

**MR imaging of temperature rise
in ultrasound fields of
diagnostic relevance**

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Abstract

The generation of heat within tissue due to exposure to ultrasound fields at diagnostic levels is a recognised safety concern. Due to the rapid development of ultrasound equipment and the large number of routine scans performed clinically, there is a need for rapid and accurate evaluation of the temperature rise caused by these spatially complex, time varying fields. While the use of directly applied thermal probes allows accurate point measurements to be made, the visualisation of complex three dimensional temperature distributions is exceedingly time consuming and the presence of the thermal probe can potentially affect the amount of heating. Magnetic Resonance Imaging (MRI) has the potential to provide a non-invasive temperature measurement system both in phantoms and *in vivo*.

To date, MRI has been used for the monitoring of thermal effects, both *in vivo* and *in vitro*, mainly in the areas related to thermal ablative therapies. As a result, much of the work has concentrated on large tissue temperature increases and rapid imaging with relatively coarse resolution. In contrast, the metrological requirements for fields of diagnostic relevance are rather different: a temperature rise of only 4°C is considered potentially hazardous if maintained for five minutes or more and the focal region may be 2 mm or less in diameter; consequently, it is necessary to measure the small temperature increases with high spatial resolution.

This report describes the development of an MRI protocol for determining the temperature distribution generated by an ultrasound transducer in a tissue-mimicking phantom with a resolution of approximately 0.5 mm and 0.2°C in less than 20 seconds. The results are compared with measurements using thin-film thermocouples.

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MR imaging of temperature rise in ultrasound fields of diagnostic relevance

1 Introduction

The work described in this report was funded by the Strategic Research programme of the UK National Physical Laboratory. It was carried out in collaboration between NPL and the School of Physics at the University of Exeter (Head of Department, Prof. John Inkson) who provided the magnetic resonance facilities and expertise.

1.1 Heating by diagnostic ultrasound

With the increasing acoustic power levels available from certain types of medical diagnostic ultrasonic equipment, there has been growing interest in estimating the degree of heating caused by the use of this type of equipment in clinical practice. Measurement of temperature elevations in three dimensions caused by ultrasonic fields will be an essential safety requirement in future years as the complexity of medical ultrasound systems increases. Development of cost-effective methods would not only have importance for metrology and safety but also would have major impact on the clinical use of ultrasound. It should also be noted that, whilst this project concentrates on the relevance to medical ultrasound, technology developed to meet this need may well be relevant to other applications such as process monitoring in the food industry.

Temperature increases are produced *in vivo* by the passage of ultrasound through tissue and it is known from *in vitro* and theoretical work that the temperature increases caused by clinical ultrasound equipment are potentially hazardous. NPL has carried out a major project funded by the Department of Health (DoH) aimed at assessing the local *in vivo* temperature rise produced by diagnostic ultrasound. This new project builds on recent work undertaken by NPL and also funded by DoH (Shaw *et al.*, 1998) which utilised the ultrasound dose standards work funded by the National Measurement System Directorate of the Department of Trade and Industry (DTI/NMSD) to show that pulsed Doppler ultrasound machines routinely used in our hospitals can produce temperature increases of up to 8°C under worst-case conditions. This compares with a recommendation of the World Federation of Ultrasound in Medicine and Biology that 4°C maintained for five minutes is potentially hazardous (WFUMB 1998).

The non-invasive mapping of 3-D temperature distributions *in situ* with good spatial and thermal resolution and on an appropriate time-scale is one of the major challenges in many areas of medicine and in numerous industrial processes (Edwards, 1997). A number of techniques have been developed which are indirect, invasive or are limited to particular applications such as hyperthermia. To date, none are able to provide millimetre spatial resolution and fractional °C sensitivity on a timescale of tens of seconds.

Measurement of temperature rise due to ultrasonic heating has been carried out by, amongst others, Fry & Fry (1954a and 1954b), Dunn *et al.* (1969), Parker (1983), Drewniak *et al.* (1989), Carstensen *et al.* (1990), Wu *et al.* (1992), Bosward *et al.* (1993), Bacon & Shaw (1993) and O'Neill *et al.* (1994). In both the recent NPL/DoH projects, these temperature increases were determined *in vitro* using a tissue-mimicking thermal test object with a single

point thermal sensor embedded within it. Whilst this technique worked well, the particular ultrasound beams tested were stationary, i.e. not scanning, and the thermal sensor was kept in the axial region of the beam, thereby ensuring the point of maximum heating could be located. A major limitation occurs when attempting to apply this test methodology to scanned ultrasound beams, such as are generated by ‘colour flow’ imaging systems, and over the enormous range of operator-controlled settings which affect the acoustic output and therefore the spatial distribution of deposition of energy (asymmetrical beams, multiple focal points, combined modes, variable sector angle, etc.). A multielement thermal sensor in the form of a linear array or, better still, a two-dimensional array would partly solve some of these problems. However, identifying the location of the maximum temperature rise in three dimensions would still be time consuming, especially for three-dimensional scanning systems which are now beginning to be commercially available. In addition, due to their invasive nature, these sensors would not be appropriate for use in determining the temperature rise *in vivo* for diagnostic examinations, although they may be appropriate for some therapeutic applications.

1.2 MR imaging of temperature rise

Ultimately, what is required is the non-invasive determination of temperature distributions in a patient *in-vivo*. The first major step towards this objective would be the development of methods of measuring the temperature rise in three dimensions caused by the deposition of ultrasonic energy in a test object.

The physical principles of Magnetic Resonance Imaging are well known and described in numerous text books such as Kuperman (2000) and in articles such as Ballinger (1998) and Horner (2003). There is also a useful animated presentation at [simplyphysics.com](http://simplyphysics.com/MRIntro.html) (<http://simplyphysics.com/MRIntro.html>). A brief overview is given in Section 2.

MRI can be used to determine temperature rises. Much of the focus on temperature dependent MRI has been driven by a need to monitor thermal methods of cell destruction, such as high power ultrasound and interstitial laser photothermal (ILP) therapies. For these techniques there is usually a high temperature thermal source located deep within a tissue and tissue conduction is responsible for the generation of a roughly spherical region of tissue necrosis. In ILP, the optical fibre tip needed to deliver the laser beam reaches temperatures typically in excess of 200°C. The key to the success of the treatment is to ensure that all malignant cells have reached a temperature sufficient to cause cell death, typically > 60°C. The visualisation of such treatments has been performed using ultrasound (US) imaging which has the advantage of speed and convenience, however the principal cause of image contrast in ultrasound imaging is the generation of micro-bubbles in the tissue which then diffuse through the tissue via the capillary supply. With training, this approach has been sufficient to allow the progress of the treatment to be assessed. With regard to MRI, it has been shown in the literature (Clemence 1994, Graham 1998) that the signal response shows a non-reversible characteristic above a certain temperature where tissue damage dominates the process. Much of the research has therefore been aimed at optimising the visual appearance of the temperature field in this high temperature regime to aid the surgeon in making the judgement of when to stop the therapy.

The literature contains numerous papers by Hynynen, Moros, Huber and others exploring MRI as a method for providing temperature information to be used during ultrasonic hyperthermia and ablation treatments (e.g. Hynynen *et al.*, 1993; Chung *et al.*, 1999). The dimensions of the ultrasound fields used for hyperthermia are substantially larger than the dimensions of diagnostic fields (focal beamwidths are typically centimetres rather than millimetres) and the temperature increases are naturally higher than would be considered safe

for diagnostic exposure. The metrological requirements are therefore different and although the best techniques currently used have thermal, spatial and temporal resolutions of the order of 0.1°C, 1 mm and 10 seconds individually, these performance levels have not been achieved simultaneously.

There are two principal effects used to monitor temperature effects, T1 changes and chemical shift, both well documented. Chemical shift determination requires the subtraction of a baseline image (taken immediately before the initiation of heating) and extensive post processing. This, in conjunction with the fact that the T1 effect leads to an exponential response with temperature (and so leads to a greater change in signal on an MR image at higher temperatures) has meant that most of the clinically based literature has concentrated on T1 weighted imaging.

Chemical shift techniques however have not been neglected (eg. Olsrud 1998, Kuroda 1998, Chung 1999) with much of the work coming from the laboratory of F. Jolesz. The paper by Chung (1999) “shows that MRI ... has significant potential for monitoring thermal exposure and evaluating tissue damage”. This group has typically concentrated on *in-vivo* measurements by a rapid spoiled gradient (SPGR) technique which provides rapid, but low SNR, images (typically an image in 4 s). However, again this work visualises high temperature changes and so their quoted uncertainty of 4°C is acceptable for this application. More recent papers (Hynynen 2000) have concentrated in tissues where the chemical shift effect is much reduced due to the lack of hydrogen binding interaction, such as fat and have returned to the T1 imaging methods.

Some of the most accurate quoted literature values for chemical shift evaluation of temperature come from the paper by Olsrud (1998). In this paper standard deviations of between 0.14°C and 0.26°C were given. However, this is over a region of interest (the exact size of which is omitted) which has been interactively chosen to minimise the standard deviations of the signal from the voxels within the volume. In addition this work was performed at a field strength of 1.5T which, as chemical shift is proportional to field strength, would improve accuracy.

1.3 Objectives

The overall aim of the work described in this report was to undertake a feasibility study into using MRI as a method for determining the heating caused by exposing a reference medium to ultrasound at clinically relevant levels. Specific objectives were to:

- establish temperature profile techniques using fixed ultrasound beams and compare with the NPL reference *in vitro* methods;
- optimise the process, aiming for the optimal combination of thermal, spatial and temporal resolution (ideally, better than 0.5 mm, 0.2 °C and 30 s for a volume slice of 10 x 1 x 2 cm);
- investigate the application of MRI to the measurement of temperature rises in scanned ultrasound beams;
- review the wider applicability of the technique as a reference method for further *in vivo* and industrial research.

2 Physical principles of magnetic resonance

2.1 Nuclear magnetic resonance

Magnetic Resonance Imaging (MRI), which is now widely used for imaging the inside of the human body, is a product of nuclear magnetic resonance spectroscopy (NMR) which was first developed in the 1940s by research groups at Stanford and M.I.T. in the USA. Over the next 50 years NMR developed into the most important spectroscopy technique available to organic chemists for determining the detailed structure of the chemicals they were synthesizing.

The NMR phenomenon is based on the fact that nuclei of atoms have magnetic properties that can be interrogated to yield chemical information. If the number of neutrons and the number of protons are both even, the nucleus has no spin. If either the number of neutrons or the number of protons is odd, then the nucleus has a half-integer spin (*i.e.* 1/2, 3/2, 5/2). If the number of neutrons and the number of protons are both odd, then the nucleus has an integer spin (*i.e.* 1, 2, 3).

For a hydrogen nucleus (single proton, spin 1/2), the magnetic moment can align with an externally applied magnetic field of strength B_0 in only two ways: either with or against the applied field B_0 . The energetically preferred orientation has the magnetic moment aligned parallel with the applied field (spin $m = +1/2$) whereas the higher energy orientation is anti-parallel (spin $m = -1/2$). If the rotational axis of the spinning nucleus is not orientated exactly parallel (or anti-parallel) with the direction of the applied field B_0 , it will precess about this field with an angular velocity, ω_0 , given by the expression:

$$\omega_0 = \gamma B_0$$

Where ω_0 is the precession rate called the Larmor frequency. The constant γ is called the gyromagnetic ratio which is defined as a constant of proportionality between the nuclear angular momentum and magnetic moment. For a proton, $\gamma = 2.674 \times 10^8 \text{ T}^{-1} \text{ s}^{-1}$. This precession process generates an electric field with frequency ω_0 . If we irradiate the sample with radio waves (MHz) the proton can absorb the energy and be promoted to the less favorable higher energy state. This absorption is called resonance (and hence the term NMR) because the frequency of the applied radiation and the precession coincide or resonate. In the equilibrium state at room temperature, the fraction of nuclei in the lower energy state slightly exceeds the fraction in the higher energy state. Consequently, on a macroscopic scale in any small volume element of material (voxel), there is a nett magnetization which lies in the direction of the applied field B_0 .

Since energy separation exists, there is a possibility to induce a transition between the various spin states. The absorption of energy during this transition forms the basis of the NMR method. Other spectroscopic methods, such as Electron Spin Resonance, IR and UV/Visible, also rely on the absorption of energy during a transition although the nature and energies of the transitions vary widely, as can be seen from the following table which gives the typical frequency ranges for the different types of transition (although NMR and ESR have also been tried at much lower frequencies, *eg* Earth Field NMR).

NMR	$6 \times 10^7 - 6 \times 10^8$ Hz	Probes nucleus' magnetic field
ESR	$1 \times 10^9 - 3 \times 10^{10}$ Hz	Probes electron's magnetic field
Microwave	$1 \times 10^9 - 6 \times 10^{11}$ Hz	Probes molecular rotation
Infrared	$6 \times 10^{11} - 4 \times 10^{14}$ Hz	Probes bond vibrations and bending
Ultraviolet/Visible	$7.5 \times 10^{14} - 3 \times 10^{16}$ Hz	Probes outer core electron transitions

Disturbing the relative numbers of nuclei in the two states in this way, changes the nett magnetization of the voxel. Nuclei in the excited state gradually return to the ground state and, as they do so, the nett magnetization returns to its equilibrium value. The timescale for this relaxation is crucial to the NMR experiment. For example, relaxation of electrons to the ground state in uv-visible spectroscopy is a very fast process, on the order of picoseconds. In NMR, because the transition energy between spin levels is so small, attaining equilibrium occurs on a much longer timescale. The timescale for relaxation will dictate how the NMR experiment is executed and consequently, how successful the experiment is. The

magnetization process is mediated through an equilibrium with a Boltzman distribution of thermal photons. It is this sample temperature which dominates both the relaxation time and the eventual equilibrium magnetization.

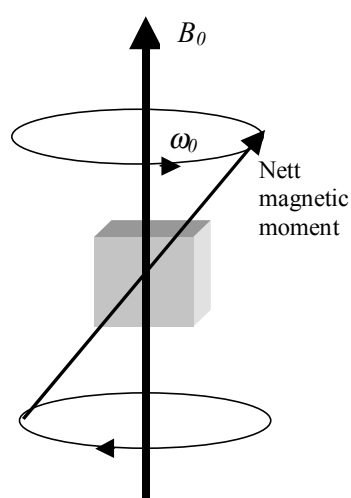


Figure 1. The nett magnetic moment of the voxel precesses about the applied field B_0 (along the z-axis) at an angular velocity ω_0 .

