain. The EPT method is more beneficial to characterizing the dielectric properties of the body, since it is more robust in the body to patient motion, given the relatively simpler structures and bigger organ sizes compared to the brain.

Non-linear registration of existing models has also been suggested. Surface-based anatomical models were proposed by IT'IS (97), and a surface-based morphing technique was introduced which registers surface elements into a target model (163). In this referenced study, the Ella and Fats models were morphed into three different BMI models based on a FEM-based morphing technique (164).

The main advantage of the morphing approach is its simple implementation. Only surface information of the various tissue boundaries is required to reproduce voxel models with different characteristics. The limitation of surface-based morphing is reported to be a difficulty of registering inner structures, such as organs, despite a good agreement in outer surface matching, which may require further information of inner structures and with a greater weighting.

Non-linear registration was previously studied by the research group from the University of Queensland using BrainWeb data and a NORMAN voxel model (165). MR data of four subjects were chosen from the BrainWeb database, and these were segmented for non-linear registration. Tissue was segmented into 11 compartments using images derived from four different MR contrasts - MR angiography, T1-, T2-, and proton density weighted MR images. Segmented tissues were used for rigid and non-rigid registration. The results of the registered models were assessed inside a model of a single-channel transmit birdcage coil tuned to 7T with EM simulation software. That study showed the effects of warping head shape and size on B_1^+ field and 1g-averaged SAR. However, the benefits of a personalised voxel model in the case of a parallel transmit MRI system remained uncertain.

The purpose of this study was to develop a personalised SAR model using non-linear warping, and apply it to both single-channel and multi-channel transmit systems. Our expectation was that by simulating a personalized model of the subject, safety margins could be reduced, which enables the scanner to operate closer to the true SAR limit. Here, we propose a method that uses non-linear registration of a high-resolution EM reference voxel model into a target head morphometry. We then sought to conduct a cross validation between EM models to evaluate the effectiveness of this procedure in the context of pTx.

In this chapter, a standard EM model (MIDA) was warped into subject-specific space. Two further EM models (Duke and Ella), representing the (subject-specific) target, were used for cross-validation. The local SAR for a parallel transmit configuration was evaluated using 5,000 randomly chosen RF shims.

6.2 Assessment of a warping to produce personalised EM models for RF safety in pTx

The method used to warp a model to a target morphometry was described in Chapter 5. In this section, the effects are analysed of a personalised SAR model on RF safety assessment in both combined (single channel) mode and for a pTx system.

6.2.1 Methods: Evaluation of predicted SAR in personalised models

EM simulations were carried out using Sim4Life at the 7 Tesla frequency of 297.2 MHz. The simulations assumed an eight-channel dipole array coil with no RF shield and driven with realistic capacitor values assumed to account for the loading effects arising from the expected morphometry. The dipole element was chosen due to its simple electrical structure. SAR simulations were performed on both the Duke and the reference models. Warped surface-based tissue compartments were loaded into Sim4Life. The same process was performed with Ella. The position of the warped MIDA model was aligned inside the RF coil to be the same as the Duke (or Ella) model, using the same amount of translation and rotation, so that the effects of warping could be observed.

For all simulations a truncated body model was used. The body of either Duke or Ella was used depending on the comparison. This was positioned at the same location under the head to provide an appropriate body loading for RF heating calculations. The amount of torso included was chosen to be the point at which 98% of the energy is absorbed, as seen in Figure 6.1.

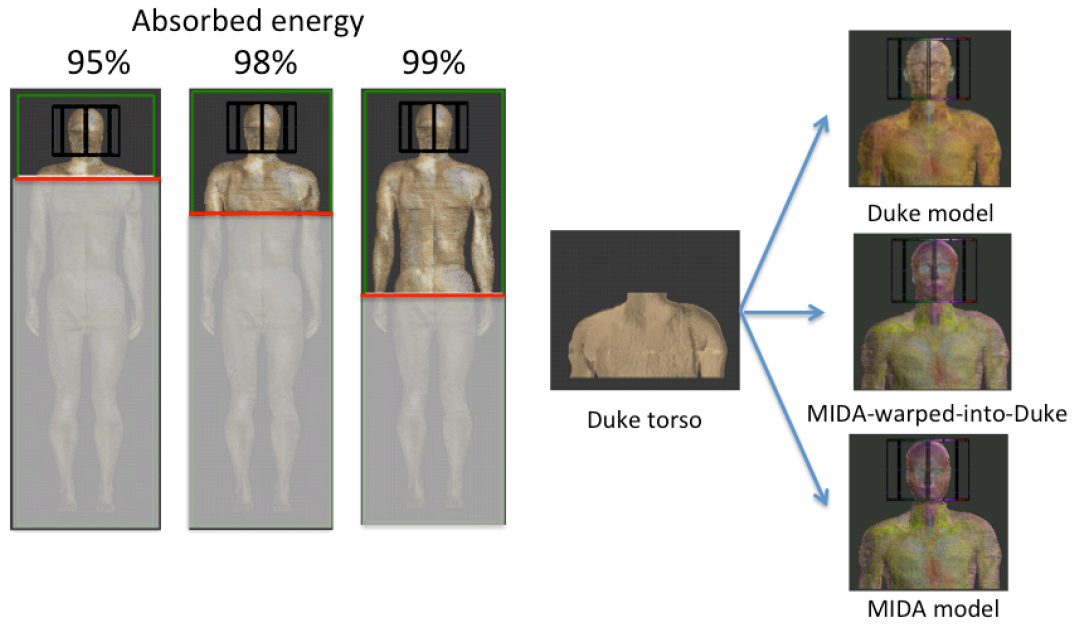


Figure 6.1: Portion of Duke body model chosen for EM simulation and illustration of volumes that absorbed 95%, 98% or 99% of the RF energy (Data from 8-channel head pTx coil as described in Chapter 3, Section 3.2).

When simulating circularly polarised (CP) mode, a harmonic simulation was performed with a 45-degree phase increment applied to each channel. The B_1^+ field, SAR and 10g averaged SAR were normalized to fields that produced 2 μT at the coil centre using an ideal current driving method (166,167). (1.957 μT is the amount of field strength require to produce a 90° flip angle in ^1H with a rectangular RF pulse of 3 msec duration (166)).

To simulate arbitrary pTx modes, a multiport simulation was performed, which calculates multiple identical simulations: this approach excites each source separately by adding 50 ohms resistances to the non-activated channels.

A Q-matrix formulism was used to calculate quickly the SAR for various RF shim combinations, as described in Chapter 2. The Q-matrix can be calculated indirectly, either from unaveraged SAR estimates, or from mass averaged SAR (67,168) which estimates where only the 10g SAR maps are needed. Full SAR results from 64 different RF shim sets are required to solve the 8×8 Q-matrices. 8 sets are used to calculate Q_{ii} (the diagonal elements), and 56 sets are needed (two sets as Q is complex, one pair for each component in the upper half of Q) to solve for the non-diagonal Q_{ij} complex components. The remaining elements can be calculated by using the conjugate characteristic of Q-matrices, as seen in Figure 6.2.

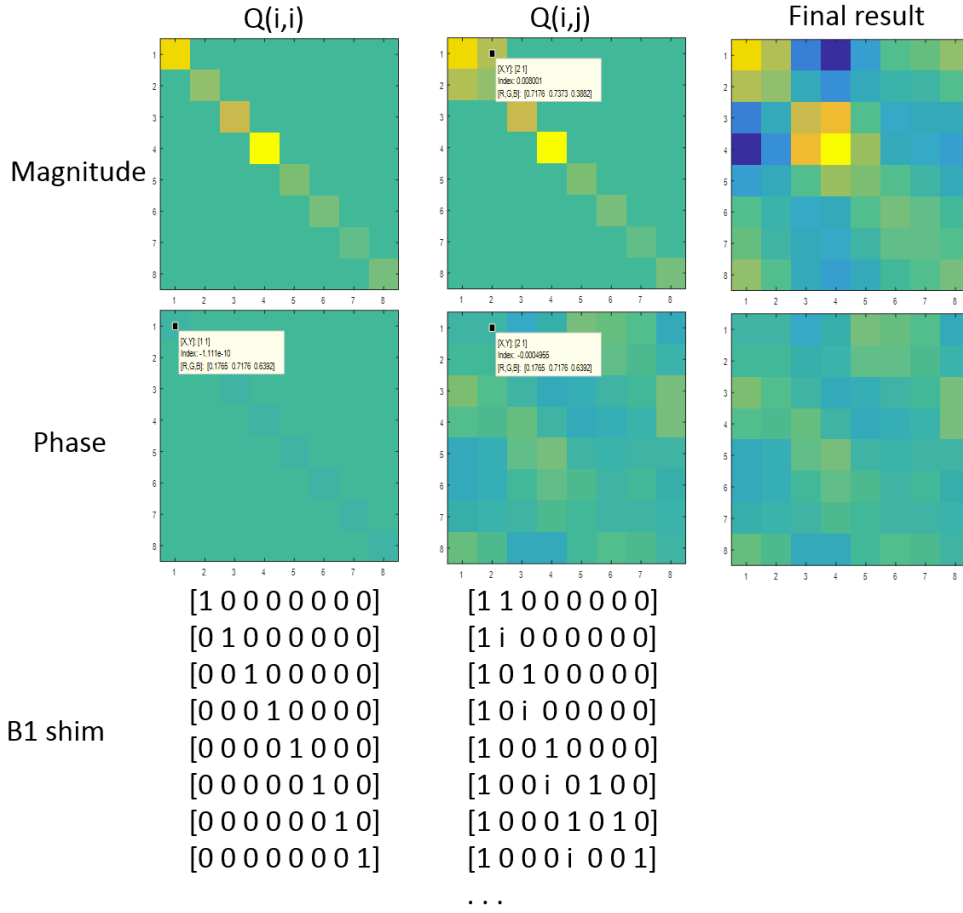


Figure 6.2: Q-matrix calculation process from SAR estimates at one voxel: eight B_1 shim sets are needed to calculate the diagonal elements (left column, containing real part only). An example complex solution for a B_1 shim set in the non-diagonal elements is also shown in middle column: real parts of Q-values can be calculated by applying (1,0) at each element (e.g. real $Q_{12} = (\text{SAR}_{[1\ 1\ 0\ 0\ 0\ 0\ 0\ 0]} - Q_{11} - Q_{22})/2$). Imaginary parts of Q-values between two elements can be verified by adding 90 degree phase in second element (e.g. imag $Q_{12} = (\text{SAR}_{[1\ 1|90^\circ\ 0\ 0\ 0\ 0\ 0\ 0]} - Q_{11} - Q_{22})/2$).

For each of the three different models the SAR results were averaged to 10g mass voxels according to the IEEE/IEC 52704-1 standard using the dosimetry tool provided in Sim4Life, which are then converted in turn to 10g averaged Q-matrices. 5,000 random B_1^+ shim sets with random normalized amplitude (0-1) and phase (0- 2π) were used to assess RF safety in pTx mode; all data were then averaged to 1 W total input power. The NRMSE difference of SAR was calculated, and several comparisons were made: Duke versus MIDA, Duke versus MIDA-warped-into-Duke (MIKE), and the same process was performed for the Ella model.

6.2.2 Results: Duke vs. MIDA-warped-into-Duke

The differences of 10g averaged SAR and Q-matrices between the subject-specific model (Duke) and the original MIDA model were compared in CP mode.

Additionally, the results of 10g averaged SAR between the subject-specific model (Duke) and the warped voxel model (MIDA-warped-into-Duke) were compared, as seen in Figure 6.3.

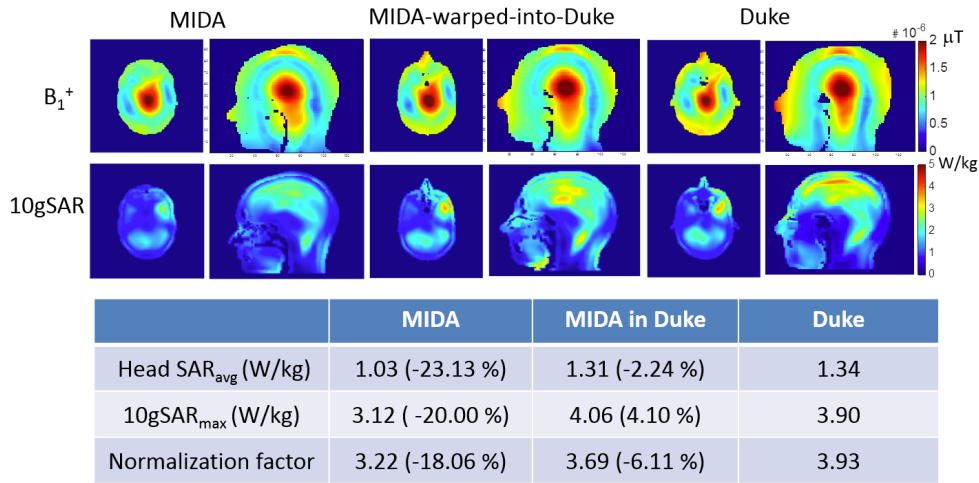


Figure 6.3: B_1^+ field distribution and 10gSAR in CP mode (normalized to $2\mu\text{T}$ at the coil centre). Differences in averaged SAR in head regions relative to the Duke model are shown in the first column, and in worst-case 10gSAR in 2nd column, and normalisation factors in the last column in parentheses.

The difference map in B_1^+ field distribution and 10gSAR in CP mode between Duke vs MIDA, and Duke vs MIDA-warped-into-Duke (MIKE) are shown in Figure 6.4.

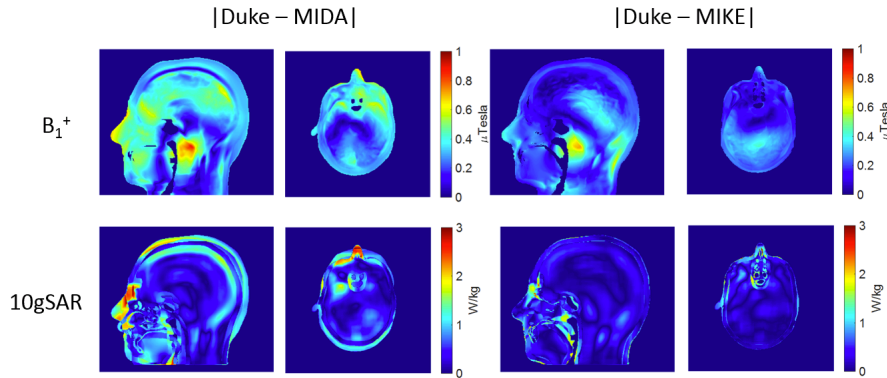


Figure 6.4: Differences in B_1^+ field distribution and 10gSAR in CP mode (normalized to $2\mu\text{T}$ at the coil centre) between Duke-MIDA, and Duke-MIKE (MIDA-warped-into-Duke)

Figure 6.5 shows Bland-Altman plots that compare the hottest local SAR predicted by Duke compared to that predicted by MIDA (calculated both for the case of the original MIDA model, and for the case of MIDA warped into Duke space) for each of the 5000 random B_1 transmit shim sets. Here, values below zero indicate an underestimation and therefore an unsafe condition where MIDA would predict a lower SAR than Duke.

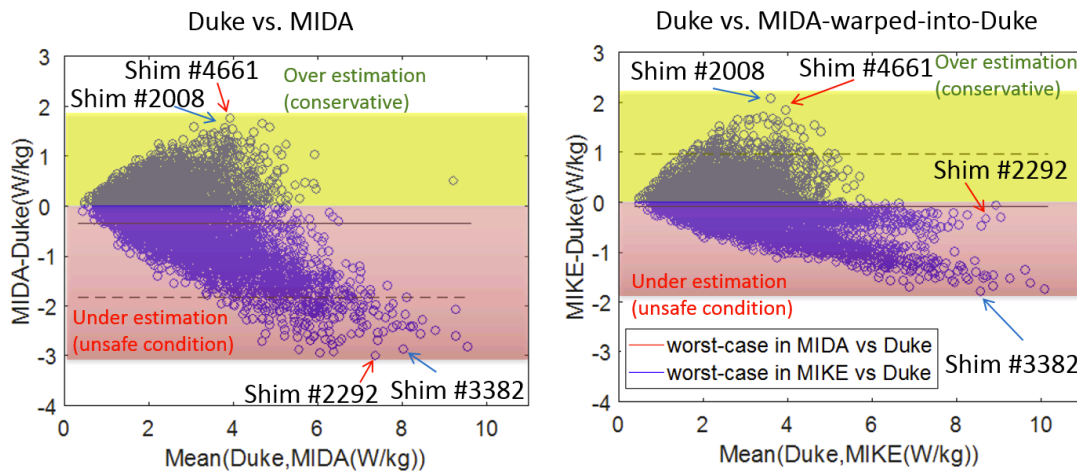


Figure 6.5: Bland-Altman plot comparing the hottest local SAR predicted by Duke to that predicted by MIDA (with and without warping) for each B_1^+ shim set. Arrows are pointing at worst-case scenario for Duke-MIDA (red), and Duke-MIKE (blue).

Figure 6.6 shows histograms of maximum 10g SAR differences among the three models. Figure 6.7 shows the location of the hottest SAR deposition for an example specific shim set (#1145).

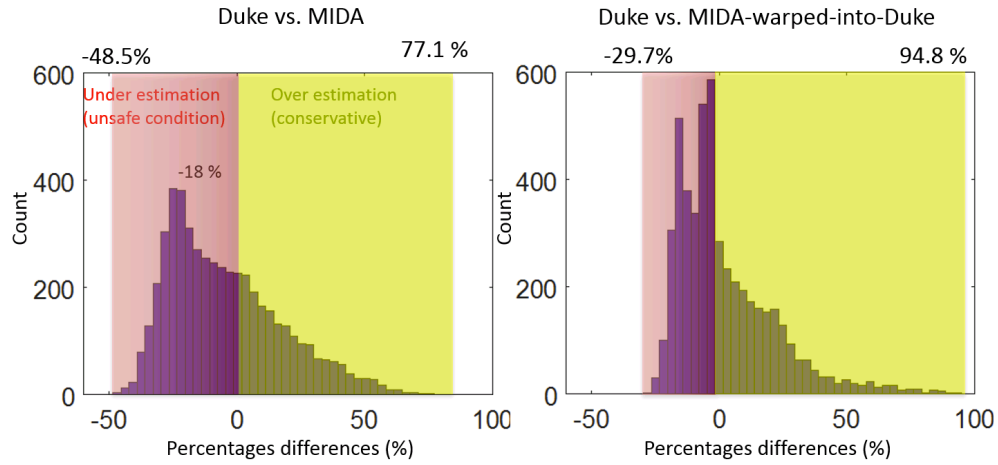


Figure 6.6: Histogram of maximum 10gSAR differences between MIDA-Duke and MIDA-MIKE (MIDA-warped-into-Duke)

	Duke (W/kg)	MIDA in Duke (W/kg)	MIDA (W/kg)
Shim #2292 (Worst-case underestimation in MIDA)	8.862 [104 37 156]	8.538 [99 38 160]	5.861 [106 51 126]

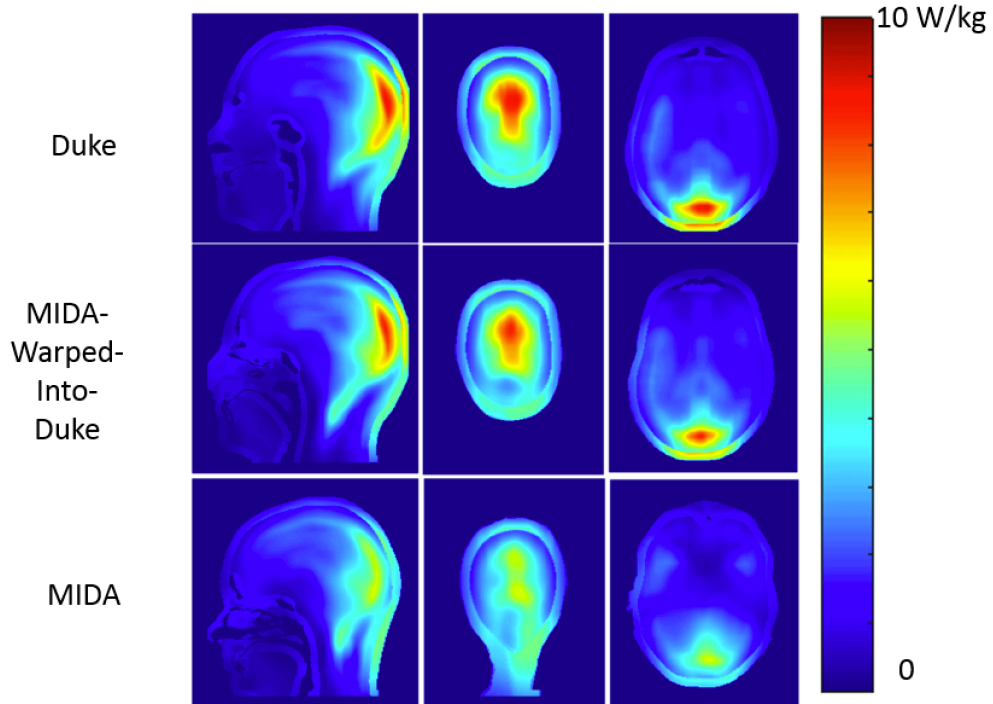


Figure 6.7: Location of hottest 10g maximum SAR among Duke, MIDA, and MIDA-warped-into-Duke for the case of a specific B_1 shim set (#3382).

6.2.3 Results: Ella vs. MIDA-warped-into-Ella

To compare the effect of warping in a standard female model, MIDA was also warped into Ella space. In this section, the results of MIDA-warped-into-Ella are compared, similar to the comparisons for Duke made above, as seen in Figure 6.8.

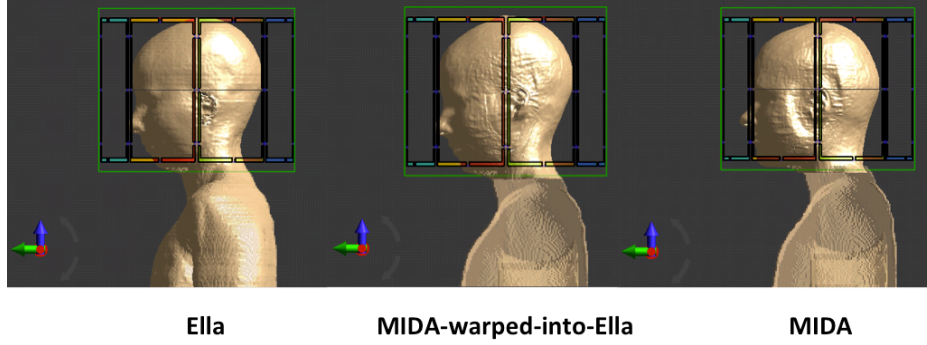


Figure 6.8: MIDA, Ella, and MIDA-warped-into Ella models located in the 8-channel pTx coil described in Section 3.2

The results of 10g averaged SAR maps calculated in CP mode are shown for comparison between MIDA (both with and without warping) and Ella in Figure 6.9.

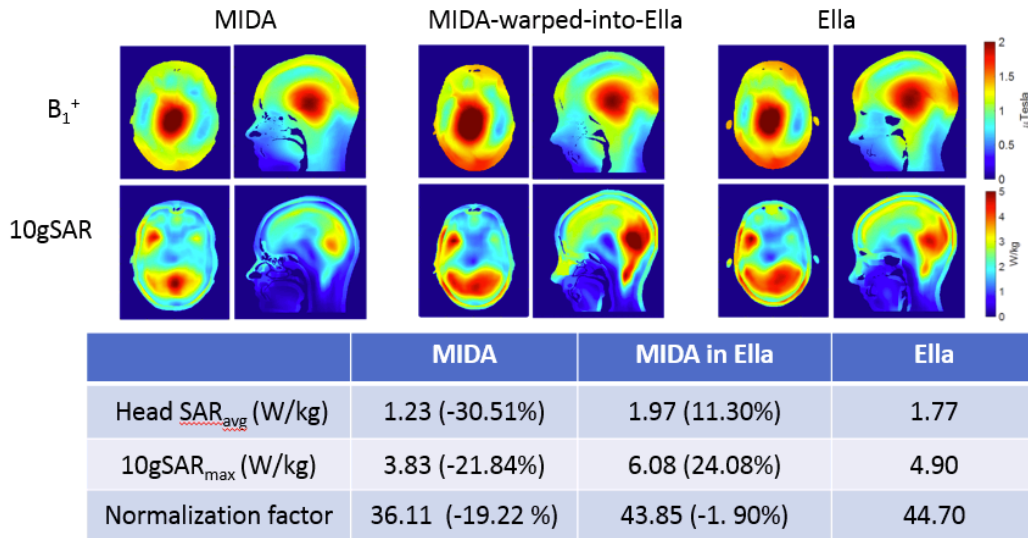


Figure 6.9: B_1^+ field distribution and 10gSAR in CP mode (normalized to 2 μ T at the coil centre). Differences in averaged SAR in head regions relative to the Duke model are shown in the first column, and in worst-case 10gSAR in 2nd column, and normalisation factors in the last column in parentheses.