There are two processes that achieve this relaxation in NMR experiments: longitudinal (or spin-lattice) relaxation and transverse (or spin-spin) relaxation. When an external electric field of the correct Larmor frequency is applied, individual nuclei make the transition between energy levels with the result that the nett magnetization of the volume element is rotated away from the B_0 direction by an angle which depends on the duration of the applied electric field. (Often the vector is rotated by 90° to the x/y-plane; in this case the RF pulse is called a 90° pulse.) The magnetization vector will now have a component in the x/y-plane as well as a component along the z-axis. In a perfectly uniform applied magnetic field and in the absence of interactions between atoms, the nett magnetization vector will precess at the Larmor frequency around the z-axis (Figure 1), losing energy and

returning to its equilibrium state parallel to B_0 . This is spin-lattice relaxation and the half-life for this process is called the spin-lattice relaxation time (T_1). This is an exponential process and T_1 can be determined by measuring the $1/e$ recovery time for the z-component of the magnetization of the volume element (see Figure 2).

In this scheme, the x/y component of the magnetization will return to zero at the same time as the z-component returns to its equilibrium value. However, in reality, it decays more rapidly than this because of two effects. Firstly, the total magnetic field experienced by each atom is the sum of the applied magnetic field and the (very much smaller) fields generated by its neighbours. Each atom therefore experiences a slightly different and time-varying magnetic environment. Consequently, the precessional frequency of each atom is slightly different and time varying. This means that the x/y-components of the magnetic moments of all the atoms, although initially compelled to be in phase by the perturbing electric field, gradually move out of phase and the x/y-component of the nett magnetization of the volume element decays to zero (see Figure 2). This is spin-spin relaxation and the half-life for this process is called the spin-spin relaxation time (T_2). In addition, the applied magnetic field is not perfectly uniform and this also leads to dephasing of the x/y-component of the nett magnetization. The overall

decay time (termed T_2^*) of the x/y-component therefore includes both effects. The second is usually the larger effect but, because it is systematic, it is possible to account for it by appropriate acquisition sequences.

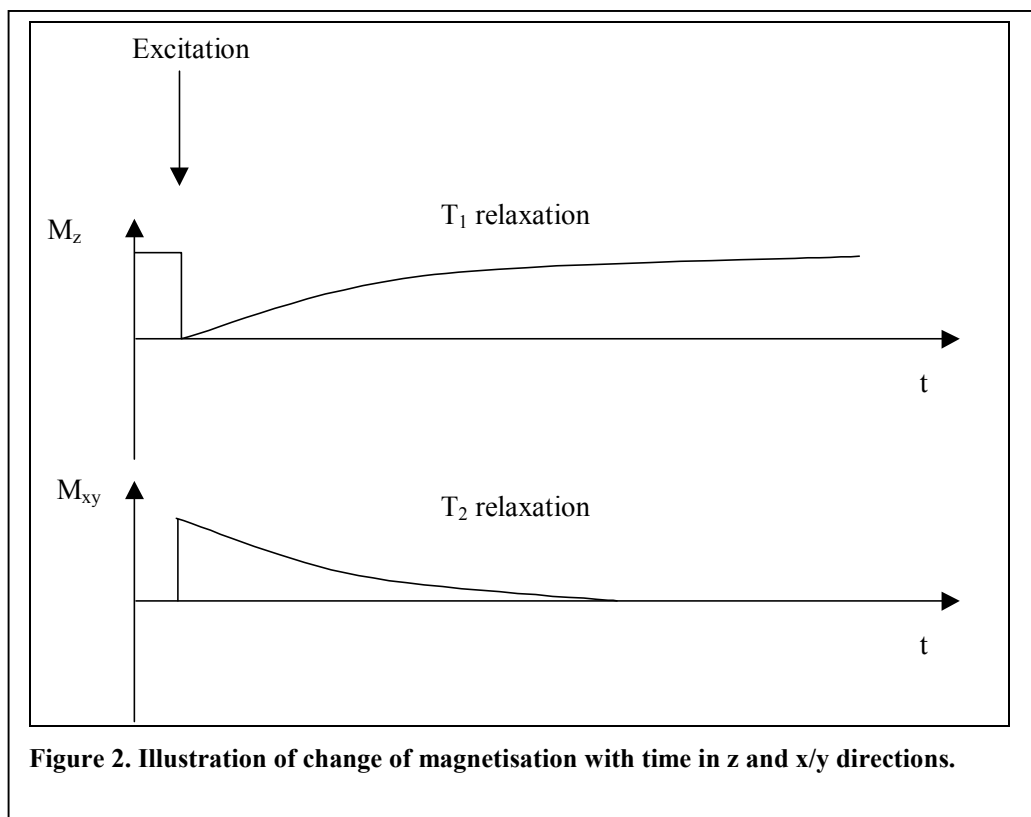


Figure 2. Illustration of change of magnetisation with time in z and x/y directions.

Both T_1 and T_2 can be shortened by the use of a paramagnetic contrast agent such as gadolinium-diethylenetriamine pentaacetic acid (Gd-DTPA) or other agents like ferric chloride and ferric ammonium citrate which have a similar effect.

A further modification of the Larmor frequency for an atom occurs because electrons are negatively charged particles that surround the nucleus. Since moving charged particles generate a magnetic field, electrons around nuclei in a molecule generate their own magnetic field; in fact, the electron's magnetic field runs anti-parallel to the external magnetic field. When this happens, the electron-generated magnetic moment will run in opposition to the magnetic moment of the external magnetic field. This has the effect of reducing the net magnetic moment affecting the proton. This electronic magnetic field effect will cause protons with different chemical environments to yield resonance frequencies perturbed from the frequency defined by the applied external field B_0 .

The Larmor frequency can therefore be re-written to include the electronic effect:

$$\omega_o = \gamma(B_o - S)$$

where S represents the change in magnetic field caused by the opposing electron magnetic moment. This is the 'chemical shift' effect which allows molecules of different types to be identified from their characteristic spectra and is the basis of NMR spectroscopy.

2.2 MR Imaging principles

An MR imaging system (Figure 3) consists of the following components:

- 1) a large (often cylindrical) magnet to generate the main magnetic field,
- 2) gradient coils to provide controlled gradient in the magnetic field and so allow spatial localization of the signal to a single voxel,
- 3) a radiofrequency (RF) coil to transmit a radio signal into the body part being imaged to flip the magnetic moment,
- 4) a receiver coil to detect the returning RF signal (often the same coil used for transmission),
- 5) a computer to reconstruct the RF signal into the final image.

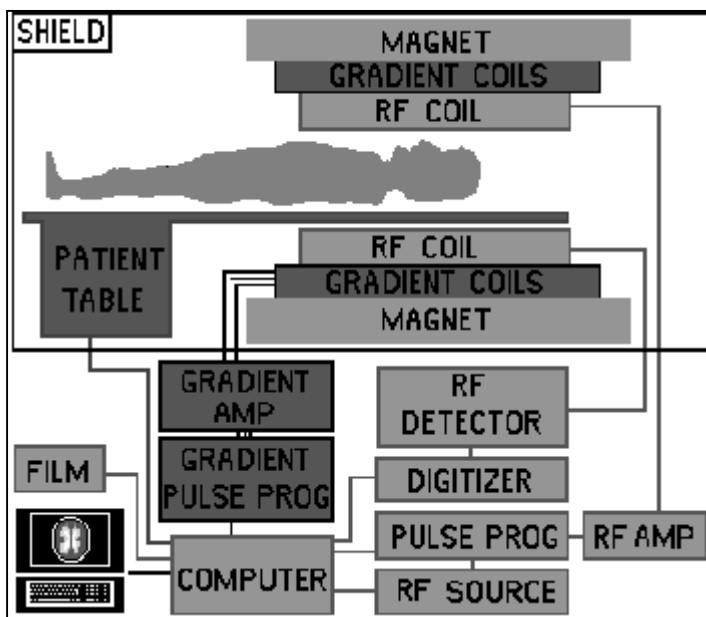


Figure 3. Schematic of MRI system (from Horner, 2003).

To use NMR principle to create an image (MRI), it is necessary to be able to identify which volume element of the body or object is radiating the electromagnetic wave caused by the relaxation processes. This is done by introducing gradients in the main magnetic field by the use of gradient coils on the x, y and z axes. Since the Larmor precession frequency depends on the external magnetic field, it is now possible to select which voxels experience the appropriate external magnetic field to be excited to the higher energy state by an RF pulse of frequency ω . The received signal during relaxation then comes from the same known voxel.

The imaging process as described would be very slow as excitation and reception have to be performed on a point-by-point basis. Considerable time savings can be made by exciting a range of frequencies (slice selection) and receiving the signals from many voxels simultaneously. The signals from individual voxels can be separated by Fourier analysis.

The current through the gradient coils are not constant but pulsed rapidly in a controlled manner to allow different voxels to be selected. The 'pulse sequence' sets the specific number, strength, and timing of the gradient and RF pulses. The two most important parameters are the repetition time (T_R) and the echo time (T_E). T_R is the time between

consecutive 90° RF pulses. T_E is the time between the initial 90° RF pulse and the echo. The signal intensity on the MR image is determined by four basic parameters:

- 1) proton density,
- 2) T_1 relaxation time,
- 3) T_2 relaxation time,
- 4) flow or diffusion.

Proton density is the concentration of protons in the tissue in the form of water and macromolecules (proteins, fat, etc.). The T_1 and T_2 relaxation times define the way that the protons revert back to their resting states after the initial RF pulse. Diffusion causes the signal to decay as excited atoms leave the interrogated voxel in a random manner; organised flow generally also reduces the signal amplitude but it is possible, in certain imaging regimes, for flow to enhance the MR signal.

2.3 Temperature dependent MRI

MRI is a two-channel technique, collecting complex data points. Thus each voxel has both a real and imaginary component, or conversely a magnitude and a phase. The temperature effects upon the magnetic vector can either effect the magnitude or the phase or both and, in principle greater sensitivity could be achieved by combining two independent mechanisms one in the magnitude and one in the phase.

The magnetic vector in a voxel rotates at a frequency ω , which is proportional to the applied magnetic field B_0 . The components of the complex magnetic vector are sampled with reference to a precision frequency reference within the imaging system. Any variations of the precessional frequency will therefore show up as a gradual phase accumulation with respect to the internal reference. As there is a finite time between excitation of the magnetic vector and its sampling (the echo time or T_E) then the accumulated phase is simply related to the resonant frequency by $\phi = (\omega_o - \omega_{ref}) \cdot T_E$. The largest effect upon the resonant frequency is due to spatial imperfections in the main magnetic field due to either magnet inhomogeneity or susceptibility variations of the sample and its containers. However an additional effect is due to the chemical shift effect of the surrounding electron shells. It has been demonstrated that there is a linear dependence of the chemical shift of water upon temperature (Ishihara 1995) and thus a phase map may be used to measure temperature changes. This method has the advantage that the sensitivity of the phase map to temperature may be altered by changing the echo time T_E (within the limits set by T_1 and T_2). However, there are number of disadvantages.

1. The phase stability of the MR equipment must be very much smaller than the phase shift one is attempting to measure over the timescale of the heating cycle.
2. It is a relative technique, not absolute and so relies on a phase reference image to be collected before heating takes place which is then subtracted from each subsequent image. This has the advantage of eliminating the effects due to susceptibility and magnet inhomogeneity but adversely affects the accuracy of each measurement, especially when the temperature difference (and hence phase shift) is small.
3. The phase map suffers from discontinuities when the phase angle wraps over from $+\pi$ to $-\pi$ and so a simple subtraction will fail to give the correct answer at these boundaries. This unwrapping procedure is not trivial.

There are two areas where noise can adversely affect the calculation of temperature from phase maps. The first is in the calculation of the initial phase map and the second when two phase maps are subtracted to get the final phase shift due to temperature.

Phase is usually calculated from the imaginary and real components using $\phi = \tan^{-1}\left(\frac{\text{Im}}{\text{Re}}\right)$. If

however, both of these values have noise superimposed upon them then ϕ will be very inaccurate if the signal is principally contained in the imaginary channel (i.e. the real channel is zero and therefore just noise). Thus for maximum accuracy, the image should principally be in the real channel. Any noise in the image, will of course lead to an error in the measured phase. It may be shown that, making reasonable assumptions about the noise distributions that

the standard deviation in the phase image is equal to $\frac{\sigma_o}{M}$ where σ_o is the standard deviation

of either the real or imaginary channel and M is the magnitude of the signal vector (following the method of Conturo 1990). This formula states that the standard deviation is inversely proportional to the signal to noise ratio (SNR) of the pixel. However, one of the assumptions is that the noise in the real and imaginary channels is uncorrelated. A typical MR system synthesises the quadrature information from a single sampled signal, rather than from two independent channels. In this case, the standard deviation will be larger than that predicted by theory.

The required phase shift, $\Delta\phi$, is the difference between two phase maps and hence as $\Delta T \propto \Delta\phi$ the required accuracy on ΔT specifies the required SNR of the image.

3 MR experimental arrangement

The experimental aim was to image a cylindrical sample of gel (described in Section 3.2) which has acoustic and thermal properties typical of soft tissue. The gel would be heated during the imaging by exposure to a continuous wave, focused ultrasound field (described in Section 3.3) with an acoustic frequency of 3.5MHz.