Figure 6.10 shows Bland-Altman plots comparing the hottest local SAR predicted by Ella compared to that predicted by MIDA (both with and without warping) for each of the 5000 randomly sampled B_1 transmit shim sets.

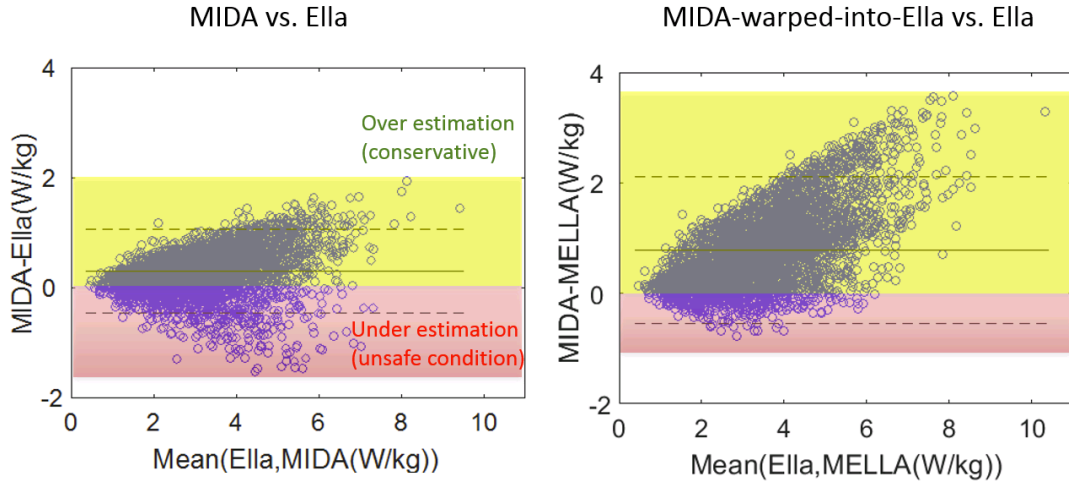


Figure 6.10: Bland-Altman plot comparing the hottest local SAR predicted by Ella to that predicted by MIDA (with and without warping) for each B_1^+ shim set.

Figure 6.11 shows histograms of maximum 10g SAR differences between the Ella, MIDA, and MIDA-warped-into-Ella models.

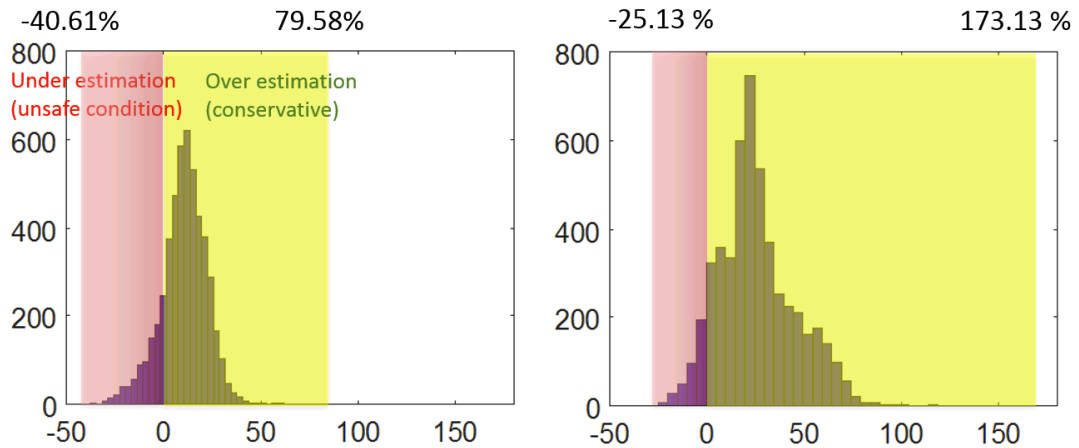


Figure 6.11: Histogram of maximum 10gSAR differences between [MIDA minus Ella] and [MIDA minus MELLA (MIDA-warped-into-Ella)]

6.2.4 Discussion

The 10gSAR results were calculated for the standard model (MIDA), and compared with Duke, Ella, MIDA-warped-into-Duke and MIDA-warped-into-Ella space.

For the CP mode analysis of Duke, the difference between the subject-specific model (Duke) and the ‘standard’ model (MIDA) was reduced both for the case of head-averaged SAR and maximum 10gSAR when MIDA was warped into Duke space. However, in the case of Ella as the subject-specific model, the amount of over-estimation in maximum 10gSAR actually increased when MIDA was warped into Ella space. It is postulated that a greater benefit is gained from warping when there is a significant morphometric difference between the subject-specific model and the standard model.

In the case of the pTx analysis of 5000 randomly chosen shim sets, the underestimate of maximum 10g SAR for Duke was reduced from 46.1% to 26.3% after the warping of MIDA into Duke space. Conversely, underestimation of Ella was increased from 21.91% to 25.16% when MIDA was warped into Ella space.

It is possible that innate differences between the two models being compared, especially the more detailed tissue descriptions in the MIDA model versus the sparser tissue characterisation of the Ella model, could lead to underestimation of SAR. In the case of MIDA warped into Ella space, due to the initially smaller morphometric differences between these two models, we speculate that the benefit of warping did not overcome the larger effects arising from the differences in how detailed tissue structures are characterised between them.

The effects of detailed tissue characterisation will be further discussed in Section 6.4 using Duke version 1.0 and 3.0.

6.3 Field warping: post-simulation warping: A way to assess improved E-field prediction by non-linear registration

In order to evaluate the effects of warping synthetic human models this section applies an additional post-simulation field warp to the un-warped simulation of MIDA. This is not done to predict the E-fields in the target space, but rather to assess the improvement in field prediction within a common geometric basis. We expect that warping of the fields after simulations will enable further understanding of the effects of morphometry on RF energy deposition by facilitating voxel-to-voxel comparisons.

6.3.1 Methods

In order to apply a warping field to the ‘standard’ model simulation results, the location and size of the field sensor region (i.e. the field-of-view and relative location of the model space used in the original EM simulation) must be reduced in size and relocated to match the available extent and location of the warping field. In this case, the results exported from the field sensor region should have an isotropic resolution that is the same as the warping field ($1 \times 1 \times 1 \text{ mm}^3$ in our case). By matching these parameters, warping of the simulation results, such as the 10g averaged SAR, E-field, and even Q-matrix maps, can be done as a simple post-processing step.

The simulation set-up for Duke, MIDA, and MIDA-warped-into-Duke, described in Section 6.2, was used to assess the post-simulation warping method. The size and location of the field sensor region was adjusted to be the same size as the field-of-view used when MIDA was registered to the subject-specific model. The results of the field sensor calculations were then resampled to $1 \times 1 \times 1 \text{ mm}^3$ iso-voxel

resolution using the ‘Resample Field’ tool in Sim4Life. The inverse warping field was then calculated as described in Section 5.3.3.

Warping the Q-matrix is done separately for the magnitude and phase, because it requires the correct handling of complex values. The values of the Q-matrix were first separated into magnitude and phase (originally scaled from $-\pi$ to $+\pi$), and then π was added to the phase values as an offset to avoid negative values in the data when using the NIFTI format.

The absolute Q-matrices can indirectly show how much energy is potentially consolidated in a certain area. Therefore, the summation of absolute Q-matrices at each voxel was done at each point and compared between the model spaces.

The MIDA post-simulation results were warped into the relevant subject spaces using their respective warping field, and then compared with the results of the fully warped voxel model. This comparison was done with E-field, 10g averaged SAR and Q-matrices.

6.3.2 Results

Figure 6.12 shows the results of 10gSAR estimation in CP mode for the four models considered: namely EM simulation of Duke (top row); EM simulation of MIDA-warped-into-Duke (MIKE, middle row); post-simulation warping of MIDA into Duke space (MIDA-results-warped-into-Duke, third row); and EM simulation of MIDA (bottom row).

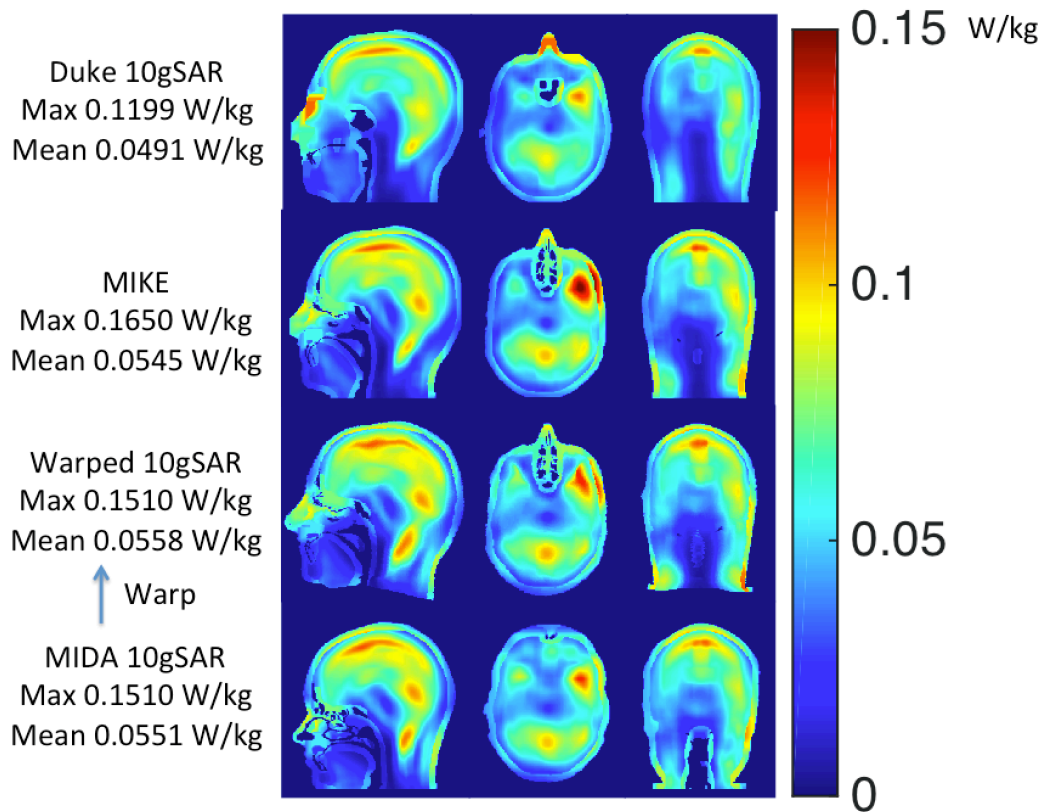


Figure 6.12: Results of EM simulations in CP mode with 1 W input power of Duke (top row); EM simulation of MIDA warped into Duke (second row); post-simulation MIDA-results-warped-into-Duke (third row); and EM simulation of MIDA (bottom row).

Figure 6.13 shows the difference in the 10g averaged SAR between EM simulation of Duke vs EM simulation of MIDA, EM simulations of Duke vs post-simulation MIDA results-warped-into Duke space, and EM simulations of Duke vs EM simulations of MIDA-warped-into-Duke (MIKE).

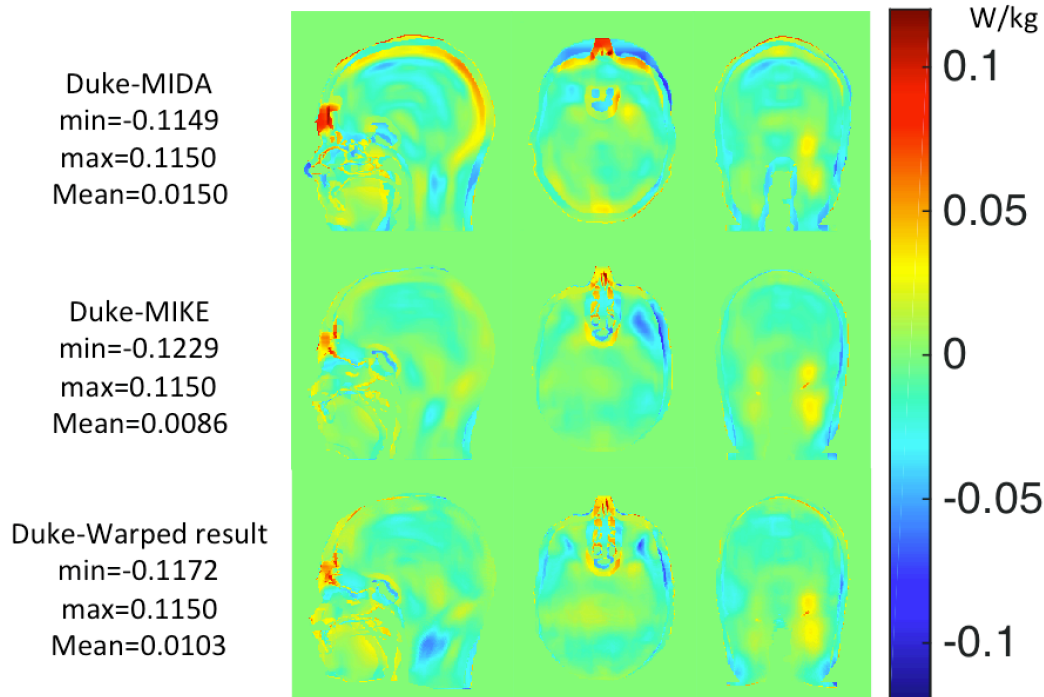


Figure 6.13: Results of difference in the 10g averaged SAR with 1 W input power in CP mode between EM simulation of Duke vs EM simulation of MIDA (top row); EM simulation of Duke vs EM simulation of MIDA warped into Duke (middle row); and EM simulation of Duke vs post-simulation MIDA-results-warped-into-Duke (bottom row).

The level of averaged error was found to be reduced from 0.0150 W/kg to 0.0103 W/kg when post-simulation MIDA-results are warped into Duke space, and further reduced to 0.0086 W/kg when a correct pre-warped model is used in EM simulation within the area of the tissue mask.

To assess full pTx performance, 10g averaged Q-matrices were also calculated from Duke, MIDA-warped-into-Duke, and post-simulation MIDA results warped into Duke, using a summation of the absolute Q-matrices done at each voxel. The results of these estimates in 10g averaged Q-matrices can be seen in Figure 6.14.

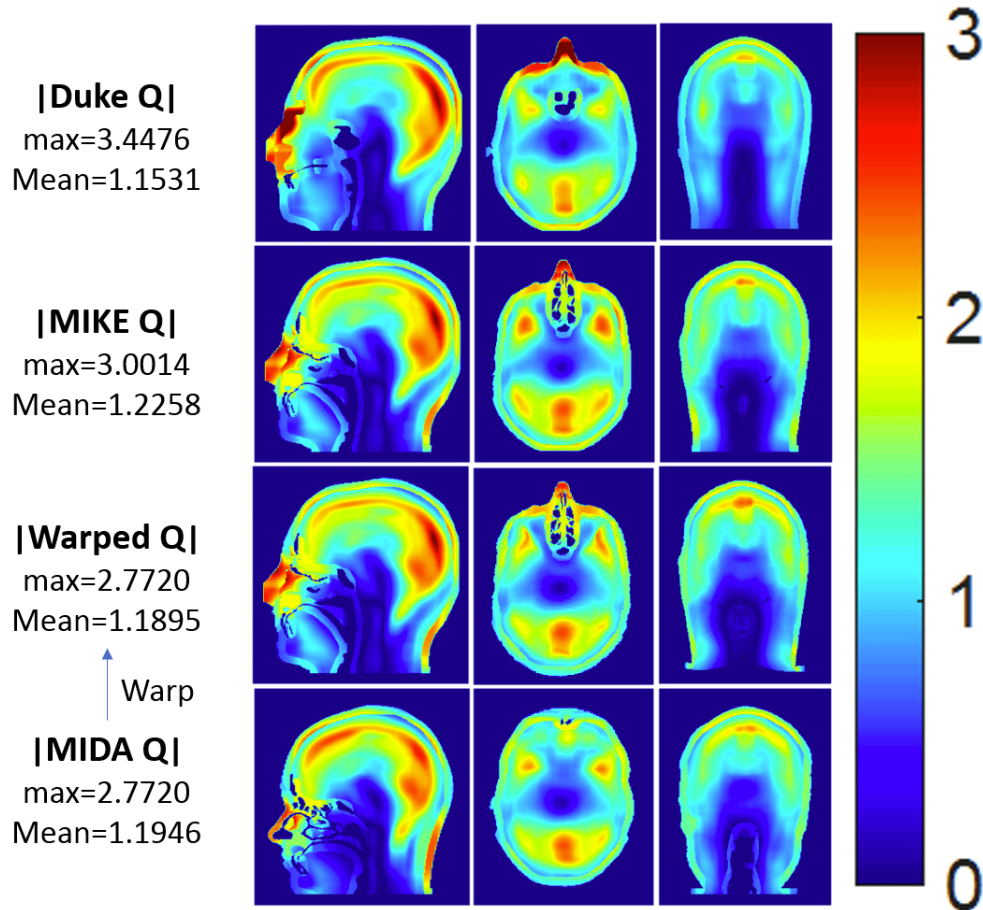


Figure 6.14: Results of 10g averaged Q-matrices, based on EM simulation of Duke (top row); EM simulation of MIDA warped into Duke (second row); post-simulation MIDA-results-warped-into-Duke (third row); and EM simulation of MIDA (bottom row). The 10g averaged Q-matrices are calculated as a summation of absolute Q.

Figure 6.15 shows the difference in the Q-matrices between EM simulations of Duke vs EM simulations of MIDA-warped-into-Duke (MIKE), and EM simulations of Duke vs post-simulation MIDA results-warped-into Duke space.

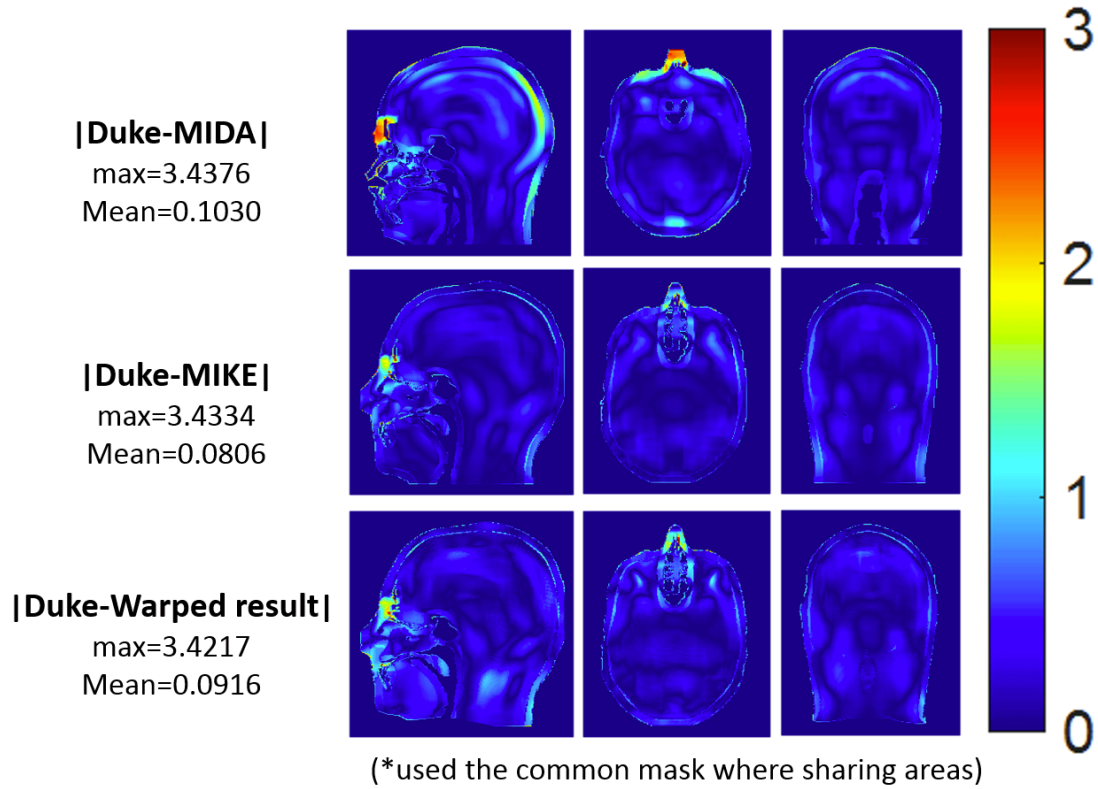


Figure 6.15: Results of differences in the Q-matrix for Duke vs MIDA (top row); Q-matrix for Duke vs Q-matrix for MIDA-warped-into-Duke (middle row); and Q-matrix for Duke vs post-simulation MIDA-results-warped-into-Duke (bottom row).

In the same regard with the results of 10g averaged SAR, the level of mean errors was slightly reduced when the EM simulation results of MIDA was warped into Duke space (from 0.1030 0.0916) and further reduced when EM simulation is performed with the correct pre-warped model (from 0.1030 to 0.0806)

6.3.3 Discussion

The SAR predictions using pre-simulation warping had smaller errors compared to post-simulation warping, however the difference was marginal. A limited amount of changes were found when the EM simulation results were warped in to subject space (Duke), which were partially caused by changes of air cavities area within the head region.

It is still unclear whether the remaining differences observed are generated from morphometric differences between Duke and MIDA, or are innate differences in how the structures of the two models were segmented and more subtle differences such as what type of material was identified. For both Q-matrix and CP-mode in both pre- and post-simulation warping a large energy deposition difference is observed on the bridge of the nose, indicative of a significant difference in tissue type of the two models. Further studies are needed to separate effects coming from segmentation of the models and morphometric differences.

The differences between the pre- and post-simulation warping are likely to be larger if the head position, rotation, inclination are more different between the subject in the scanner (Duke) and the ‘standard’ model (MIDA), since the full pre-warping before EM simulation accounts for the relative position of the head within the coil, whereas the post-simulation results only consider a single relative position of the head (MIDA) within the coil.

Since only the one post-simulation MIDA-results-warped-into-Duke-space was analysed (model was positioned in the centre of the coil), the results and effects are less representative than if the subjects had been in a different position in the coil compared to the ‘single’ MIDA simulation. The more extreme circumstances are needed to be assessed in future (e.g. the subject is squeezed against the front of the

coil)

6.4 Assessment of different tissue compartments: Duke v1.0 v2.0 v3.0

The effects of warping were discussed in previous sections (6.2 and 6.3). The morphometric differences between the two models ('subject-specific' and 'standard') were minimized using non-linear registration, and under-, or over- estimation of SAR was evaluated in the maximum 10gSAR estimates.

However, warping was observed to sometimes produce a higher overestimation than non-warping, especially for the case of MIDA-warped-into-Ella space, which indicates that there could be effects coming from segmentation differences between the three models (MIDA, Duke, Ella).

In this section, the magnitude of effects coming from the specifics of tissue compartment characterisation was studied using three different versions of the Duke model, which have differing compartmental descriptions, but otherwise identical morphometric information.

6.4.1 Methods

The three versions of the Duke model (v1.0, v2.0, v3.0) that were used in this study are compared in Table 6.1.

	Duke 1.0	Duke 2.0	Duke 3.0
Type	Voxel	Surface	Surface
Number of tissue compartment	78	22	78 (230 bones)

Table 6.1: Comparison of the different versions of Duke model

Duke version 1.0 is a voxel-based model that was introduced in 2011, with 78 tissue compartments. Despite its higher version number, Duke 2.0 is actually a simplified version of Duke 1.0, provided to 3rd party users. Duke 3.0 was introduced in 2015 with a surface-based format and a larger number of segmentations and bone compartments, whereas the total number of tissue compartments remained the same as for Duke v1.0.