3.1 MR measurements

The gel sample was mounted in a sealed Perspex tube and held firmly in position by a rigid foam annulus at one side and a polythene pipe at the other. This is illustrated schematically in

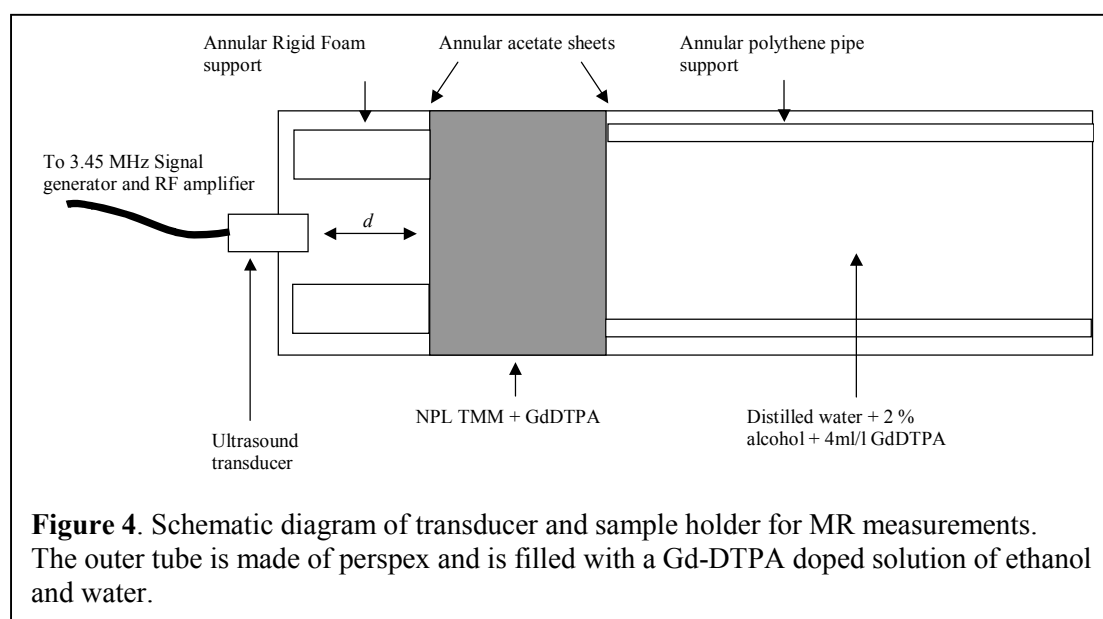


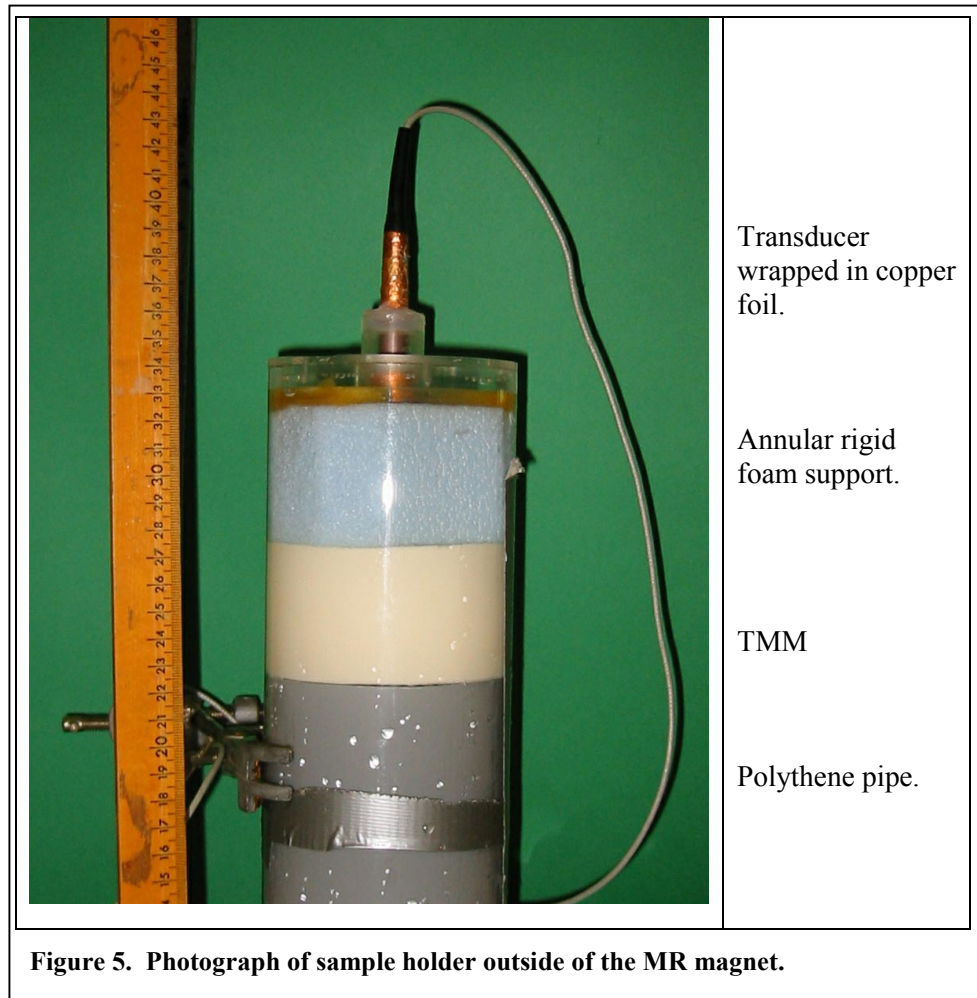
Figure 4 and there is a photograph of the arrangement in Figure 5. Two annular acetate sheets were used to spread the load on the gel. The transducer was mounted in one end of the tube and sealed in place with silicone rubber; the axis of the ultrasound beam was approximately co-axial with the perspex cylinder. The distance from the transducer face to the gel surface was approximately 45 mm. The assembly was mounted horizontally along the axis of the bore of the main magnet in the MR system.

The rapid imaging sequences used require rapid changes in the applied electric fields. This is very demanding on the R.F. power amplifiers used to generate the electric fields and may therefore cause substantial heating of both the internal gradient coils, which surround the sample, and the amplifiers, causing the general laboratory temperature to rise. However, the temperature at the sample surface was monitored using a conventional thermocouple and was shown to vary by no more than 0.5 °C during the course of the experiment at an example ambient temperature of 22.6 °C.

Care must also be taken not to introduce additional RF noise at or around the MR system operating frequency when using external apparatus such as the ultrasound transducer. Most research MR installations will have the magnets installed within Faraday screens to limit stray interference. The ultrasound transducer has a resonant frequency of approx. 3.5 MHz (compared to the proton resonance at 22 MHz) however substantial noise was introduced through the cabling. Consequently, a 22 MHz notch filter was constructed and placed at the

junction of the cable to the ultrasound transducer and Faraday cage. No appreciable attenuation of the ultrasound driving voltage was observed with the filter in place and the noise of the MR system returned to that measured without the ultrasound transducer in place.

A second, more serious consequence of placing the ultrasound transducer within the magnet bore is due to the fact that the transducer has a residual magnetism, due to the materials used in its construction. The interaction of this residual magnetism with the main applied magnetic field leads to inhomogeneities in the total field and produces a range of unwanted features in the MR image. When the inhomogeneities in the magnetic field induce phase shifts of more than π across a voxel, substantial signal loss occurs due to partial cancellation of the signal



across the voxel. When the induced phase shift is less than π , the phase measurement is distorted but, since the distortion is systematic, this can be accounted for in the reference baseline measurements. If the field distortion is high enough, signals from voxels are displaced in the image causing crescent-shaped areas of signal enhancement. This effect is most commonly referred to as ‘susceptibility artefacts’. If MRI is to be used generally on a range of transducers, the effects of this residual magnetic field must be mitigated as it is unreasonable to assume that manufacturers will make MR compatible equipment. (It should also be noted at this point that there was no observable attractive force on the ultrasound transducer; it would normally be considered “non-magnetic”).

3.2 TMM properties

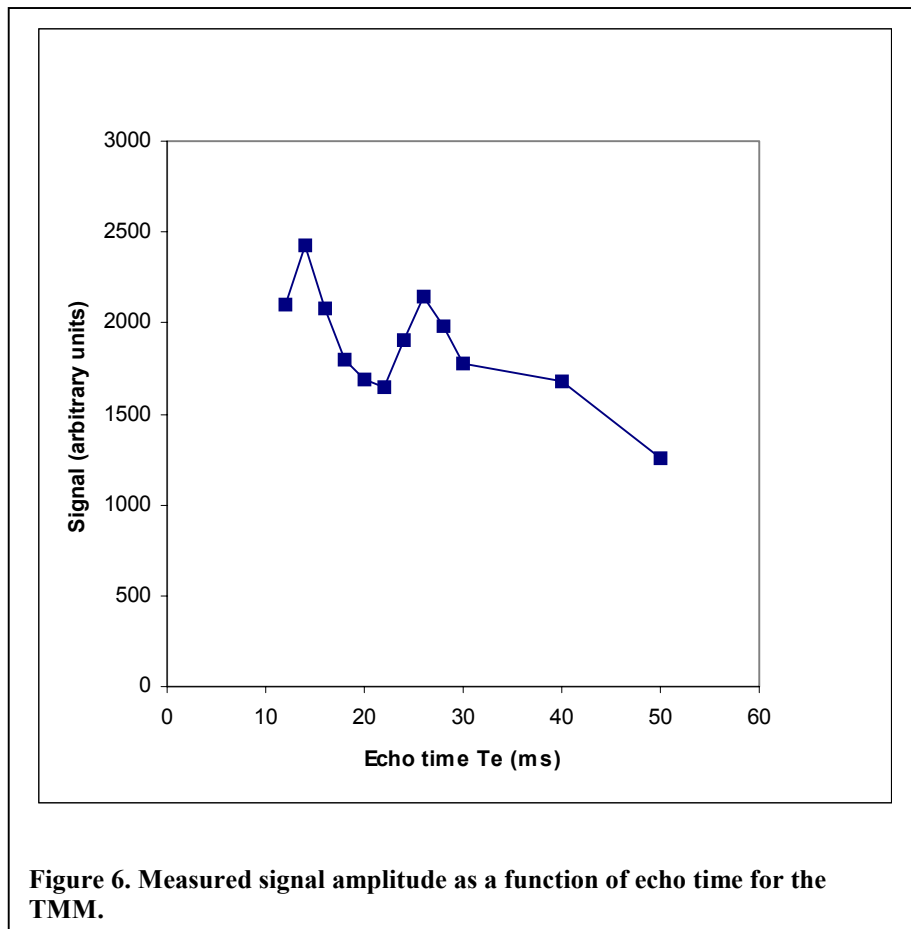
The tissue mimicking material has been described previously (Madsen *et al* 1982; Ruf *et al.* 1988; Bacon & Shaw 1993). It is a gel made from animal hide gelatine dissolved in water; the important physical properties of the gel are given in Table 1 and compared with typical values for soft tissue. The attenuation coefficient can be controlled by adding varying quantities of castor and olive oil to the solution to form an emulsion; formaldehyde and alcohol are also added to fix the gel after setting and to inhibit bacteriological degradation. For the measurements reported in this paper, the gel was doped with approximately 4 ml l⁻¹ of Omniscan™ clinical Gd-DTPA contrast agent to shorten T_1 and T_2 . This reduces the repetition time T_R and so allows the imaging sequence to be completed more rapidly.

Table 1. Acoustic and physical properties of the TMM gel compared with typical values for soft tissue.

Property	TMM	Soft tissue
Volume heat capacity (MJ K ⁻¹ m ⁻³)	3.9	3.8-3.9
Thermal diffusivity (10 ⁻⁷ m ² s ⁻¹)	1.33	1.2-1.4
Thermal conductivity (W m ⁻¹ K ⁻¹)	0.52	0.47-0.56
Speed of sound (m s ⁻¹)	1540	1560-1590
Typical attenuation coefficient at 5 MHz (dB cm ⁻¹)	2.45	2.2

A pure water/agar gel would be a simpler material to study and have a greater sensitivity to temperature changes. However, the oil/water suspension in the chosen TMM is more representative of soft tissue which contains a significant fat content. When studied using MRI this suspension of water and oil may be considered as two separate, non-interacting spin pools with their own individual NMR parameters (resonant frequency ω , T_1 and T_2). The water pool will normally be considered to be “on-resonance” and the resonant frequency, ω , of the system will be adjusted to match that of water. However, the exact frequency of resonance is dependent upon the temperature of the water and forms the basis of this temperature measurement technique.

The resonant frequency of the protons in the oil is not sensitive to temperature and is approximately 72 Hz lower than that of the water pool (at 0.5 Tesla). The Gadolinium contrast agent is insoluble in oil and will therefore not substantially effect the relaxation times of the oil. When made correctly so that the emulsion does not separate out, the gel forms a mixture with droplet sizes much smaller than the imaging resolution and therefore the signal from within a pixel is formed from the vector sum of the magnetisation of the two proton pools. This can clearly be seen if detailed relaxometry is performed. Figure 6 shows the result of attempting to measure the T_2^* of a similar gel mixture by looking at the variation of signal with echo time but using a finer spacing of echo times than would usually be performed.



In a simple sample mixture we would expect this signal to be exponential in nature decaying with a time T_2^* . There are however, clear oscillations of the signal. This is due to the magnetisation of the two pools becoming first in phase and then out of phase because of the 72 Hz difference in resonant frequencies of oil and water. The period of a 72 Hz oscillation is 14 ms and it can be seen that peaks occur at 14 ms and the next at 28 ms. When characterising the material, these effects must be properly accounted for.

In addition, the response to doping will be different in each of the spin pools. At short imaging times, the doped pool material will produce greater signal than the undoped one, i.e. the temperature dependent water signal will dominate. At longer times, more signal will be acquired but the extra signal will not only come from the water but will increasingly be contaminated by non-temperature dependent signal from the oil pool (since the signal from the water pool decays more rapidly). The signal in any pixel is the vector sum of the two pools and the temperature information is encoded in the phase of that vector. Thus the presence of the oil pool will reduce the temperature sensitivity and change the coefficients of the relationship between phase and temperature. This implies, unlike for pure water, that the absolute calibration of temperature depends upon the exact composition of the phantom, the doping and the sequence imaging times. However, this mixture of two pools is more representative of biological tissue than is pure water.

3.3 Transducer properties

The transducer selected for continued study was the Irex type 136597H with a single concave piezoelectric element. The transducer was driven in continuous wave mode from a separate signal generator with a sinewave of peak-to-peak voltage 9V (measured at the end of the

integral cable). The output characteristics were measured with an NPL Ultrasound Beam Calibrator and are given in Table 2. Acoustic output at the drive voltages used for the MR studies were calculated using the relationships in the right-hand column.

Table 2. Transducer acoustic output properties.

Drive voltage (peak-to-peak)	9.0 V	
Acoustic frequency	3.5 MHz	Independent of voltage
Transducer diameter	13 mm	Independent of voltage
Focal distance	5.6 cm	Independent of voltage
-6 dB beamwidth at focus	2.75 mm	Independent of voltage
Peak pressure	200 kPa	Proportional to voltage
Spatial-peak temporal-average intensity	1100 mW cm ⁻²	Proportional to voltage squared
Total power	61 mW	Proportional to voltage squared

4 MR system

4.1 Choice of imaging sequence

The signal exploited in conventional MRI originates from the nuclei of hydrogen. The amplitude of the signal is modulated according to both the timing details of the experiment and the physical properties of material of which the hydrogen nuclei are a component. As many of these properties are temperature dependent, accurate measurement of the changes of these MR parameters may be related to temperature rises. There are three groups of temperature dependent MR parameters of principle interest.

- For a given sample it is possible to quantify how the induced magnetisation changes with time. Once the sample is placed in a large static magnetic field, the magnetisation may be divided into two components of interest, an axial and transverse component. If perturbed, each component returns to equilibrium with a characteristic time denoted T_1 and T_2 respectively, both of which are temperature dependent.
- MRI utilises the ability to encode the position of a sample in the phase of the magnetic signal associated with the hydrogen nuclei. Under extreme position sensitisation it becomes possible to modulate the signal amplitude by the distance nuclei have moved by diffusion effects. The change in diffusion coefficient with respect to temperature can therefore be found.
- The frequency of the signal from a nucleus is dependent on the static magnetic field which the nucleus experiences. The surrounding electrons have the effect of screening the nucleus and hence changing the resonant frequency. A perturbation of the electron field will therefore have an effect on the resonant frequency and is termed the chemical shift effect. The chemical shift of water shows a marked temperature dependence due to the effect of transient hydrogen bonding.

There are therefore several approaches that may be used for temperature measurement using MRI or magnetic resonance spectroscopy (MRS):

- Quantitated T_1 , T_2 or diffusion imaging techniques in 1, 2 or 3 dimensions providing voxel-based temperature rise measurements
- Imaging techniques which modulate the phase of the signal through chemical shift effects. This may be extended to combine imaging techniques which modulate both the

amplitude and the phase of the signal using two different mechanisms (e.g. Diffusion and chemical shift).