However, despite having the same overall number of tissue compartments, Duke v1.0 and v3.0 each have their own special tissue compartments, which are only available in each version, as seen in Figure 6.16.

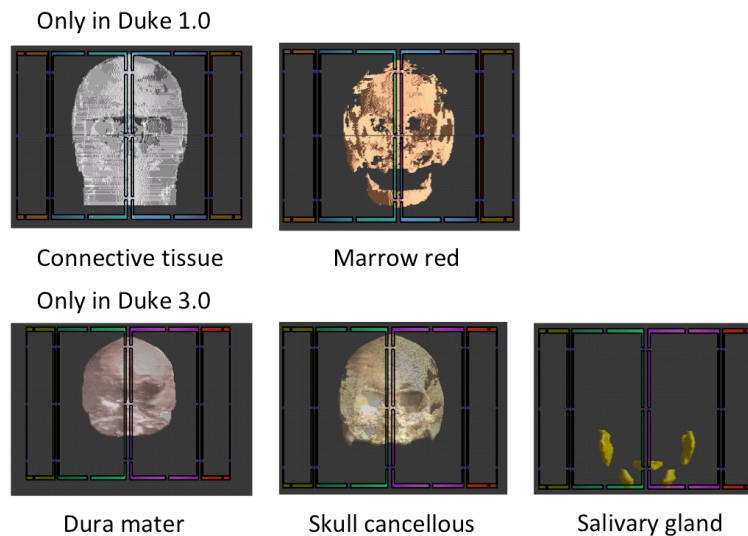


Figure 6.16: Special tissue types only available in Duke v1.0 (top) and Duke v3.0 (Bottom)

Duke v1.0 contained a large volume of connective tissue around the bone regions, which is eliminated in Duke v3.0. Instead of connective tissue, Duke v3.0 newly introduced Dura mater. Marrow red in Duke v1.0 was replaced with cancellous skull and salivary gland regions in v3.0, which also have different dielectric properties.

Duke v1.0 and v3.0 were compared by modelling them inside the 8-channel head pTx coil (Juelich, Germany) which previously described in Chapter 3, Section 3.2.

6.4.2 Results

Figure 6.17 shows the differences in conductivity and density between Duke v1.0 and v3.0.

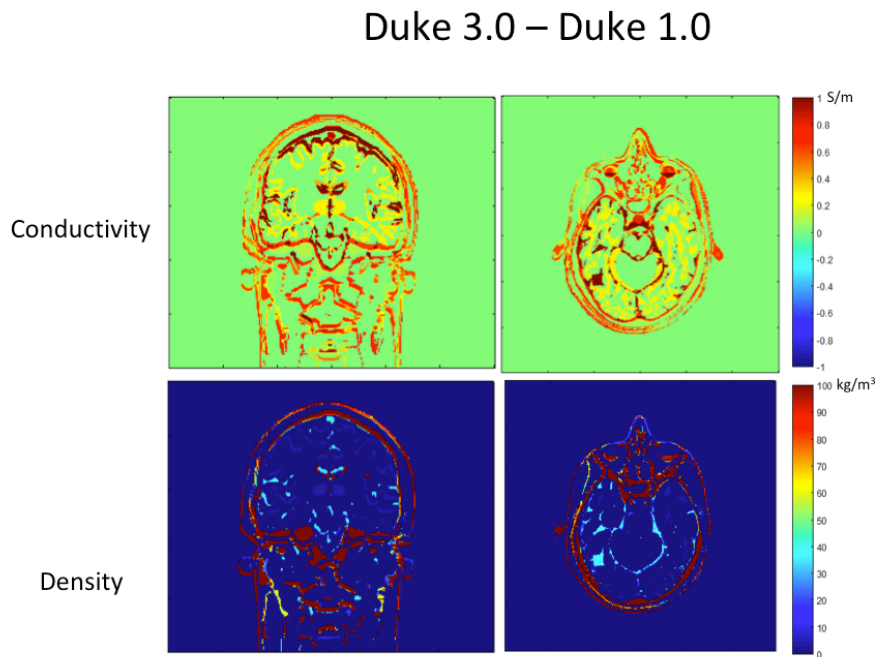


Figure 6.17: Difference in conductivity and density between Duke v1.0 and v3.0

Further detailed differences were found in brain grey-matter and white-matter regions, as well as differences at the edges that could potentially arise from model modification, or from differences coming from the voxel-based model versus the surface-based model.

Figure 6.18 shows the results of the differences in maximum 10gSAR between the v1.0 and v3.0 Duke models assessed using 5,000 random B_1 shim sets, expressed as a Bland-Altman plot (left) and as a histogram (right).

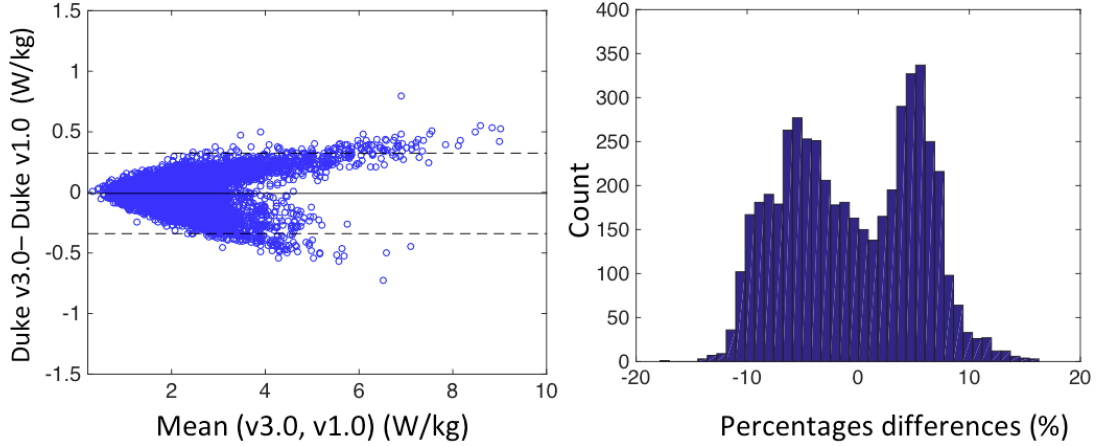


Figure 6.18: (left) Bland-Altman plot of 10g maximum SAR difference between Duke v1.0 and v3.0; (right) histogram of percentage difference in 10g maximum SAR between Duke v1.0 and v3.0.

6.4.3 Discussion

The results of EM simulation between Duke v1.0 and v3.0 were assessed. These models share identical morphometry, but have slightly different tissue segmentation. The results showed that maximum 18 % differences in worst-case SAR can be found by having a slightly different tissue segmentation. This observation highlights that use of Duke v2.0, a simplified version of Duke v1.0 and v3.0, or other voxel models with the limited number of tissue segmentation can cause uncertainties in RF safety assessment in pTx MRI even with morphometric warping effort. Further studies are needed to understand the cause of these differences and the impact that the segmentation of different tissue compartments has on the calculated fields.

6.5 Overall Discussion and Conclusions

6.5.1 Overall Discussion

The potential benefits of using a personalised voxel model have been described, especially in the context of pTx safety assessments, where the deposition of electromagnetic energy can cause unpredictable hot spots in different head sizes and shapes.

Assessment of post-warping effects after simulation was demonstrated by observing the 10g averaged SAR (for CP mode) and summation of the 10g averaged Q-matrix (for pTx mode). SAR prediction by warping the fields of an EM simulation marginally improved the SAR prediction compared with using only a reference model. However, this still has limitations in correctly identifying the hot spots of the underlying subject in the MRI scanner.

Development of personalised models potentially enables users to operate the scanner closer to the scanner's true SAR limits, albeit with additional safety margins to account for uncertainties such as motion.

The process of developing a subject-specific voxel model by warping before EM simulation was evaluated and assessed for its potential benefits. The synthetic MR images were generated by replacing the tissue compartments with pre-defined intensities to try to match a T1-weighted scan. However, these signal intensities do not represent the true contrast differences that would arise in a real scanner from system imperfections, such as coil sensitivities, shim inhomogeneities, or B_1 transmit field inhomogeneities. For these reasons, the registration process may be inefficient in finding robust warping vectors between images with perfect contrast versus realistic contrasts. This could be addressed by using the original T1-weighted images from which MIDA was generated. However using MIDA's original MR images does

not overcome contrast differences between different parameters used in T1-weighted pulse sequences or differences in contrast between 3T and 7T (MIDAs reference images were acquired at 3T) (169). In light of the above arguments, using the original MR images from the MIDA model for non-linear registration is still limited, but could be considered to improve the quality of registration between MR T1-weighted images of a specific subject and the MIDA reference model.

Using the original MR data for the MIDA model was not an option for this study as it is not accessible to the wider scientific community due to an agreement with the institutional review board (IRB) that acquired the original data, limiting access only to the U.S. Food and Drug Administration (FDA, United States).

In this study, a truncated body from Duke was connected to both MIDA and MIDA-warped-into-subject space. It is possible that local SAR hotspots occur in the shoulders of a subject and personalisation of the torso could be considered in the future. In this study care was taken to ensure the warped model matched well to the Duke body at the level of the neck. This was done to avoid discontinuity in the model. However for future work it may be preferable to choose different body loading models based on a subject's sex and BMI.

A limitation of the proposed warping and simulating approach is that it is slow, taking on the order of a day to complete all steps. Thus, this pipe line must be applied in advance of a pTx scan. With the aid of fast computational hardware personalised RF safety in real-time may be possible for future applications.

This method could possibly be extended to MRI applications that require careful safety assurance, such as deep brain stimulation (DBS) and implant safety. In a DBS study, the position of the lead in the brain plays an important role in assessing RF heating. By having an accurate depiction of the subject, and a model of the lead, a

safety margin could perhaps be determined and unexpected hot spots and excessive energies delivery can be prevented.

An alternative to non-linear subject registration is segmentation of T1-weighted MR images. The segmentation of T1-weighted images has the limitation that it cannot easily separate CSF and air. Both compartments have nearly zero intensities in an MP-RAGE sequence. To address this, additional MR images, such as T2-weighted or Turbo-Spin-Echo (TSE) scans may be required. Despite several algorithms that offer auto-segmentation, such as thresholding, gradient, or marching cube-based edge-detection, segmentation is a non-trivial process. Furthermore, verification and manual correction are usually required to avoid errors due to outliers or imperfect image quality.

The personalised voxel model could also be used in other validation studies, such as comparing B_1 field predictions against flip angle measurements. Having different orientations or locations of the subject can improve the degree of validation of this type of assessment.

The personalized voxel model can be used in other applications, such as B_1 shimming or sequence contrast simulation. B_1 shimming is a method used to mitigate B_1 transmit field inhomogeneity. Due to the shortened wavelength of tissue in ultra-high-field MRI (approximately 11 cm for ^1H signals at 7 Tesla), the B_1 transmit field pattern shows complex behaviour. This personalised approach could be used to generate a pool of multiple voxel models, B_1 shimming techniques could be tested and simulated in advance. In the process of functional tests of an RF coil, a flip angle (FA) map is usually acquired and compared with simulation data. In practice, a head-shaped phantom is used for this validation, but a biological head-shaped voxel model could instead be used for validating the simulation results of the B_1 transmit field

with experimental data. Theoretically, a personalised voxel model could be generated and assessed for RF heating in real-time during the scan with high performance computing. Assessing the RF safety of patients with implants or tattoos is also possible with a subject-specific model. In such a scenario with an implanted device or tattoo pigments it is imperative to accurately estimate the possible risk of patient RF heating, assuming the dielectric and thermal properties of the implanted device or tattoo pigmentation is known. A subject-specific voxel model could greatly increase the confidence level in assuring RF safety in this scenario.

6.5.2 *Summary Conclusion*

In conclusion, the process of warping to form a personalised voxel model was evaluated in the context of pTx.

- Methods to assess under- and over-estimation of SAR predictions in the context of pTx were presented. Bland-Altman and histogram analysis methods were used to assess the range and rate-of-occurrence of under and over estimation.
- By warping MIDA into Duke or Ella the under-estimation of SAR was significantly reduced. This is relevant for safety as it enables a reduction in the safety margin used to account for variations in morphometry. A proposed reduction from a 50% safety margin (without warping) to 25% (with warping) could be achievable.
- However, the maximum over-estimation increased marginally for MIDA-warped-into-Duke and significantly for MIDA-warped-into-Ella, with both presenting a conservative SAR prediction for a number of pTx configurations.