- Potentially, spectroscopic techniques, which look either at the whole sample or at low spatial resolution, can identify through the chemical shift effect, the range of temperature rises present.

For preliminary testing, an agar gel phantom was built hot and cold water running through it in two embedded pipes. This arrangement sets up a known temperature gradient through the phantom which can be compared with the with measured change in the MR signal.

Figure 7 below shows the change in phase taken from a line profile for an experiment with the following parameters:

- Agar Gd-doped phantom with a T_1 of 95 ms
- 128 x 64 image (0.6mm x 0.6mm x 2.0mm)
- Echo time, T_E , 15ms.

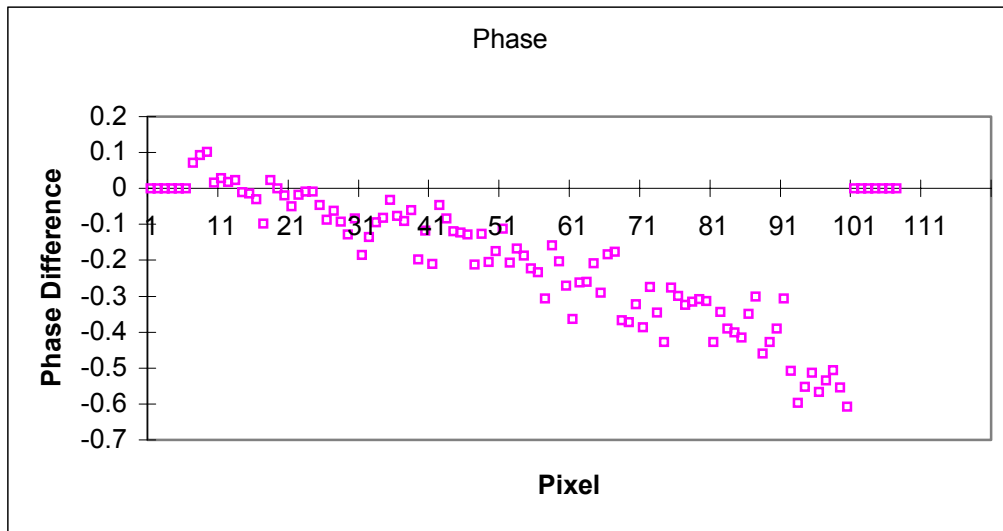


Figure 7. Phase profile between two water pipes in an agar phantom.

The temperature at the two ends of the profile were measured with calibrated thermocouples to be 12.5 °C and 22.4 °C so, for this experiment, the sensitivity was calculated to be

$$\Delta phase / \Delta T = 0.069 \pm 0.021(\text{std.dev}) \text{ rad } ^\circ\text{C}^{-1}$$

which gives a standard deviation in temperature, derived from the signal to noise of the image, of approximately 0.3°C. Assuming several degrees heating by ultrasound, a total phase change in the range of tenths of a radian would be expected.

The phase sensitivity of the NPL TMM to change in temperature will be largely controlled by the signal from the water component, so the sensitivity should be similar to this value but may be reduced somewhat and the SNR decreased by the presence of the fat component.

Finally, two imaging sequences – termed GEFAST and GELBW - were chosen. GEFAST and GELBW are acronyms for modified versions of the basic 2DFT imaging sequence that was originally available on the console. GEFAST was a modified Gradient Echo 2DFT experiment which allowed shorter repetition times and hence faster imaging. GELBW was a low bandwidth acquisition version of GEFAST which improved signal to noise by extending

the acquisition period. In both cases the modifications were machine/implementation dependent but both sequences are variations on GE-2DFT.

A rapid imaging sequence was used for single-slice measurements and consisted of:

- GELBW– based on 2DFT gradient echo.
- Spectral width 6.25 kHz
- 128x128 image matrix Fourier interpolated to 256x256
- 2 averages for DC offset correction by RF phase cycling
- T_R 55 ms, T_E 40 ms, single 5mm slice.
- Total imaging time 17 sec ($128 \times 2 \times 0.055 \text{ s} + 3 \text{ s}$ for machine setup delay)

For multislice imaging, the sequence used consisted of:

- GEFAST – based on 2DFT gradient echo.
- Spectral width 25 kHz
- 128x128 image matrix Fourier interpolated to 256x256
- 2 averages for DC offset correction by RF phase cycling
- T_R 200 ms, T_E 40 ms, 3 slices 5mm.
- Total imaging time 55 s ($128 \times 2 \times 0.200 \text{ sec} + 3 \text{ s}$ for machine setup delay)

4.2 Temporal stability.

The technique of proton resonant frequency temperature imaging relies on being able to remove a large spatially varying phase distribution from the small differences produced due to the temperature changes. This is achieved by collecting a phase reference at the beginning of the experiment, which is then subtracted, from all subsequent images. It is expected that machine drift will gradually render this phase map less applicable with time and this will limit the length of time that can be studied in one experiment. A crucial purpose of the phase reference is to remove the large (in the range zero to ten radians) phase shift due to the presence of the ultrasound transducer in the magnet allowing the much smaller shifts due to heating to be observed. If this were not the case, it would be possible to correct the phase map using an internal phase reference in each image, i.e. an area of the gel not expected to rise in temperature.

The imaging protocol was used to scan continuously the sample without applying any ultrasound to evaluate the long-term stability of the phase map. Data taken from a one dimensional profile taken through the gel phantom typically has a standard deviation of 0.025 radians but the mean can drift with time. This is shown below in Figure 8 for several voxel locations, indicating that the changes with time are similar at different locations.

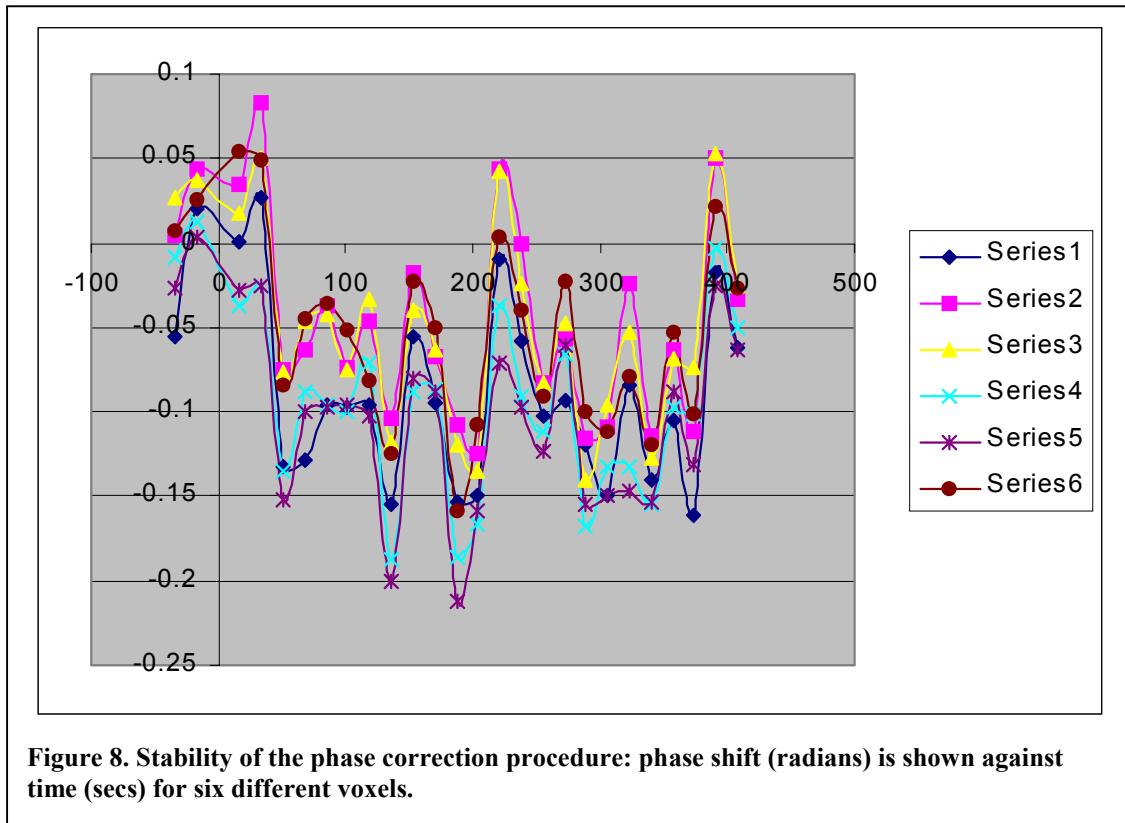


Figure 8 shows the profile along a line of voxels close to the centre of the volume at different times over an experimental period of 408 s (nearly 7 minutes). Ideally, following phase shift correction, the phase from each voxel should be constant with time and close to zero. While this is true initially, Figure 8 shows that there was a sudden step change after 50 seconds to a new mean value of -0.1 radians. This is in comparison to a maximum observed phase change due to ultrasound heating of 0.25 radians (at a transducer drive voltage of 24 V). Such baseline shifts when they occur can obviously invalidate the temperature values derived from the image. Such changes however affect the whole phase map image equally and can be corrected at any timestep by comparison with the phase change in an area of the gel which experiences no temperature rise. The correction for the large, spatially varying component remains valid during these periods. Thus both corrections are required, in summary

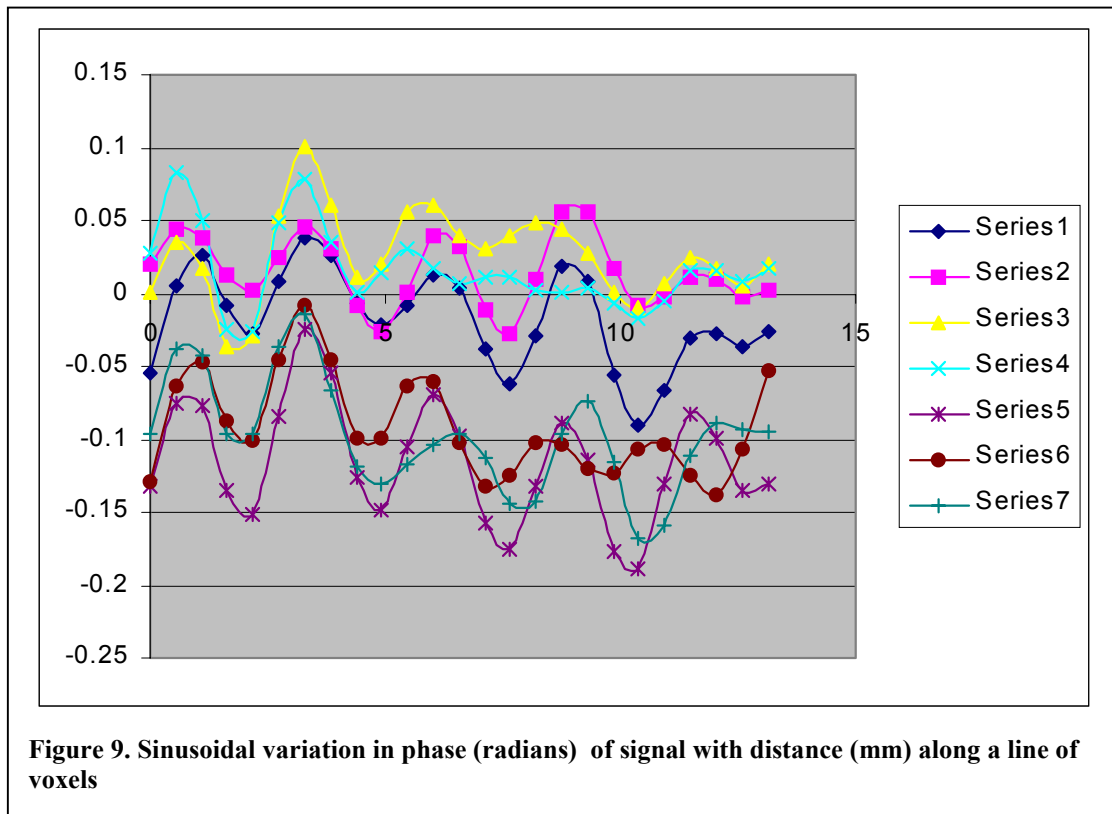
- Subtraction of the phase reference image to remove the large phase shift due to the transducer.
- Correction of the baseline using an internal reference to set the zero correctly to compensate for machine drift.

It is expected that more modern machines would suffer from this to a much lesser extent.

For this protocol, the phase of the signal from a given pixel was found to be approximately normally distributed with a standard deviation of 0.028 radians. Where necessary, this value has been used as the error bars on phase graphs. The standard deviation rises to 0.04 when a thinner slice has been used.

4.3 Spatial homogeneity

When examining the phase variation along a line of voxels in the image acquired at the same time-step, there is a clear sinusoidal spatial-variation with a periodicity of approximately 2.6 mm (equivalent to 5 voxels). Figure 9 shows this for a single line of voxels at each of seven time-steps. This may be a real variation in the properties of the TMM on a scale of millimetres; alternatively, it may be a spatial-variation in the applied magnetic field (although a variation on this scale is unlikely) or it may be an artefact related to the input signal filters or to Fourier transformation of the received signal. If any of the latter, it is expected that more modern machines would suffer from this to a much lesser extent.