- The subtlety of different segmentations of the same model were analysed and found to introduce for some pTx configurations a 10% SAR under-estimation and for other configurations a 10% SAR over-estimation. Future work should investigate if this is caused by tissues with high electrical conductivities (e.g. CSF) or from small, hard-to-segment tissue compartments causing sudden changes in dielectric properties (e.g. bone marrow).

Overall, the personalised voxel model applied to RF safety assessment was capable of reducing the safety margin of SAR prediction in operation by providing a lower degree of under-estimation of SAR at the expense of an increased over-estimation for some pTx configurations.

7 Discussion and Conclusions

7.1 General Discussion

7.1.1 RF safety modelling for pTx MRI and its validation

Methods developed for RF safety modelling in the context of pTx and its validation were discussed in Chapters 3 and 4. B_1 transmit field and thermal elevation maps were measured in order to validate the RF pTx safety simulations. However, additional validation methods can also be considered. The measurement of E-fields could be an alternative method for validation of the RF safety simulations, since E-fields are directly related to SAR, when combined with density and electrical conductivity values (170). Measurement with E-fields reduces uncertainties compared to when validation is done using B_1 transmit fields, since a specific B_1 field distribution could theoretically arise from more than one E-field distribution. Combining direct-E field measurements along with thermal elevation measurements would therefore be an ideal way to validate EM simulations, although at present direct E-field and temperature measurement methods only support point evaluation using E-field and optic fibre probes.

Phantom design procedures were also introduced in Chapters 3 and 4. A phantom was designed to have similar dielectric properties to averaged brain white matter and grey matter and was also designed to be compatible with MRI PRF thermometry. Notwithstanding, further efforts are needed to design a more realistic inhomogeneous phantom for RF safety assessment. The EM field behaviour and thermal behaviour become more complicated in non-homogeneous objects, which can introduce boundary effects between several different tissue types.

The method of PRF-based MR thermometry was described and compared with

simulation data in Chapter 4. The most popular method to experimentally measure temperature changes uses proton resonance shift, but one can also measure the chemical shift using a more sensitive chemical additive, such as TmDOTMA⁻, with a spectrometer (85). TmDOTMA has a larger alpha coefficient than protons, and this chemical has to be added to a phantom to monitor the temperature changes. Despite its high accuracy, and temperature sensitivity, it is not widely used due to its high cost.

There are also other approaches to measure temperature using conductivity changes. A method of temperature monitoring in a clinical setting using conductivity imaging has been introduced for RF ablation studies (171). Conductivity is a temperature dependent property, so accurately measuring and monitoring conductivity changes could give us information about temperature changes. But it requires specialised hardware for impedance measurement, and requires injection of electrical currents into the sample which may introduce another safety issue.

Also, due to perfusion and time-varying heating deposition in real tissues, the accurate thermal simulation and validation of a human voxel model is challenging.

The main RF safety consideration in conventional low field MRI usually focuses on assuring whole-body SAR, extremity SAR, and head SAR, since a whole-body transmit coil is the typical configuration inside the MRI bore (up to 3T). This allows a considerable simplification of RF safety assurance. Only a small number of simulations are required, such as head and body-centred loading in the circularly polarised transmit mode, since the main RF heating consideration is regarded as coming from the transmit coil. However, the introduction of ultra-high field ($\geq 7\text{T}$) MRI requires regional transmit coils, and each different design of transmit coil requires a specific RF coil model, meaning that safety assurance and simulation

validation become much more difficult.

Parallel transmit MRI further increases the complexity of the EM field evaluation and SAR deposition, making safety assurance due to RF heating even more challenging. Despite many studies that have relied on SAR for safety assurance, measuring and assessing temperature elevation provides a more direct measure of RF heating, which could be used for additional assurance and for relaxing conservative safety controls. Direct E-field measurement using an optical probe can be a robust way to validate a simulation, which can be used in place of measuring the B_1 transmit field.

Our RF heating experimental data were assessed only with activation of a single transmit element. With confidence in the safety assessment approach and validation of each single transmit element, the complex form of thermal behaviours in different RF shimming conditions can also be predicted and validated in phantom studies.

Understanding of thermal behaviours *in vivo* is more challenging. It requires further understanding of thermal regulation by blood flow, and accurate accounting for tissue compartments. So that the validation of thermal simulations should be done using phantoms first, then thermal simulation can be more plausible. In the case of field behaviours and thermal elevation in non-homogeneous phantoms the heat transfer mechanism between two different materials needs to be further studied.

Studies of SAR using thermo-acoustic information are showing promise of direct spatial mapping of SAR experimentally (172). This result can be converted into temperature mapping in a transient heating experiment and used for cross validation with PRF MR thermometry. Additional hardware is required to measure SAR based on thermo-acoustic mapping, but this can be used as a real-time SAR safety monitoring method in the future. The possibility of measuring SAR using the

temperature dependence of the water diffusion coefficient has also been proposed (173).

7.1.2 Development of a Personalized SAR Model

A method describing a personalized voxel model was proposed and its future application was discussed in Chapters 5 and 6. Discrepancies in the conventional approach for SAR estimation between patients who undergo MRI and the voxel model used for EM simulations requires a safety margin of up to 1.5 (150%) to return a probability of less than 1% of exceeding the safety limits (132). Since individual differences have been studied and considered in clinical studies, the need for more accurate safety modelling and further safety monitoring would allow operation of the scanner closer to the true SAR. This would hence enable diagnosis of patients more accurately with advanced sequence techniques, and with sufficient driving power to excite protons in the region of interest.

The proposed method uses synthetic MRI images of a high-resolution EM voxel model for registration, which has the flexibility to replace tissue contrasts depending on the MR images that are acquired in the subject. This contrast can be varied by the type of MR sequence, sequence parameters, and the MRI vendor's specific image reconstruction scheme. Subject images using an MPRAGE T1-weighted sequence were used for registration in our method, but other contrasts, such as T2-weighted imaging, diffusion tensor imaging, and vascular images can also be used to improve the quality of registration. A sequence simulator tool, such as SYSSIM in Sim4Life, can be used to generate synthetic MR images. Coil sensitivities, coupling between elements, and different sequence parameters can also be included to generate synthetic MR images for registration.

Access to the original MR images of the MIDA model could be the ultimate solution to improving the quality of registration. Provided users have access to MRI data that matches as closely as possible the original MIDA data (174), the remaining discrepancies between the contrast in the synthetic MIDA T1-weighted images and the MR images of the subject can perhaps be reduced. Currently, though, data access is limited to use in the US Food and Drug Administration (FDA, USA), so that the chances of potential benefits are limited.

The position of the subject's head is important for RF safety, as well as the size and shape of the head. When coil loading conditions change, the RF coil response also changes. The RF coil uses an L-C circuit to resonate at a specific frequency, which is optimised for a specific loading condition to minimize reflection at the port. Small variations in the subject's position could result in different patterns of energy deposition, leading to changes in the location of hot-spots. Thorough studies are needed that incorporate the measured scattering matrix into SAR estimation.

Our proposed method does not require tissue segmentation, since T1-weighted images are used directly in registration. However, segmented tissue compartments may provide better registration for specific tissues by weighting segmented tissues in specific masked regions in the registration. Further studies are needed to understand which tissue compartments are sensitive in the SAR simulation and play an important role in obtaining adequate EM simulation results. Any regions identified in this manner could be given an increased weighting and further registration.

The concept of a personalised voxel model can also be used in hyperthermia treatment studies (175,176). The current pipeline used by the Berlin Ultrahigh Field Facility (BUFF) group obtains images from two modalities, CT and MRI, and segments tissue compartments in both modalities (176). Providing our proposed

warping process can be adapted, patient tissue compartments containing pathological tissue can be rigidly captured and more realistically assessed. RF safety control with minimum safety margin can be achieved by removing uncertainties resulting from un-segmented regions.

The increasing number of open data studies enables access to big data. Examples include the UK-Biobank (177), Human Connectome Project, etc., which offers the possibility of relating RF safety estimation to big data. Providing the personalised voxel model pipeline could be connected with big data, the relationship between RF deposition and individual morphometric differences across the population can be thoroughly studied along with its correlation with different cohort groups – sex, ages, ethnic background, history of certain disease - and used to estimate a suitable safety margin or transfer function in RF safety. Also, machine learning could aid in operating the scanner closer to the true SAR limit by correctly identifying the morphometry and location of the patient, and capturing SAR changes by motion and scattering matrices.

Personalized voxel model studies have now been extended to whole-body safety simulation, safety in different BMI studies, and also safety modelling of the foetus (IT'IS). Since the standard model does not represent differences across the population, the safety margin to account for individual differences, position of the subject, and incorrect characterisation of segmentation has been studied. Our ongoing efforts to assess accurately individual differences in RF safety assurance will allow further understanding about thermal behaviours, and RF safety in MRI.

More RF safety studies need to be performed to develop cohort data sets which represent the RF safety factor over a population of patients with different morphometric information, ages, sex, and ethnic background. The advantage of using

such a cohort as a database can be validated by simulation of a specific dataset with a large number of voxel models, with this data set, such as a localizer, or previous medical imaging dataset, chosen at the beginning of the scan session. By having a cohort dataset of RF safety models, the current safety margin could possibly be reduced, and more confidence in RF safety can be achieved. Furthermore, a personalized model can be used for assessing RF safety in specific applications, such as implant patients (e.g., deep brain stimulation, DBS) which requires further accurate safety assessment to reduce the risk.

7.2 Overall Conclusion

In this work we have shown that uncertainties in the prediction of SAR for 7T pTx arise from several sources with varying degrees of significance. The introduction of uncertainties in the phantom evaluation process were assessed and found that simulating with measured, rather than expected, electrical and thermal properties improves the level of agreement by 10%. When choosing capacitor values for simulating loop elements it was found that matching the simulated to physical capacitor values produced the most similar heating profiles, but still struggled to replicate precisely the heating measured in the phantom.

A proton resonance frequency (PRF) shift MR thermometry method was proposed, it was found that using a TIAMO acquisition strategy significantly reduced the thermal errors in regions of ' B_1^+ dropout' and enables an acquisition strategy that does not require scan specific B_1^+ adjustment. By averaging four echoes a marginal improvement in temperature measurement was observed, which became significant in regions of low signal. It was found that a simple 15 minute stabilisation scan mitigated B_0 field gradient drifts, allowing the correction of non-RF heat-related field

drift more accurately without dedicated hardware set-up.

This work found that the differences in SAR prediction between two models are significant for a number of pTx configurations when compared to that for a single transmit setup.

The work set out to reduce the subject-specific uncertainty using non-linear warping to personalise a synthetic human model. It was found that achieving accurate morphometric results required the registration to focus on gross anatomy rather than fine structures. This process produced models similar in appearance but with residual differences in many structures such as the grey/white matter in the brain, muscles, and tissues in the nasal cavity region.

Non-linear warping reduced the degree of SAR underestimation in both models evaluated. Underestimation of SAR is safety critical and reflects the magnitude of safety margin required to represent one model with another across the spectrum of possible pTx transmit configurations. This reflects a reduction in the required safety margin from 50 % to 25 % when using non-linear warping to personalise an EM simulation for pTx. Over estimation of SAR remained after non-linear warping in both of the models evaluated, this results in a conservative RF energy limitation for some pTx configurations.

It was found that the manner in which the same model is segmented introduces pTx-related under- and over-estimations of ± 10 %.

This work has found that uncertainties in SAR prediction from pTx can be reduced by considering simulation parameters such as resolution, capacitor values, and RF shields. When physically verifying a simulation environment using a phantom the electrical and physical properties should be measured after production. It was found that while the effects of head morphometry play an important role, large

discrepancies in SAR predictions remained, this highlighted the importance of the model segmentation process for pTx RF safety.

With improved confidence in assessing patient safety, the state-of-the-art MR imaging techniques can be pushed further to produce better images of patients in clinical and research 7T MRI.

7.3 Future work

7.3.1 *Assessing which tissue compartments are critical to accurate SAR estimation*

Perhaps the greatest finding in this thesis was that brain morphometry is outweighed by the importance of segmentation for pTx SAR prediction. A future study is needed to evaluate the level of accuracy required for various tissue compartments to minimise uncertainty in SAR prediction.

7.3.2 *RF safety modelling with pTx MRI using Personalised model*

Our proposed workflow is to warp the MIDA EM model into the subject underlying the MRI scan. The warping method introduced in Chapter 5 can be applied to a T1-weighted image obtained from the subject, as seen in Figure 7.1.

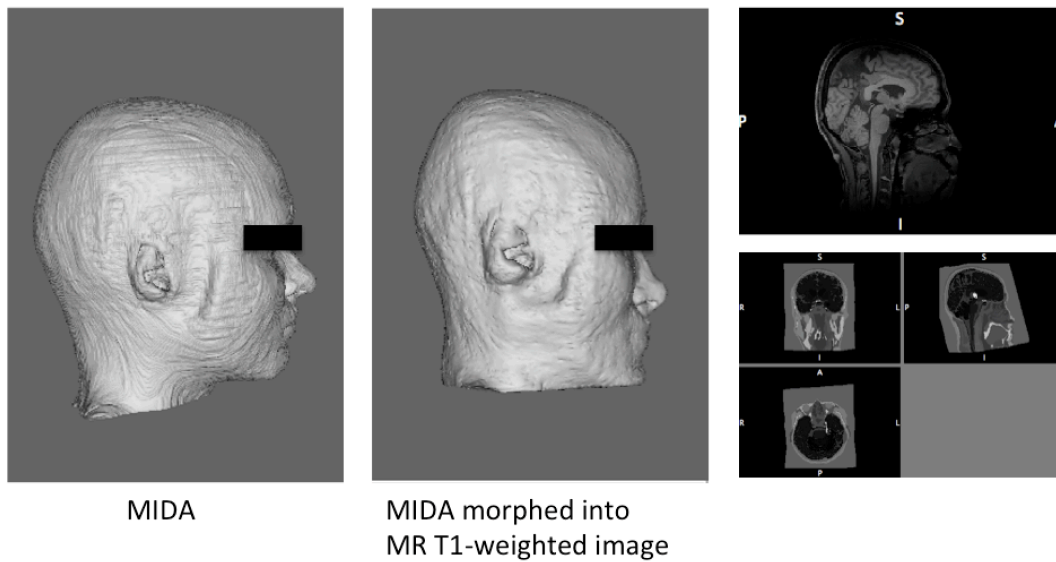


Figure 7.1: MIDA voxel model warped into T1-weighted image that was acquired at 3T (TR: 2380 ms, TE: 3.96 ms, IT:1200 ms, FA: 8°)

In order to register the brain and non-brain structures of MIDA into the subject, the field of view should be chosen to include the nasal cavity and chin, which are not

always chosen for T1-weighted imaging.

The effectiveness of non-linear registration using T1-weighted images of a subject can be assessed by using segmentation of the grey- and white matter compartments from the T1-weighted MR images of subjects (segmented using the FSL tool FAST, and compared with the results of the MIDA voxel model) to assess warping performance.

As discussed in Chapter 6, use of MIDA's MR data could be considered for future application. However, due to data sharing restrictions, MR images of MIDA are not open to public usage. This study could, however, be done through collaboration with the Food and Drug Administration (FDA, USA). The use of the actual MR images could increase the performance of non-linear registration instead of using synthetic T1 contrast.

The development of MR imaging techniques has introduced numerous advanced neuro-imaging methods for research and clinical studies, such as functional MRI (fMRI), diffusion tensor imaging (DTI), MR angiography and more. Different contrasts are provided by different imaging modalities, such as Computed Tomography (CT), positron emission tomography (PET), or the various imaging techniques in MRI, which could potentially contribute to high-quality segmentation and provide high-quality reference data for personalised models. Direction beyond RF safety for patient comfort

The approach used here to address RF heating concerns in brain tissues can be extended to simulation of peripheral-nerve-stimulation (PNS). The pipeline of deploying a personalised voxel model for SAR estimation could instead be used for assessing a personalised nerve model, which would contribute to patients being scanned without undesirable PNS caused by the gradient coil (178).

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9 Appendix. Code used for Non-linear registration

The following are screenshots of the command lines used for linear- and non-linear registration. These can be run in MATLAB by launching MATLAB via the terminal. Alternatively, the ‘!’ symbol can be removed at each command line so that the commands can be passed directly from the terminal application (Mac).

(run Matlab via terminal: /Application/MATLAB_R2014b.app/bin/matlab)

```

1  # name of reference image
2  # --ref=/usr/local/fsl/data/standard/MNI152_T1_2mm.nii.gz
3  --ref=Fake_T1_2mm
4  # name of file with mask in reference space
5  # --refmask=/usr/local/fsl/data/standard/MNI152
6  --refmask=brain_mask_2mm
7  # If =1, use implicit masking based on value in --ref image. Default =1
8  --imprefm=0
9  # If =1, use implicit masking based on value in --in image, Default =1
10 --impinm=1
11 # Value to mask out in --ref image. Default =0.0
12 --imprefval=0
13 # Value to mask out in --in image. Default =0.0
14 --impinval=0
15 # sub-sampling scheme, default 4,2,1,1
16 --subsamp=4,4,2,2,1,1
17 # Max # of non-linear iterations, default 5,5,5,5
18 --miter=5,5,5,5,10
19 # FWHM (in mm) of gaussian smoothing kernel for input volume, default 6,4,2,2
20 --infwhm=8,6,5,4.5,3,2
21 # FWHM (in mm) of gaussian smoothing kernel for ref volume, default 4,2,0,0
22 --reffwhm=8,6,5,4,2,0
23 # Weight of membrane energy regularisation, default depending on --ssqlambda and --regmod switches. See user documetation.
24 --lambda=300,150,100,50,40,30
25 # Estimate intensity-mapping if set, default 1 (true)
26 --estint=1,1,1,1,1,0
27 # Apply the mask if set, default 1 (true)
28 --applyrefmask=0
29 # Apply the mask if set, default 1 (true)
30 --applyinmask=1
31 # (approximate) resolution (in mm) of warp basis in x-, y- and z-direction, default 10,10,10
32 --warpres=10,10,10
33 # If set (=1), lambda is weighted by current ssq, default 1
34 --ssqlambda=1
35 # Model for regularisation of warp-field [membrane_energy bending_energy], default bending_energy
36 --regmod=bending_energy
37 # Model for intensity-mapping [none global_linear global_non_linear local_linear global_non_linear_with_bias local_non_linear]
38 --intmod=global_non_linear_with_bias
39 # Order of poynomial for mapping intensities, default 5
40 --intorder=5
41 # Resolution (in mm) of bias-field modelling local intensities, default 50,50,50
42 --biasres=50,50,50
43 # Weight of regularisation for bias-field, default 10000
44 --biaslambda=10000
45 # If =1, ref image is used to calculate derivatives. Default =0
46 --refderiv=0

```

Appendix Figure S1.1: Configuration set-up for non-linear registration

```

%Non-linear registration
%set FSL environment
setenv('FSLDIR','/usr/local/fsl'); %this to tell where FSL folder is
setenv('FSLOUTPUTTYPE','NIFTI_GZ');%this to tell what the output
type

!fslroi Fake_brain tmp1 0 -1 0 -1 0 175 % Zero-padding below
!fslroi Fake_brain tmp2 0 -1 0 -1 175 -1 % brainstem
!fslmaths tmp1 -mul 0 tmp1
!fslmerge -z tmp3 tmp1 tmp2
!immv Fake_brain Fake_brain_old
!immv tmp3 Fake_brain
!rm tmp1 tmp2
%% Reference downsampling (0.5 mm -> 2 mm)
%% Header file generation
!fslcreatehd 87.5 120 120 1 2 2 2 1 0 0 0 64 refspace
%% Downsampling to 2mm
!applywarp --in=Fake_T1 --ref=refspace --super --superlevel=4 --
interp=spline --premat=eye.mat --out=Fake_T1_2mm

!applywarp --in=Fake_brain --ref=refspace --super --superlevel=4 --
interp=spline --premat=eye.mat --out=Fake_T1_brain_2mm

%% Linear registration (calculating affine matrix)
!flirt -in Fake_brain -ref Fake_T1_brain_2mm -omat sample2fake.mat -
out test

!fnirt --ref=Fake_T1_2mm --in=Sample --aff=sample2fake.mat --
config=T1_2_Fake_T1_2mm.cnf --cout=sample2fake_warps --
iout=sample_fnirted2fake --fout=sample2fake_field -v

```

Appendix Figure S1.2: Command lines for linear and non-linear registration of voxel-based model

```

1  %% Make 3D affine transform for CAD to Nii
2  cad2nii = diag(ones(4,1));
3
4  niiMK = load_untouch_nii('MIDA_in_space_of_Duke.nii.gz');
5  niiMida = load_untouch_nii('MIDA_label.nii.gz');
6
7  mask = niiMida.img>0;
8  niiMK.img(niiMK.img==50)=0; mask3= niiMK.img>0;
9
10 %% plotting MIDA nifti
11 figure(1);p1 = patch(isosurface(permute(mask,[2 1 3]), 0.0001),'EdgeColor','none');
12 view(3); axis tight;daspect([1,1,1]); camlight left;camlight; lighting gouraud;
13 xlabel('a1');ylabel('a2');zlabel('a3'); % axis of second image dimension
14
15 % Orientation of MIDA (resolution is 0.5)
16 % X, Left +ve : Right to Left
17 % Y, Nose +ve : Posterior to Anterior
18 % Z, Feet -ve : Feet to Head
19
20 %% Find range in each axis
21 ind = find(sum(sum(mask,2),3));
22 range_a1_nii = [min(ind),max(ind)];
23 ind = find(sum(sum(mask,1),3));
24 range_a2_nii = [min(ind),max(ind)];
25 ind = find(sum(sum(mask,1),2));
26 range_a3_nii = [min(ind),max(ind)];
27
28 %% plotting MIDA surface (Resolution is 1mm)
29 fv = stlread('~/MIDA_v1.0/MIDA_v1_surfaces/Epidermis_Dermis.stl');
30 figure(2) patch(fv,'FaceColor',[0.8 0.8 1.0],'EdgeColor','none','FaceLighting','gouraud');
31 material('dull'); axis tight;xlabel('a1');ylabel('a2');zlabel('a3');
32 daspect([1,1,1]); view(3);camlight left;camlight;lighting gouraud;
33 % Orientation of CAD file
34 % X, Left -ve : Left to Right
35 % Y, Feet -ve : Feet to Head
36 % Z, Nose -ve : Anterior to Posterior
37
38 %% plotting MIKE voxel
39 figure(3); p1 = patch(isosurface(permute(mask3,[2 1 3]), 0.0001),'EdgeColor','none');
40 view(3);axis tight;daspect([1,1,1]);camlight left;camlight;lighting gouraud;
41 xlabel('a1');ylabel('a2');zlabel('a3');axis(ax);view(3)'; % axis of second image dimension
42
43 %% Range
44 range_a1_stl = [min(fv.vertices(:,1)), max(fv.vertices(:,1))];
45 range_a2_stl = [min(fv.vertices(:,2)), max(fv.vertices(:,2))];
46 range_a3_stl = [min(fv.vertices(:,3)), max(fv.vertices(:,3))];
47
48 % Make rotation transform
49 % Transform STL to nii system, using above observation of coordinates
50 % X -> -X
51 % Y -> -Z
52 % Z -> Y
53 scale = inv([niiMida.hdr.hist.srow_x(1:3);niiMida.hdr.hist.srow_y(1:3);niiMida.hdr.hist.srow_z(1:3)]);
54 stl2nii_rot = [ 1 0 0; 0 0 -1; 0 1 0]*scale;
55
56 %% Make translation trasform
57 lim = stl2nii_rot*[range_a1_stl; range_a2_stl; range_a3_stl];
58 translation = [range_a1_nii(2),range_a2_nii(2),range_a3_nii(2)]- max(lim.'');
59
60 stl2nii = diag(ones(4,1));
61 stl2nii(1:3,1:3) = stl2nii_rot;
62 stl2nii(1:3,4) = translation;