4.4 Ultrasound transducer compatibility

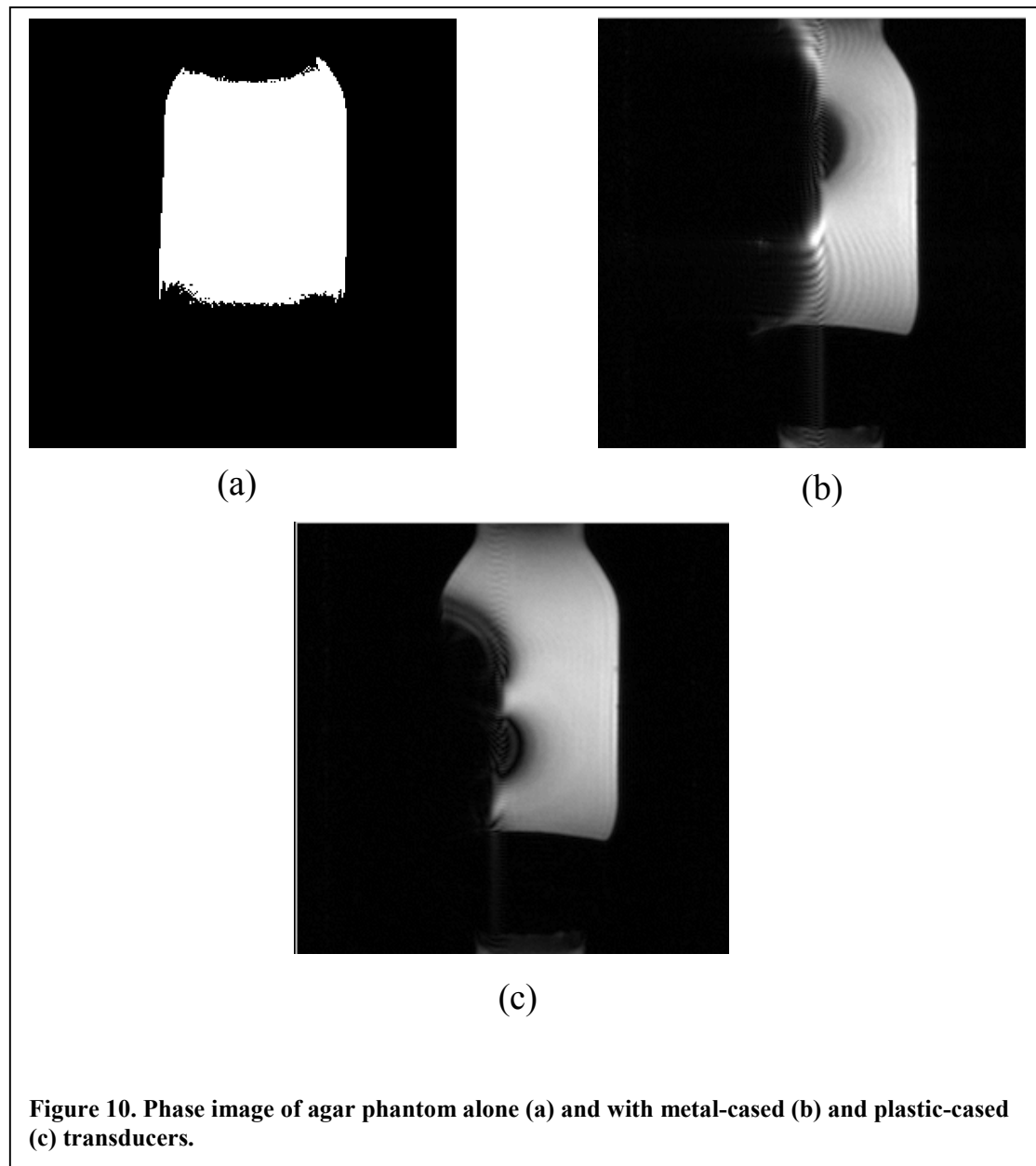
In preliminary experiments using an 3.5 MHz clinical imaging transducer, significant image distortion due to the presence of the transducer was found. The transducer did not show any appreciable force of attraction to the magnet. However, the phase sensitive imaging sequences used in these experiments are very sensitive to magnetic field inhomogeneities and a very small residual magnetic field can have significant effects on the image. Two non-clinical transducers were imaged next to an agar phantom and the results shown in Figure 10.

The two transducers tested were

- metal cased, Panametrics type M7-12-F50 320266
- plastic cased, Irex corporation type 136597H 3.5MHz 13mm.

In neither case was there a detectable force of attraction to the magnet. Image (a) above shows a 75 mm diameter agar phantom imaged with a gradient echo sequence ($T_R = 500$ ms,

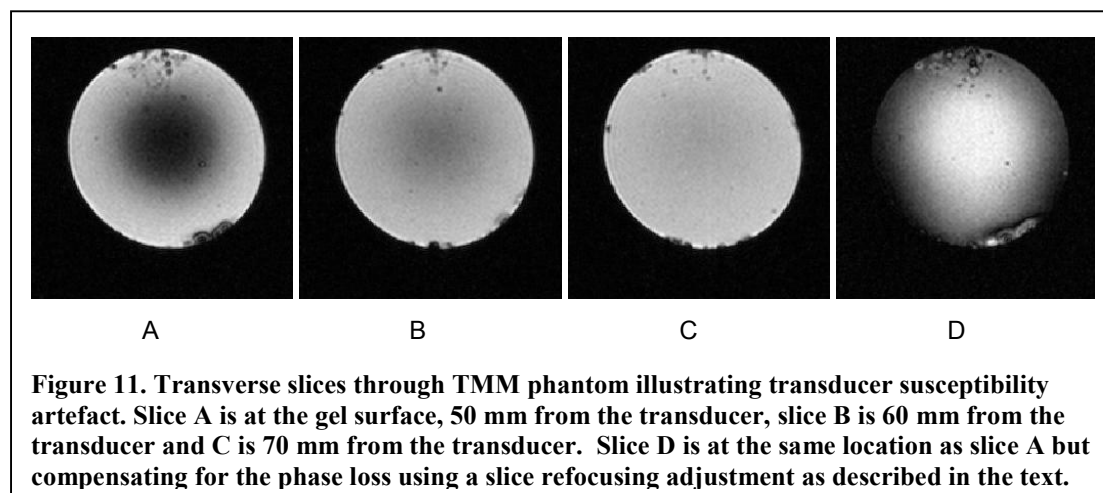
$T_E = 20$ ms). After the transducer has been placed alongside the object the image distortion can clearly be seen. Image (b) is the metallic cased transducer, image (c) the plastic one. The plastic transducer shows less image disturbance, with the unusable area of the image extending approximately 20mm beyond the end of the transducer. The metallic cased transducer, while worse still shows some area of useable image. From earlier experiments with a stripped down 3.5MHz transducer (identified by MIF NE 4383 75573H) that the effects are caused by some aspect of the ultrasound transducer itself rather than the casing: a common cause is nickel which is often used to provide tinning surfaces on components.



The susceptibility artefact caused by the presence of the ultrasound transducer spoils the homogeneity of the MR main field. This leads to signal loss due to through-slice dephasing. This signal may be recovered through adjustment of the slice-refocusing gradient but not for all slices simultaneously. As a result, time efficient multi-slice imaging sequences are less applicable as only one slice can effectively be imaged at a time. To illustrate this, the images in Figure 11 were collected. These images show a set of transverse slices through a gel phantom (x-y plane, perpendicular to the ultrasound transducer axis) at increasing distance

from the transducer. Slice A is at the gel surface, 50 mm from the transducer, slice B is 60 mm from the transducer and C is 70 mm from the transducer. The loss of signal due to the ultrasound transducer is clear from the dark region at the centre of slice A; the effect drops off with increasing distance from the transducer.

It should also be borne in mind that the maximum heating in this configuration will be near

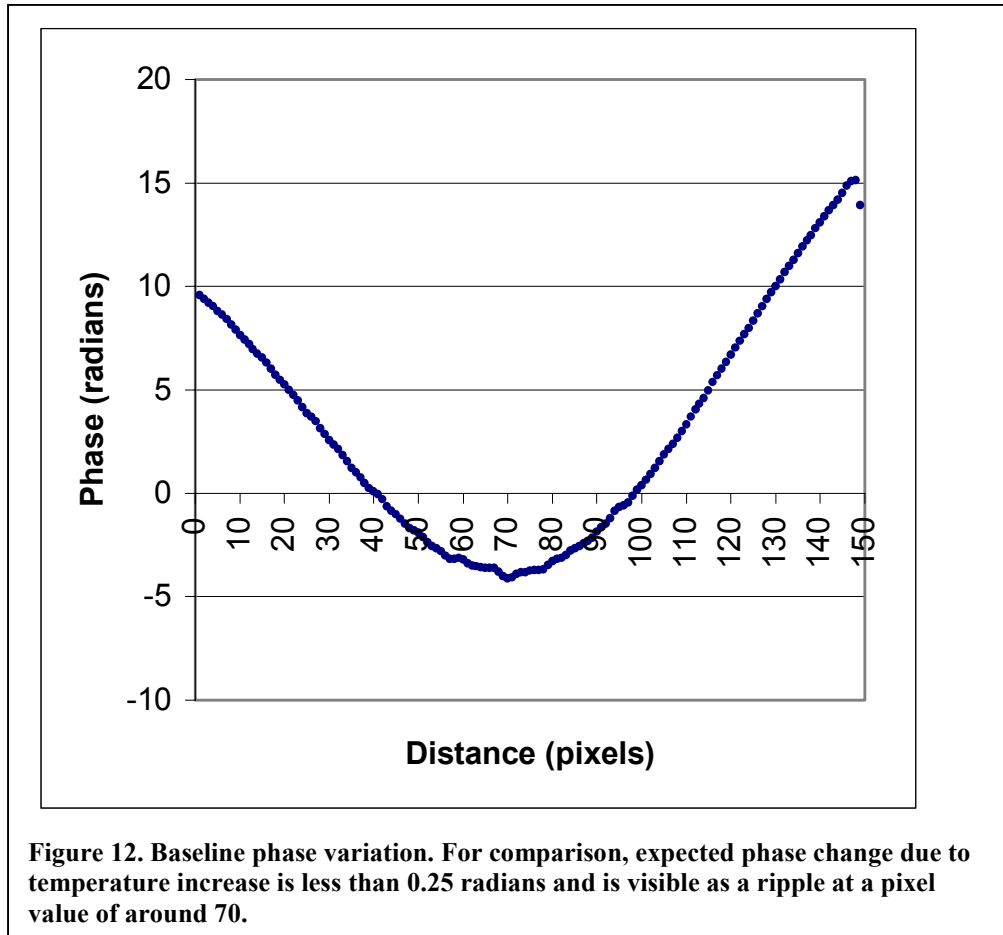


the gel surface and centrally located within the slice, just where the signal loss is worst. Slice D is at the same location as slice A but compensating for the phase loss using a slice refocusing adjustment. This shows that the Exeter system can recover the signal in the central region but, in the process, signal from the edge of the slice is lost and images of the other slices would be rendered useless.

More flexible systems than those at Exeter are equipped with additional magnetic field coils which generate various spatial variations of field (“shim coils”). These coils can be adjusted to compensate over a volume for the presence of field artefacts such as these, however correction of such large artefacts would probably be at the limit of such adjustments.

The susceptibility artefact is proportional to the strength of the main magnetic field. It would be desirable to use a large magnetic field as both the base signal and the temperature dependent effect increase with increasing field strength. The increased artefact would however wipe out any gains. For example, when the ultrasound transducer was imaged on the 1.5 T imaging system, the artefact was found to extend some 150 mm from the transducer.

Finally, even where the signal is of sufficient magnitude to allow good phase determination to take place, there is a large background phase shift superimposed upon the temperature dependent phase (Figure 12). Thus the variation in phase due to ultrasound heating is of the order of 0.1 rad superimposed upon a baseline variation of 10 rad. This imposes tighter constraints upon the positioning stability of the gel phantom as small shifts of the phantom in such a field can lead to phase shifts comparable to those we desire to observe.



4.5 Data analysis

Two methods of analysis were tried: fourier analysis and a simpler method which relies on using non-insonated regions of the sample as stable temperature references.

4.5.1 Fourier Filtering.

In the absence of ultrasound, the signal from a line of voxels (or profile) at a given distance from the gel surface and perpendicular to the ultrasound beam axis show a periodic fluctuation of the background with a period of 5-7 pixels depending upon the location of the profile. A Fourier transform was applied (based on the routing *four1* from Numerical Recipes in C 2nd Edition, Flannery and Press) to various lines but no clear spectral peak was obtained. Narrow band filtering was therefore not applied but a broader spectral editing was investigated. This method was chosen because, if successful, it will have the added benefit of allowing the MR imaging sequence to be shortened.

In order to apply this sort of filtering, *a priori* assumptions about the form of the expected profile are required. In the sagittal plane (perpendicular to the propagation direction of the ultrasound beam) the temperature profile is approximately gaussian in form. The effect of low pass Fourier filters of various widths was evaluated by comparing a Gaussian profile with the

result after removal of the higher spectral components. A “figure of merit” was chosen based on the integrated squared differences between the pre- and post- profiles.

Figure 13 shows the pre-filtering profiles chosen. Each has a central maximum value of 100 and has the width expressed a number of pixels standard deviation.

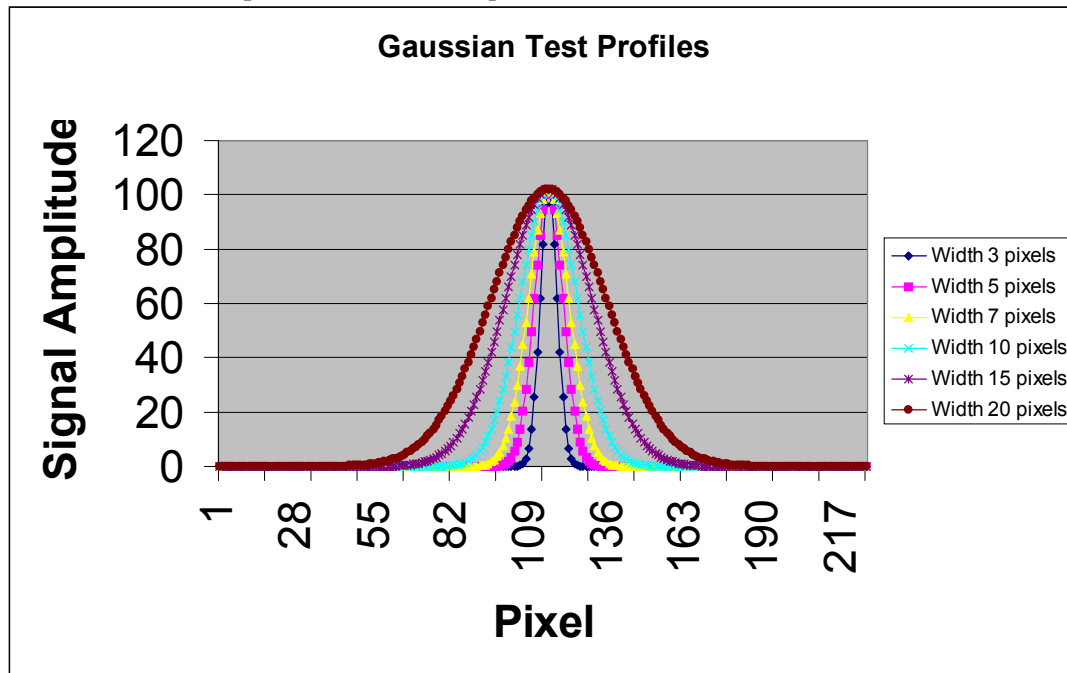


Figure 13. Gaussian test profiles.

After Fourier transformation, this profile of 256 pixels is converted into real and imaginary data each of which is 256 pixels in length with the DC component located at pixel 128 and the highest negative and positive frequency components in pixels 0 and 255 respectively. The Fourier filter is defined in this data space and has a flat pass band centered on the central (DC) pixel with a width w (also expressed in pixels) with smoothed edges formed from semi-Gaussians with a standard deviation of 3 pixels. An example is shown in Figure 14 for a filter width of 20.