```

Appendix Figure S1.3: Code lines to register CAD-based model to nifti space

```

64 % Check that the limits agree after transform
65 limSTL = stl2nii*[range_a1_stl; range_a2_stl; range_a3_stl; 1 1]
66 % note order will be reversed, but number should be the same for the limits
67 limNii = [range_a1_nii; range_a2_nii; range_a3_nii]
68
69 %% transform STL to Nii coordinates
70 ndp = size(fv.vertices,1);
71 fvNii.vertices = stl2nii*[fv.vertices, ones(ndp,1)].';
72 fvNii.vertices(4,:) = [];
73 fvNii.vertices = fvNii.vertices.';
74 fvNii.faces = fv.faces;
75
76 % Plot figure to check it looks the same
77 figure(5); patch(fvNii,'FaceColor',[0.8 0.8 1.0],'EdgeColor','none');
78 camlight('headlight'); material('dull'); view([0 0]);daspect([1,1,1]);view(3);
79 axis tight;xlabel('a1');ylabel('a2');zlabel('a3');title('STL in Nii system');
80
81 %% Apply warping field (Original, none-inverse)
82 niiWarp = load_untouch_nii('Warping_field_1mm.nii.gz');
83
84 %% bring back to STL position
85 x = round(fvNii.vertices(:,1));
86 x(x<1) = 1;x(x>size(mask,1)) = size(mask,1);
87 y = round(fvNii.vertices(:,2));
88 y(y<1) = 1;y(y>size(mask,2)) = size(mask,2);
89 z = round(fvNii.vertices(:,3));
90 z(z<1) = 1;z(z>size(mask,3)) = size(mask,3)';
91 ind_vert = sub2ind(size(mask),x,y,z);
92 sz = size(mask);
93 warp_field = reshape(niiWarp.img,[prod(sz(1:3)),3]);
94
95 fvNiiWarp.vertices = fvNii.vertices + warp_field(ind_vert,:)*diag([-2 2 2]);
96 fvNiiWarp.faces = fvNii.faces;
97
98 % Take back to STL coordinate system
99 fvWarp.vertices = inv(stl2nii)*[fvNiiWarp.vertices, ones(ndp,1)].';
100 fvWarp.vertices(4,:) = [];
101 fvWarp.vertices = fvWarp.vertices.';
102 fvWarp.faces = fvNiiWarp.faces;
103
104 % Display it for check
105 figure(6); p2=patch(fvWarp,'FaceColor',[0.8 0.8 1.0],'EdgeColor','none');
106 view([180 0]);l2=camlight('headlight'); material('dull');
107 xlabel('a1');ylabel('a2');zlabel('a3');title('STL warped');daspect([1,1,1]);axis tight;
108
109 %% Save to binary .stl
110 stlwrite('epidermis_new.stl',fvWarp)

```

Appendix Figure S1.4: Code lines to apply warping field to surface-based model

10 Appendix. MRI RF safety in tattooed skin

Despite many reports of skin burns in the region of tattoos, there are few safety studies concerning RF heating caused by tattoos. Manufacturers of tattoo ink are numerous and use various dye ingredients, making it difficult to assess the electromagnetic properties of each ink pigment. As a pilot study, an anchor-shaped tattoo was modelled 1 mm under the skin layer in the region of the cervical spine to predict a possible skin burn generated by an RF coil. A simulation model of RF

heating in tattoo pigment is proposed, which shows that certain tattoo pigments may lead to severe skin burns when performing high field MRI.

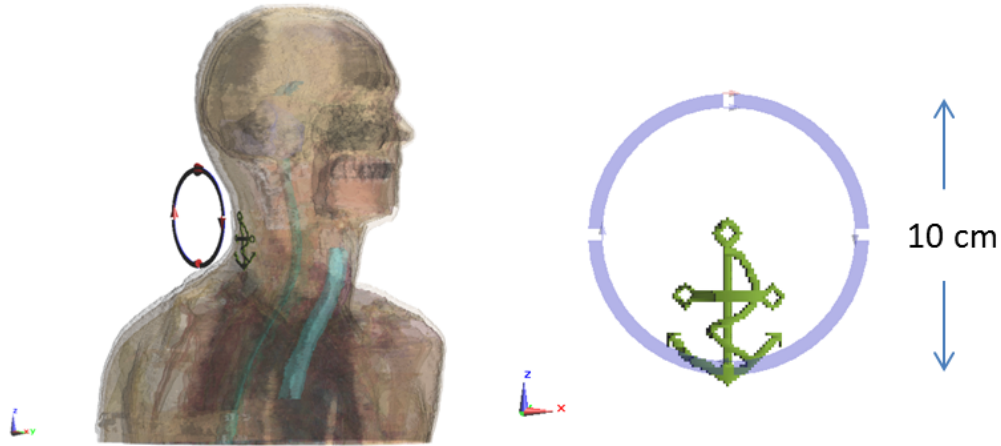
Electromagnetic simulation of specific absorption rate (SAR) and temperature elevation in subjects scanned with MRI have been studied for many years, with the previous introduction of a ‘cumulative equivalent minutes at 43°C’ (CEM₄₃) tissue damage threshold to ensure MR safety (71). Despite many reports of skin burns in the region of tattoos, there are few safety studies concerning RF heating caused by tattoos (179–181). Nevertheless, the possible cause of a skin burn during an MR scan has been reported to be related to iron oxide, which is potentially magnetic and an electrical conductor (180). Iron oxide exists in different chemical states: Fe₃O₄ is a known ingredient of black ink pigment, along with Fe₂O₃ and FeO for red and yellow, respectively, as seen in Appendix Table S2.1 (182).

	Skin	D.I. water	Fe ₂ O ₃	Fe ₃ O ₄	4.3 % Fe ₃ O ₄ * in black ink ⁶
Relative permittivity	49.93	78.26	3.22 ^[183]	2.4 ^[184]	74.41*
Conductivity [S/m]	0.64	5.5x10 ⁻⁶	0.025 ^[189]	25,000 ^[185]	1275.2*
	Skin	Tattoo ink pigment ^[183]			
Density [kg/m ³]	1109	1200			
Heat capacity [J/Kg/K]	3390.5	1888			
Thermal conductivity [W/m/K]	0.372	66			

Appendix Table S2.1: Thermal and dielectric properties of tattoo ink pigment ingredients (297.2 MHz, 310 K) (* Values are assumed using the averaged properties of 4.3 % Fe₃O₄ and 80 % water)

SEMCAD X (Speag, Switzerland) was used to calculate SAR, CEM₄₃ values, and to solve the Arrhenius model for thermal change. A single loop surface coil was modelled with four equally spaced capacitors and with a diameter of 100 mm and a

width of 10 mm. The coil was positioned 5 cm away from the Duke human model(97) with a resolution of $(1\text{ mm})^3$ and tuned for 7 T ($S_{11} < -25\text{ dB}$) (Appendix Figure S2.1).



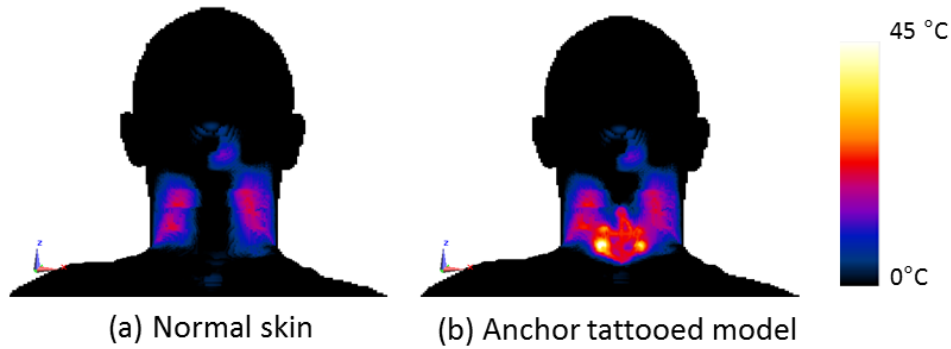
Appendix Figure S2.1: Location of coil and anchor shaped tattoo ink pigment

An anchor-shaped tattoo was modelled 1 mm under the skin layer in the region of the cervical spine using iSEG (ZMT, Switzerland) with longitudinal and lateral lengths of 60 mm and 40 mm, respectively. The model in the region of the tattoo shape was adjusted until a single layer of tattoo pigment was located 1 mm under the outmost skin layer in the 3D slices. The maximum local SAR for normal skin was calculated for a standard permitted thermal simulation input power ($10\text{gSAR}_{\text{max}}=9.8\text{ W/kg}$ at 43 W input power).

The dielectric properties of black tattoo ink pigment have not been reported, so the concentration of Fe in black tattoo pigment (186) was used to estimate its dielectric properties (σ : 1275.2 S/m, ϵ_r : 74.41 in). The thermal properties of tattoo ink pigment were assigned from previous studies (187). To estimate any skin burn effect, the Arrhenius model was used and its parameters for skin were assigned from literature values (A : $2.2 \times 10^{124}\text{ 1/s}$, $\Delta E=187.1\text{ kcal/mol}$) (188).

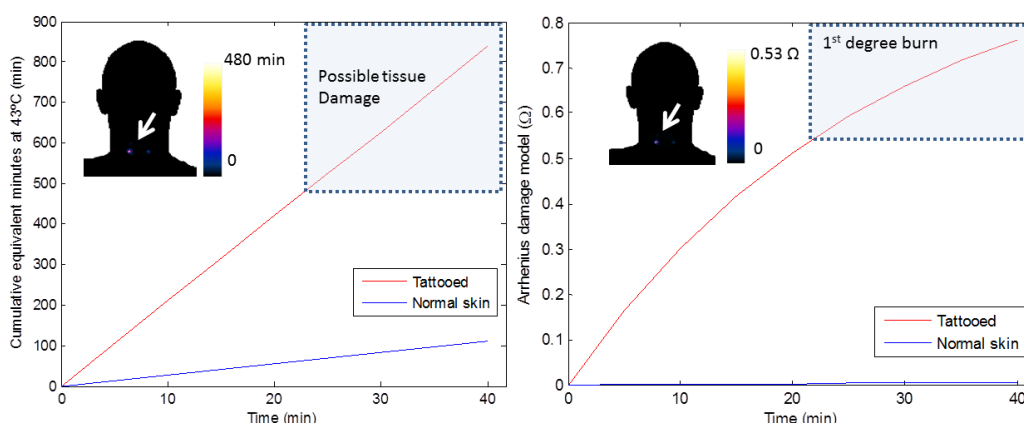
RF safety in tattooed areas have been reported in prospective studies (189,190),

but RF safety in the tattoo itself has not been actively studied. RF heating was calculated during 20 min of simulated surface coil transmission with 43 W input power. Regional temperature elevation was predicted in the bottom of the tattoo region, especially at its edges in Appendix Figure 2.2.



Appendix Figure S2.2: Surface temperature elevation in 10 minutes of heating ($T_0=37^\circ\text{C}$)

A CEM_{43} simulation was performed and showed that the left side edge of the tattoo was heated the most (200 CEM_{43} for 10 min, 409.5 CEM_{43} for 20 min, respectively, as seen in Figure 7.4. It is expected that heating of between 480 and 960 CEM_{43} would cause an immediate superficial burn (191). The Arrhenius tissue damage model was calculated to estimate the potential severity of the skin burn, and showed an increase to 0.3 Ω and 0.51 Ω for 10 min heating and 20 min heating, respectively, in the case of a sharpened anchor shape in .



Appendix Figure S2.3: Results of Maximum CEM43 and Arrhenius tissue damage model in 40 minutes of heating

The RF heating safety of tattoo ink pigment was investigated. A possible source of skin burn could be caused by a specific form of iron oxide, Fe_3O_4 , which is known to have 10^6 times higher electrical conductivity than Fe_2O_3 due to electron exchange between the Fe^{II} and Fe^{III} centres (192,193). Fe_3O_4 is also known as CI pigment black 11, which is insoluble in water and may have impurities, so caution should be used in estimating the dielectric properties of tattoo ink pigment without direct measurement. RF modelling predicted a possible skin burn in an area close to the RF coil copper strip, observed as locally generated heating at the edge of the tattoo shape. For the Arrhenius model, 0.53Ω is known to equate to a 1st degree burn, and 1 ohm is reported to equate to a 2nd degree burn (194), so more heating could lead to the subject suffering a severe skin burn. Future studies are needed to evaluate different tattoo pigment shapes and more realistic dielectric properties of the ingredients. In summary, a simulation model of RF heating in tattoo pigment is proposed, which shows that certain tattoo pigments may lead to severe skin burns when performing high field MRI.