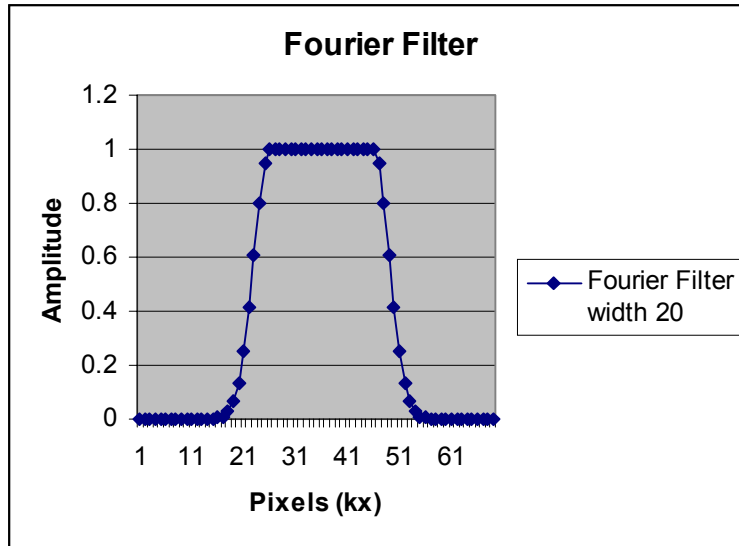


Figure 14. Example Fourier filter width 20.

The FFT of the test profile is multiplied by the filter profile and the inverse FFT calculated to produce the post-filtered dataset.

The effect on the test profiles of filters of varying widths is shown in Figure 15. The figure of merit is calculated as follows:

1. Pre- and Post- filtered profiles are subtracted from each other on a pixel by pixel basis
2. The deviations are squared (to ensure all are positive) and summed.
3. The result is square rooted and normalized to the area of the pre-filtered profile and expressed as a percentage.

The following guidelines can be determined for the use of Fourier filtering.

- Narrow filters will improve noise characteristics at the expense of accuracy of the profile shape.
- Wide profiles are affected less than narrow profiles.
- Choice of the filter size depends upon the expected width of the beam profile.

Using the sagittal scans as a basis a filter width of 20 was chosen. The profiles in the sagittal direction can be approximated by a Gaussian of width 10 to 20 pixels and a filter of width 20 will preserve profiles of down to about 5 pixels standard deviation to a figure of merit of 5%.

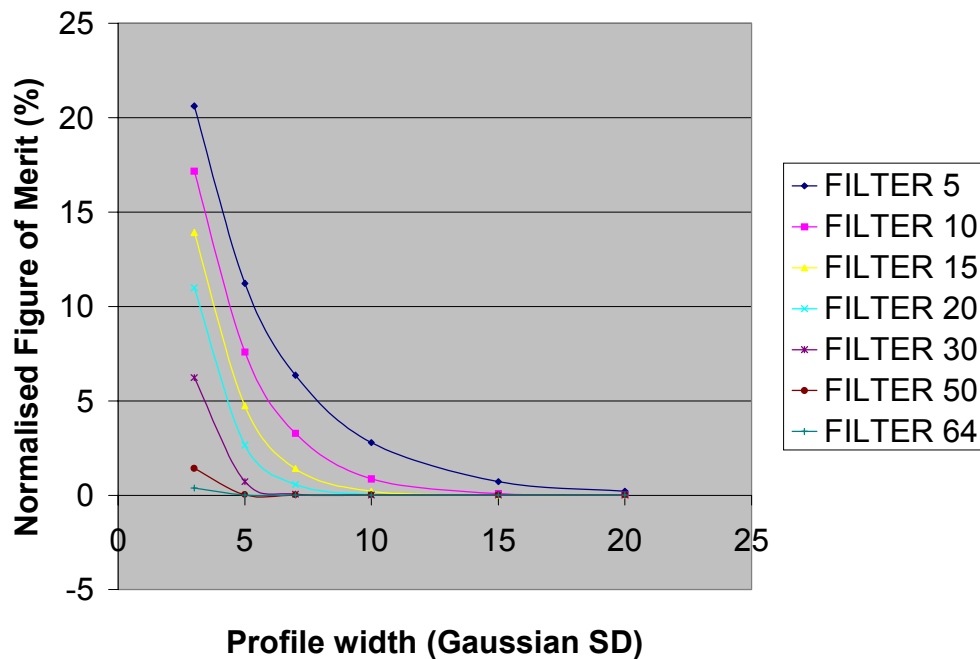


Figure 15. Deviations from the test profile caused by Fourier filtering.

4.5.2 Use of stable reference regions

As an alternative to the Fourier filtering method described above, this method makes two assumptions about temperature profiles across the sample: first that the temperature rise at each end of the profile is zero; and second that the MR image contains a periodic fluctuation with periodicity 5 voxels (see Figure 9) which is superimposed on the underlying temperature profile.

The sequence used here for post-processing of the MR image was:

- a) Remove the background phase variation described in Section 4.3.
- b) Removal of spatial variation by taking a running average of 5 voxels along each line perpendicular to the axis of the ultrasound beam.
- c) Remove temporal-variation by assuming that the ends of each line of voxels have not changed temperature since the diameter of the ultrasound field is much smaller than the measured volume (*i.e.* the periphery of the measured volume is used as a stable reference region).

5 Thermocouple measurements

Temperature rise was measured using the NPL Thermal Test Rig (Shaw *et al* 1999). A thin-film thermocouple (TFT) was sandwiched between layers of tissue mimicking material (TMM) (Bacon and Shaw, 1993); this is essentially an open version of the Thermal Test Object (Shaw *et al.*, 1999). The output of the thermal sensor was connected via a low-noise pre-amp to a digital voltmeter. The TMM sandwich was mounted on a stepper-motor positioning system in a test tank below the transducer. Data acquisition and movement of the test object was controlled by a PC, allowing the test object to be scanned through the field to locate the centre of the beam at any selected distance from the transducer.

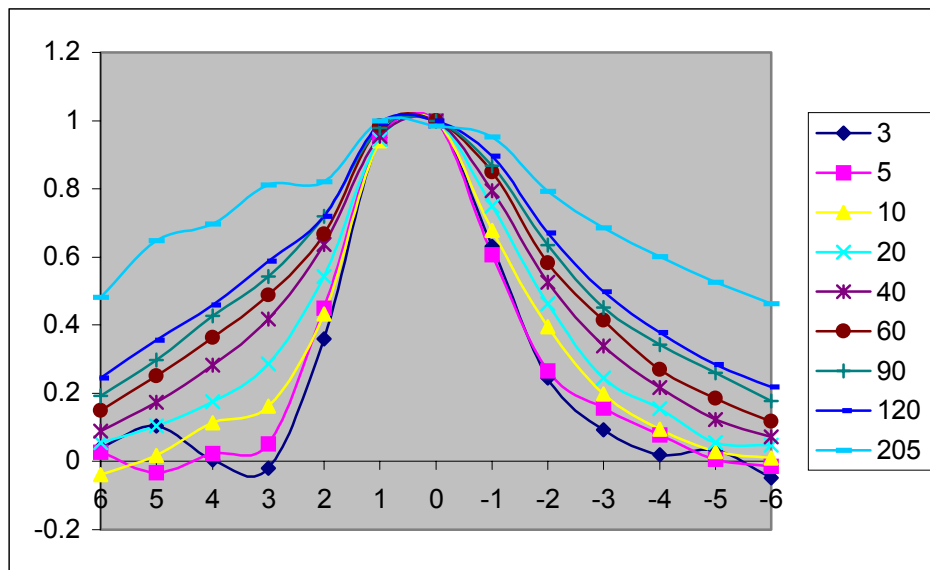


Figure 17. Radial thermocouple profiles at different times (in seconds) against distance from the beam-axis (mm) on the horizontal axis – normalised to peak value of 1.

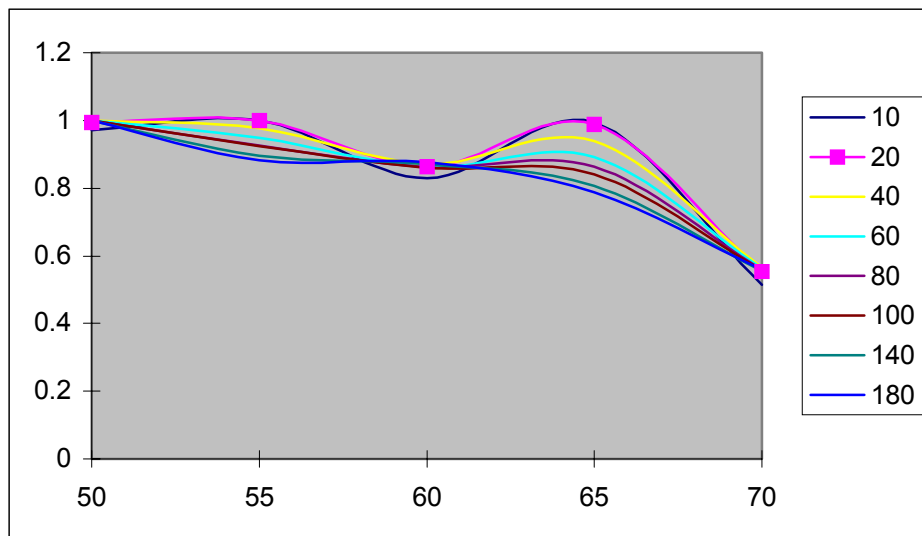


Figure 17. Axial thermocouple profiles at different times (in seconds) against distance from the transducer face (mm) on the horizontal axis– normalised to peak value of 1.

The thin-film thermocouple eliminates the potential major problem of viscous heating (*e.g.* Fry & Fry, 1954a and b): it consists of electrodes evaporated onto a thin (0.006 mm) plastic substrate; the electrodes overlapped over a region of approximately 0.2 mm x 0.2 mm at the centre of the film which was supported by a 3 mm thick plastic ring. The outer diameter of the ring was 85 mm and the inner diameter was 50 mm.

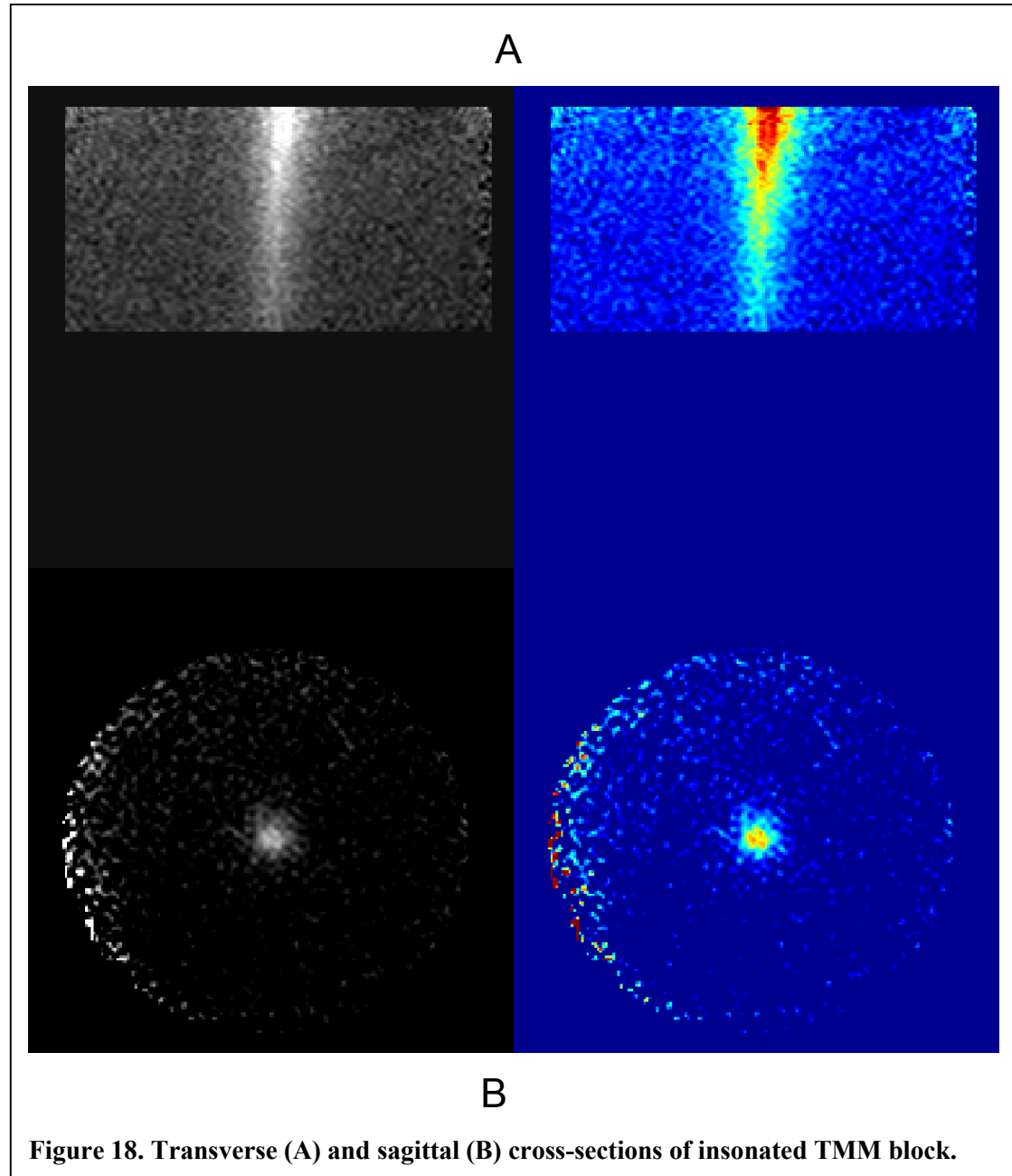
The TMM was positioned in a water bath so that there was a water path of 45 mm between the transducer and the top of the TMM. A total thickness of at least 25 mm of TMM was used, divided into discs of approximately 5 mm thickness so that the distance of the TFT from the top of the TMM could be changed.

The maximum temperature rise in the focal plane for a drive voltage of 24 Vp-p was approximately 3.5°C; this equates to 2.1°C at 18.5 Vp-p and 1.3°C at 14.55 Vp-p, assuming that temperature rise is proportional to total ultrasonic power output which is in turn proportional to the square of the drive voltage.

The temperature increase during insonation was measured as a function of distance from the beam-axis with the TFT at the focal distance of approximately 55 mm. Figure 16 shows the temperature elevation measured across this diameter of the field after different insonation times: the profiles at different times are normalised to highlight the change in the width of the thermal distribution with time. The temperature increase was also measured on the beam-axis as a function of distance from the transducers. The top surface of the TMM was 45 mm from the transducer and the TFT was positioned at five locations in the range 50 mm to 70 mm, which is the approximate distance of the gel sample from the transducer in the MR experiments). Figure 17 shows the temperature elevation measured along this axis after different insonation times: the profiles at different times are again normalised and show that the shape of the distribution axially is not strongly time-dependent; however, the distribution is smoother at longer times due to the effects of thermal conduction. Note that there are five points on each curve (for clarity, the locations of these points are indicated only for a single curve).

6 Results

For the results presented in the following section, a single slice gradient echo sequence ($T_R = 55$ ms, $T_E = 40$ ms) using a low bandwidth acquisition (GELBW) was used. Using 128×128 acquisition matrix Fourier interpolated to 256×256 with two averages produced a total imaging time of 17 s: 2 s for machine initialisation and 15 s for acquisition. The method of Fourier interpolation has been shown to be valid subject to certain assumptions which are known to apply to the MR systems at Exeter and provides a real increase of a factor of two in the spatial resolution of the image.



For the sagittal imaging direction, the performance of the power amplifiers controlling the field gradient restricted the 2D volume thickness to a minimum of 10 mm. In the transverse direction 5 mm thick slices were used. In both cases a field of view of 140 mm was used leading to an in-plane resolution of 0.547 mm. In all cases one or more baseline images were collected to provide a phase reference and the analysis methods previously described in Section 4.5 applied to the remaining images of each data set. For a visual comparison, Figure 18 shows a temperature field generated by the previously described ultrasound transducer driven using a 24 Vp-p sine wave at 3.45 MHz. The image was acquired in 17 s and heating had been applied for 165 s prior to the image being collected.

6.1 NPL method

Each line in Figure 19 below is the phase change measured across a 40mm diameter of the MR thermal image. The profiles are normal to the beam axis, 10.9 mm from the gel surface. The red and blue lines are true repeats: both were collected using a ultrasound driver voltage of 24 V but were collected in separate experiments 45 minutes apart; the agreement is excellent between the two experiments. The green and pink were measured when the transducer was driven at lower drive voltages.

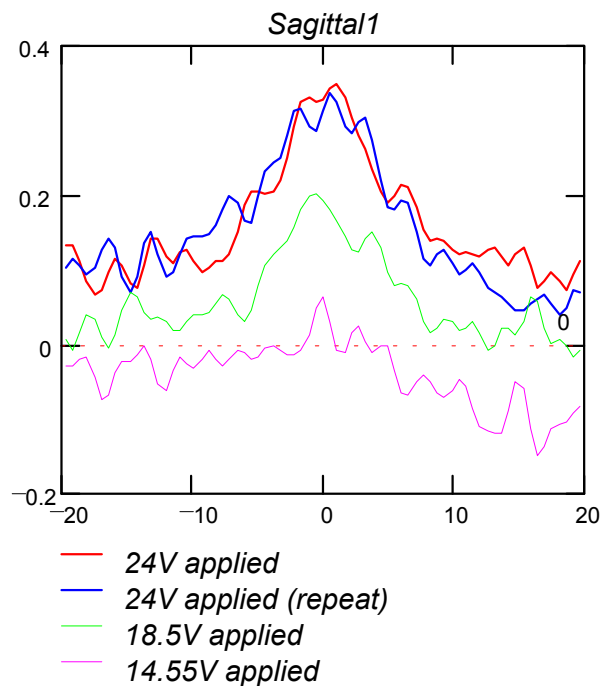


Figure 19. Phase change measured across a 40 mm diameter of the MR thermal image.

These basic profiles are smoothed with a running average of 5 pixels to reduce the regular pattern observed when evaluating the spatial-uniformity of the MR system (see Figure 9). In addition, since the edges of the region are expected to be unheated by the ultrasound field, the profiles are detrended such that each end is close to zero (Figure 20). There is good repeatability between the two measurements at 24V.

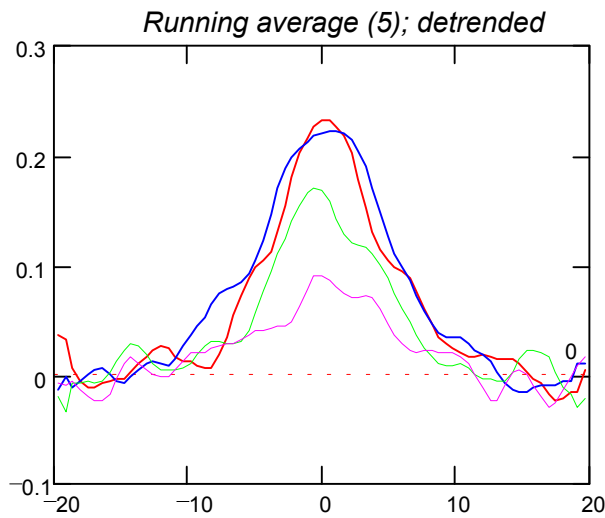


Figure 20. Smoothed and detrended phase profiles.

The output power of the transducer should be proportional to the square of the applied voltage. Scaling each profile by the square of the applied voltage (Figure 21) shows good agreement between profiles obtained over a range of temperature rise, indicating that the sensitivity is constant with respect to temperature over the range tested..

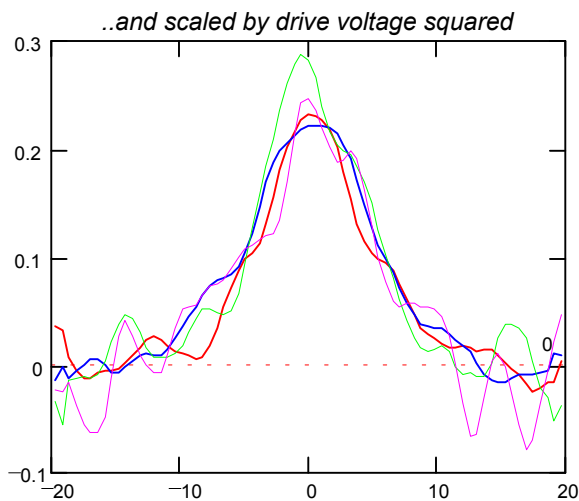


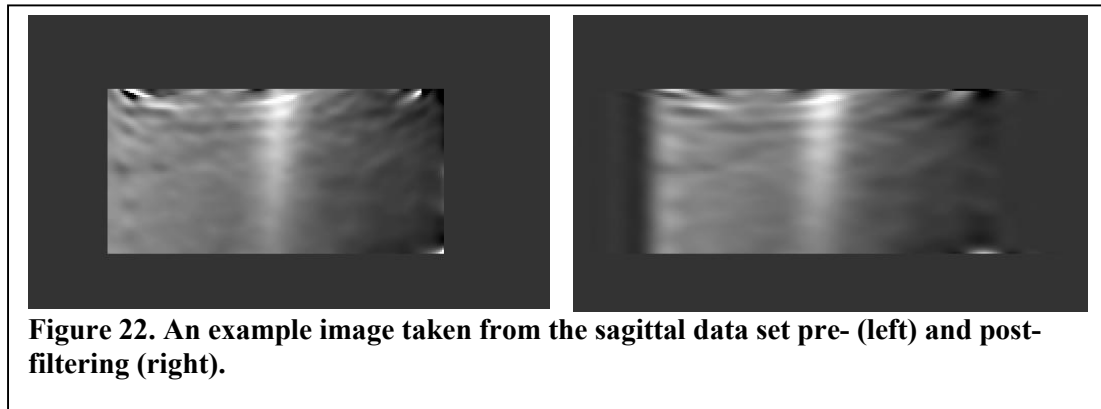
Figure 21. Phase profiles scaled to the acoustic power.

6.2 Exeter Fourier smoothing method

From the raw images the following processing steps have been applied.

1. Gaussian blurring as described in Section 4.5.1 (an example of the effect of this blurring on the MR image is shown in Figure 22).
2. Masking of image to exclude background
3. Phase mapping and unwrapping
4. Subtraction of baseline phase map from each time point

5. Horizontal Fourier filtering as described in 4.5.1.



In addition to the steps above, after profile extraction there is also a 1st order baseline phase correction (to compensate for machine drift) applied based on the first and last five pixels of the profile where the temperature rise is assumed to be zero.

Phase profiles across the sample measured at different transducer drive voltages are shown in Figure 23. The four profiles are normalised to the total acoustic power. Comparison with Figure 21 suggests that both methods give similar results but the NPL method may be more consistent.

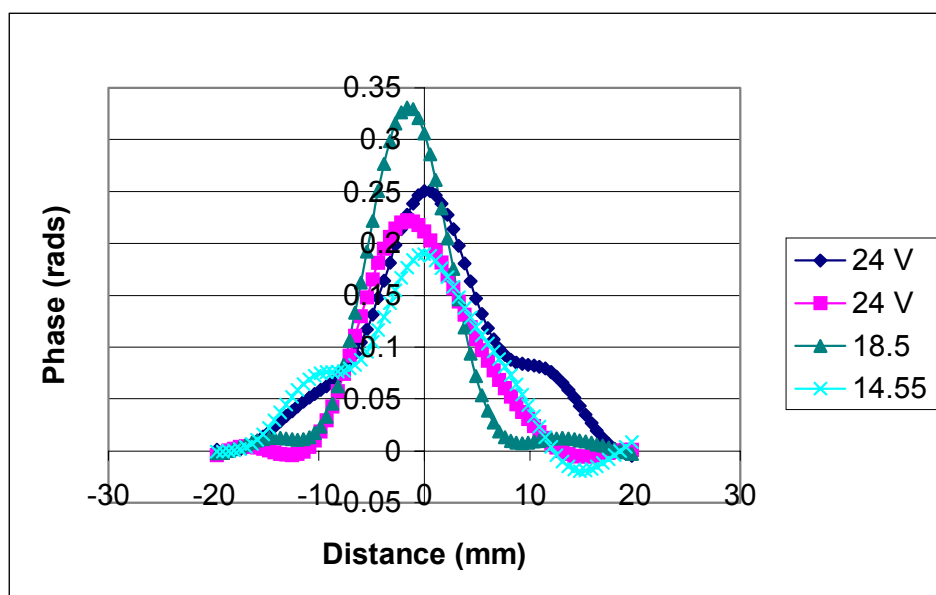


Figure 23. Phase profiles as a function of drive voltage after processing according to Exeter method and scaling for acoustic power.

6.3 Temporal variation of temperature

The temporal dependence of the phase of a single pixel 5.47 mm below the surface of the gel is shown in Figure 24 during heating and cooling using an ultrasound driving voltage of 24 V.

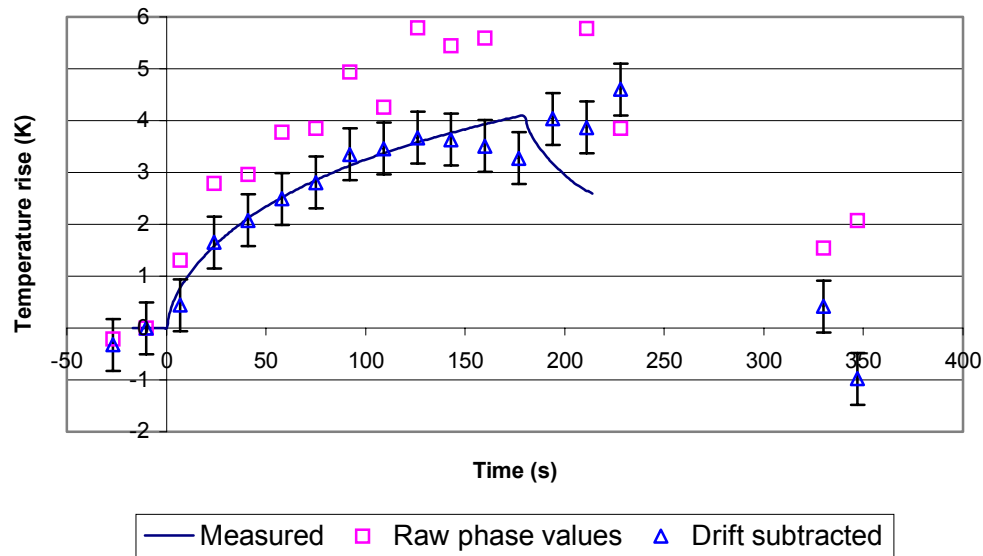


Figure 24. Phase change from a single pixel during insonation scaled by $0.06 \text{ rad } ^\circ\text{C}^{-1}$ and compared with the TFT-measured temperature.

The raw phase values (Figure 24, pink squares) cannot be used alone because of the spatial and temporal variability exhibited by the MR system (see Figures 8 and 9). It is necessary to first reduce these systematic effects by averaging and comparison with the phase change in an unheated region of the sample (Figure 24, blue triangles). The curve shows a rapid heating up when the drive was turned on (at $t = 0$) and then a levelling off at 120 s, and then cooling once the drive was switched off at time $t = 230$ s. This time variation is consistent with that obtained from thermocouple measurements over a period of 180 s insonation (Figure 24, solid line) and gives a best fit thermal sensitivity of approximately $0.06 \text{ rad } ^\circ\text{C}^{-1}$, which is consistent with value expected from the agar gel calibration. The gap in the data set between 250 and 320 seconds is due to one of the MR system gradient amplifiers becoming unstable and rendering the images unusable for that period.

6.4 Comparison of thermocouple and MR-derived temperature profiles

When the profiles for an input signal of 24 Vp-p are compared in Figure 25 between the MR

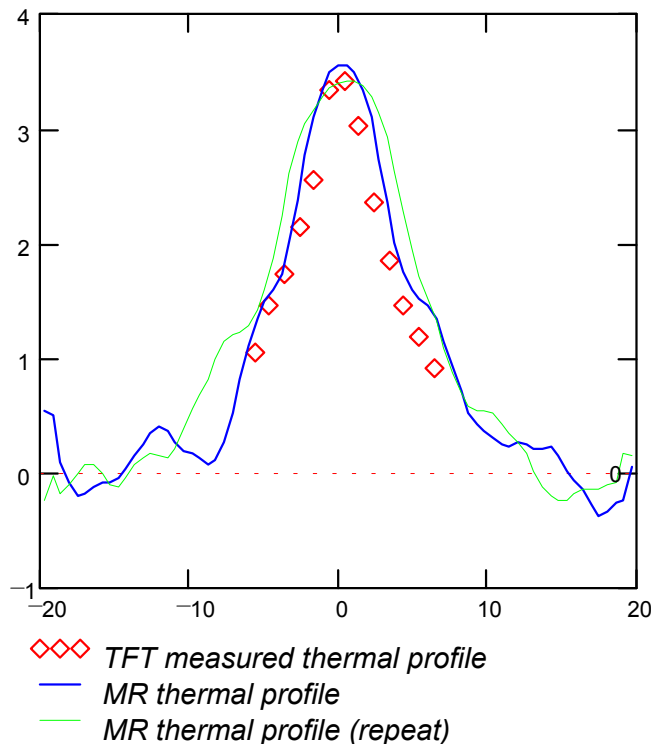


Figure 25. Temperature rise profile (°C) measured with thin-film thermocouple compared to MR thermal profile using a thermal sensitivity of 0.065 rad/°C.

method (NPL analysis) and the thin-film thermocouple method at approximately the same insonation time, there is clearly good agreement between the shapes of the profiles and the best-fit thermal sensitivity is again in the range 0.06 to 0.07 rad °C⁻¹.

6.5 Overall performance

Using the 0.5 Tesla MR scanner at Exeter University, the following performance levels were achieved: voxel volume of 0.57 x 0.57 x 3 mm³; typical noise level (specified to be the standard deviation of the signal from a population of voxels allowed to reach thermal equilibrium with their surroundings after processing to reduce known system effects) of 0.3°C; overall measurement time 15 seconds (for one plane through the phantom). Agreement with thin-film thermocouple measurements was within ±15% (±0.5°C) in the focal region of a 3.5 MHz beam with a -6dB beamwidth of 2.75 mm.

7 Performance limitations

7.1 MRI System choice.

When a sample is placed within a magnetic field, the field within the sample differs from the applied external field according to the magnetic susceptibility of the sample material. The imaging process encodes the position of the signal within the sample by modulating the magnetic field. Variations in the applied field therefore manifest themselves as distortions in the image which are termed susceptibility artefacts.

The hardware design, consisting of RF coil system, pre-amplifier and digitising system, is taken as a given starting point. In our case, the 0.5 T system at Exeter is of considerably lower specification than currently available commercially, in part due to its age and in part to the “home built” design. However, as it is possible that this work may be continued on other systems some comments with respect to the suitability of MR systems will be made. There has been a trend to increasing field strength in commercial imaging systems: now 1.5T systems are considered the standard for clinical imaging with 3T becoming increasingly common for research purposes. This move is driven by the fact that the baseline MR signal amplitude (S_0) is proportional to field strength. The clinical gains are not as clear cut as the tissue relaxation parameters (T_1 and T_2) become more similar at high fields reducing tissue contrast. For this project high signal is desirable: however, the downside is that image size of the artefacts due to susceptibility increases.

The design of ultrasonic transducers typically includes ferromagnetic elements that modulate the static B_0 . In MRI, the magnetic field is used to encode position and hence variations in B_0 lead to two principal artefacts. The most significant is that the slice profile is no longer planar and adequately re-focussed over the whole volume and hence signal magnitude is reduced. This has been discussed in some detail earlier in this report.

A second problem relates to spatial encoding of the signal and will be detailed in the next section, however it should be noted that all of these problems become more significant at higher field strengths so that use of a high field system (>1.5 T) is not necessarily desirable.

7.2 Noise

There are four principal sources of noise in MRI which originate from the RF receiver coil, the sample, the pre-amplifier and the environment respectively. The RF coil and the sample under study manifest themselves as a resistance in the receiver system and are Johnson noise sources. Of these, only the sample conductivity is easily manipulated, the others will usually be designed as best as possible for a given location and machine hardware. In the case of this project the sample constituents are fixed to be the NPL TMM material with only a small margin for adjustment of MR relaxation times. In order to understand the relationship between sequence design and SNR it is necessary to determine the relationship between the imaging process and the physical NMR signal. The key concept is that position is encoded using frequency through spatial modulation of the magnetic field. The frequency of the NMR signal is proportional to the applied field:

$$\omega = \gamma B(x)$$

If the magnetic field is made to vary linearly with a spatial direction by application of a magnetic field gradient such that

$$B(x) = B_0 + G_x x$$

then the magnitude of the signal in the frequency band $\omega + \Delta\omega$ is directly proportional to the number of spins in the corresponding strip $x + \Delta x$.

More importantly if we wish to image an object of a certain size L , with a given gradient strength G_x this implies that the NMR signal will have a certain bandwidth equal to $\gamma L G_x$ which will be centred on ω_0 . If we are to reconstruct the spatial distribution using Fourier means, the signal must be sampled according to the Nyquist criterion. As the noise sources in MR are broadband in nature, a suitable bandwidth filter is applied to prevent unnecessary aliasing of noise into the signal band.

It is therefore possible to increase the SNR by reducing the bandwidth of the experiment. This may be achieved by simultaneously reducing the gradient strength G_x and changing the sampling rate and bandwidth filter to match. However, this has two side effects

- 1 Lowering the gradient strength makes the image more sensitive to susceptibility variations in the main magnetic field. This can be seen by considering that a given gradient strength corresponds to a fixed $\Delta\omega$ per pixel in the image. For geometrically accurate images, the $\Delta\omega$ produced by the applied gradient must dominate any $\Delta\omega$ due to imperfections in the main field. If not, those imperfections will shift signal into pixels where it does not belong and a distorted image will be produced.
- 2 If image resolution is to be maintained, then the same number of sample points must be collected but now at a lower frequency and hence the time taken to acquire the signal becomes longer. The imaging time increase is negligible but the MR signal is decaying rapidly due to T_2^* effects and so a longer acquisition window can result in less signal due to relaxation effects. Asymmetric sampling of k-space can mitigate this problem but this can also introduce resolution errors and will not be considered here.

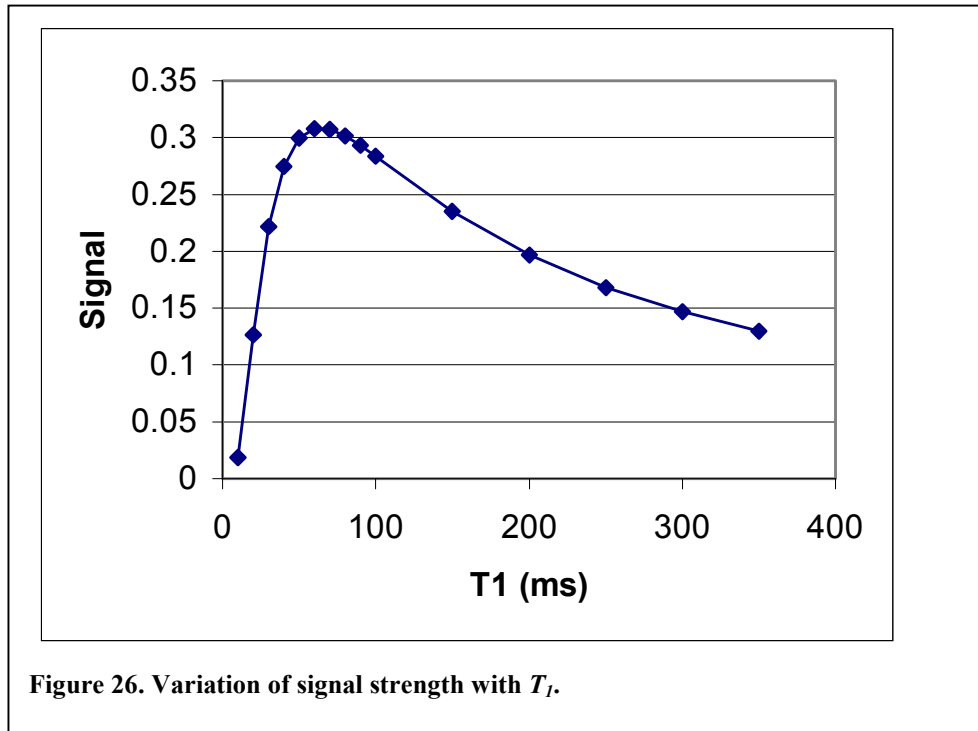
The pulse sequences initially used had a bandwidth of 25 kHz (40 μ s per complex sample point). The lower bandwidth form (GELBW), which was used for the measurements presented in Section 6, the bandwidth was reduced to 6.25 kHz providing a measured reduction in the average background noise by a factor of 1.97.

7.3 Relaxation effects

The MR signal is derived from the equilibrium magnetization of the sample M_0 . This magnetization is converted (by RF excitation) into an observable signal S . After the magnetization has been converted to the observable form, there has to be a delay for the equilibrium magnetization to re-establish itself. The MR signal returns to its equilibrium value through two separate mechanisms. It is convenient to consider the MR signal as being composed of two components, a longitudinal component M_z and a transverse component M_{xy} . The process of RF excitation converts the unobservable M_z and converts it into an observable M_{xy} in the process setting $M_z = 0$. The M_z then grows exponentially to its equilibrium value with a characteristic time T_1 while the observable component decays to zero with a characteristic time T_2 . This is illustrated in Figure 2.

Therefore, for maximum observed signal one should wait between excitations a time T_R such that the system has fully relaxed to equilibrium between excitations which in practice can be taken as $T_R > 3 T_1$. However, for conventional 2DFT imaging sequences an image will require

N_{PE} excitations (typically 128) to produce an image and hence long T_R implies long imaging times. Clinically the relaxation times are fixed in large part by the human anatomy however for this project we have some freedom to choose the relaxation properties. A clinical Gadolinium based MR contrast agent (such Omniscan™ or Magnevist™) can dramatically shorten the T_1 relaxation times of solutions into which it is mixed and hence allow greatly reduced imaging times with little signal penalty. Unfortunately once again there is a tradeoff limiting how short the T_1 can be made. A fundamental relationship exists that T_1 must be larger or equal to T_2 . As T_2 determines how long the observable MR signal persists, T_1 must not be shortened too far or no observable signal will remain at an echo time sufficiently long to measure the temperature dependent phase map.



Thus for a given time between excitations, which determines total imaging time, there is an optimum sample relaxation time. If the sample is doped with relaxation agents such that the T_1 is substantially reduced then the T_1 and T_2 are approximately equal. Figure 26 shows the theoretical signal obtained under these conditions for a fixed T_R of 55 ms. Note that on this scale, the maximum possible signal would be 1 and would occur for a sequence that had a long T_R and a short T_E . A T_R of 55 ms corresponds to an imaging time of 17 s (128 excitations with 2 averages i.e. $128 \times 2 \times 0.055 \text{ sec} + 3 \text{ s}$ setup time). It can be seen that the optimum T_1 of the phantom material would be between 50 ms and 100 ms. If the imaging time constraint can be removed then the signal will improve but the peak will remain at roughly the same point. Figure 27 shows the variation in signal (again compared to a fully relaxed sequence with unity signal) as the imaging time is extended using a T_1 of 80 ms for the phantom material.

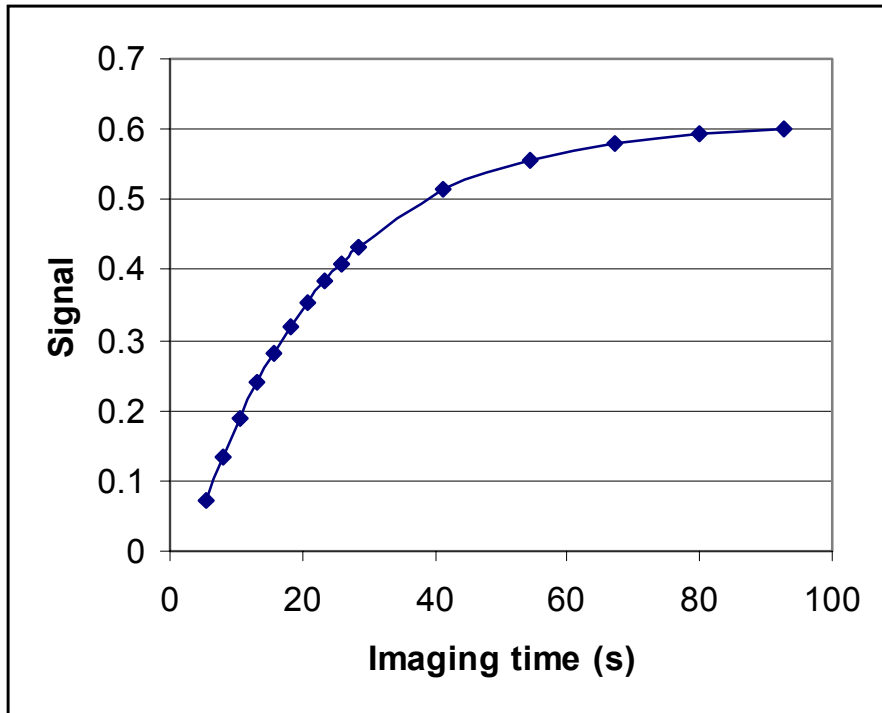


Figure 27. Variation of maximum achievable signal strength with increased overall imaging time.

7.4 Commercial MR scanners

On commercial systems, there are many imaging sequences available that were not available at Exeter. Many of these, such as EPI and SENSE offer significant increase in imaging speed over conventional 2DFT sequences. EPI for example can collect a single slice image in typically less than 100 ms. There are also faster multiplexed versions of the conventional 2DFT sequence (such as TURBO-GE and TURBO-SE) which can offer speed up factors of 4 to 16 times. However, all of these methods will incur SNR penalties over the 2DFT sequence. While the exact details vary from sequence to sequence the theory behind these penalties is as described in this report. Improved hardware and software processing will offset these penalties to a significant degree. The contrast mechanisms in the 2DFT sequence are simple to calculate and predict whereas the behaviour of many of the more advanced sequences rely upon the establishment of a steady state magnetisation and spin refocusing techniques which can result in images which are difficult to process quantitatively.

8 Conclusions and recommendations

Despite the time taken to complete this project, the scientific outcome has been generally successful. The thermal distribution produced by a diagnostically relevant ultrasound field in a Gd-doped phantom material representative of fatty tissue has been measured with MRI. The following conclusions can be drawn:

- Agreement with thin-film thermocouple measurements was within $\pm 15\%$ ($\pm 0.5^\circ\text{C}$) in the focal region of a 3.5 MHz beam with a -6dB beamwidth of 2.75 mm.
- Using the 0.5 Tesla MR scanner at Exeter University, the following performance levels were achieved: voxel volume of $0.57 \times 0.57 \times 3 \text{ mm}^3$; typical noise level (specified to be the standard deviation of the signal from a population of voxels allowed to reach thermal equilibrium with their surroundings after processing to reduce known system effects) of 0.3°C ; overall measurement time 15 seconds (for one plane through the phantom).
- It is anticipated that a modern, clinical grade 1.5 Tesla system using the same imaging protocol would achieve a significant improvement in SNR for the same voxel volume and slice measurement time.
- The temperature sensitivity of the oil/water emulsion phantom (representing fatty tissue) is dependent on the echo time due to the interaction of the signal from the water and oil pools.
- It is anticipated that a water-based phantom without oil (representing lean muscle or liver for example), would provide a SNR improvement of approximately a factor of two and should have a temperature sensitivity which is almost independent of the imaging echo time.
- Susceptibility artefacts caused by magnetic components in the transducer are a major limitation on the extent of the region that can usefully be examined with MRI.

Based on these conclusions, two main recommendations for follow-up studies can be made:

- The performance of a similar imaging sequence carried out on a modern, high quality, higher field-strength MR scanner should be tested, and the extent to which the spatial and temporal resolutions can be optimised should be explored.
- The susceptibility artefacts produced by a range of clinical imaging transducers should be evaluated. The extent to which the components responsible for the artefacts can be modified or replaced without affecting the acoustic output should also be investigated. This would require collaboration, or at least cooperation, from a transducer manufacturer.

These follow-ups should involve an MRI centre with an active interest in temperature determination: Hammersmith Hospital (now part of Imperial College) or the Royal Marsden Hospital would be two possibilities. Collaboration could take the form of an academic-led Research Council proposal with part funding by the National Measurement System Directorate of the UK Department of Trade and Industry.

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