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UTE: Past, Present and Future

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SUMMARY

There are now a variety of new techniques available to detect signal from tissues with short or ultrashort T2s and T2*s. There are also many methods of developing image contrast between tissues in the short or ultrashort T2 or T2* range which can provide visualization of anatomy and pathology which has not previously been seen. Particular methods have been developed to target susceptibility effects and provide accurate quantitation by compensating for anatomic distortion produced by these effects. Specific methods have been developed to image the effects of magnetic iron oxide particles with positive contrast. It is also possible to correct for loss of signal and image distortion near to metal due to gross susceptibility effects. These methods are likely to increase the range of applications of MR imaging.

1 INTRODUCTION

During the first year of clinical MR imaging only steady state free precession, T1-weighted and proton density-weighted clinical images were available [1-3]. Heavily T2-weighted spin echo (SE) sequences arrived suddenly in early 1982 and transformed the practice of MR [4-6]. Images obtained with these sequences detected intermediate or long T2 relaxation components in tissue. Even with the subsequent development of new classes of sequences such as fast SE, clinical diffusion weighted imaging and fluid attenuated inversion recovery, detection of signal from intermediate and long T2 relaxation components remains the dominant form of MR imaging for diagnosis of parenchymal disease in the brain and much of the rest of the body.

However even when clinical MR imaging began very short mean T2 relaxation components were recognized in cortical bone by Smith et al [7] and Edelstein et al [8]. This tissue showed no MR signal. The lack of signal was useful in providing a low signal background against which abnormalities in cortical bone with mean T2s sufficiently long to result in detectable signal could be recognized, but the absence of signal from normal cortical bone meant that there was no possibility of measuring normal values of mobile proton density (ρ_m), T1, or T2. Nor was it possible to study normal perfusion, and there was no opportunity for active contrast manipulation, little or no distinction between adjacent short T2 tissues, and no means of visualizing normal contrast enhancement. As a result study of cortical bone and other MR "invisible" short mean T2 tissues such as tendons, ligaments and menisci has been far more limited than that of tissues and organs such as brain, liver and muscle where tissue mean T2s are longer and MR signal from them can be readily detected with conventional clinical sequences. However even these longer mean T2 tissues contain significant proportions (e.g., 5-30%) of

“invisible” or undetectable short T2 relaxation components when they are imaged with conventional approaches.

To image short or ultrashort mean T2 tissues which produce no detectable signal with conventional sequences indirect methods have been used in which signal is obtained from surrounding or associated longer T2 tissues. When the low or zero signal tissue is surrounded by longer T2 tissue, signal from the latter tissue can be used to define the boundaries of the zero signal tissue. It is also possible to characterize some short T2 tissues by observing the impact their difference in susceptibility from that of a surrounding longer T2 tissue has on the signal obtained from the longer T2 tissue. For example some features of trabecular bone can be inferred by the effect this tissue has on the MR signal of adjacent red or yellow bone marrow [9]. A third indirect method of imaging short T2 components is possible when short and long T2 relaxation components are associated, and undergo magnetization exchange. The effect of saturation of the invisible short T2 components on this exchange can be observed on the signal from the detectable longer T2 components [10] and so inferences can be made about the short mean T2 tissue and/or the exchange between the shorter and longer T2 tissue components.

An alternative to using conventional sequences to study short T2 tissues in these indirect ways is to employ methods which directly detect signal from them. These usually involve the use of short or ultrashort echo time (UTE) sequences so that their MR signals can be detected before they have decayed to zero. There are now a variety of sequences of this type available in the clinical domain.

While T2 is a property of tissue which reflects dipolar and other nuclear (and electronic) interactions, frequently the effects seen with MR imaging are described more accurately by the observed T2, or T2*. This includes effects such as intravoxel dephasing due to Bo field inhomogeneity, tissue susceptibility differences, and chemical shift. Tissue susceptibility effects reflect the fact that solid tissues such as bone are generally more diamagnetic than soft tissues and that some tissues and fluids may be paramagnetic. The effects of some of these differences can be partly or almost wholly reversed by the use of spin echo (SE) sequences.

In some situations T2* effects may dominate and it is useful to recognize several different approaches to imaging of short T2/T2* components of tissue, fluid and materials.

(i) The first approach essentially sees the problem as one of imaging short or ultrashort T2 components and the basic approach has been to use short or ultrashort TEs to acquire and encode MR signals before they decay to a low level. This may be appropriate in situations where they are only minor tissue susceptibility effects present.

(ii) The second is magnetization transfer (MT) in which typically shorter T2 components are partially or completely saturated and the effect of this on longer (detectable) T2 components is observed. With short T2 tissues, and short and ultrashort TE data collections the definition of shorter and longer T2 components may change. Also off resonance MT pulses may directly saturate short T2 components of interest.

(iii) The third is susceptibility weighted imaging (SWI), where magnitude and/or phase data are used to recognize loss or change of signal from tissue due to susceptibility

effects. It can be direct and/or indirect (where tissue T2s* become too short to detect) and is qualitative. Quantitative Susceptibility Imaging or Susceptibility Mapping recognizes the fact that susceptibility differences effect slice selection and frequency encoding of MR signals and endeavours to correct for this, and to calculate values of T2* which accurately reflect both T2 and susceptibility effects.

(iv) Positive Contrast and White Marker Imaging. These techniques address the specific problem of imaging the effects of magnetic iron oxide particles (MIOPs) which shorten T2 and produce local disturbances of the magnetic field. The aim is to detect the presence of particles with positive signal, and at least in part address the problem of field distortion and so achieve credible recognition and quantification of the concentration of MIOPs.

(v) The fifth group of techniques is targeted at imaging in the presence of metal. Metals may have very large susceptibility differences from tissues and can produce very large susceptibility effects with loss of signal due to T2* shortening and gross image distortion. The primary objective in this situation is to deal with the image distortion and restore image integrity to a sufficient degree to make the images clinically useful.

There is overlap between these approaches, and they may be combined. In some situations it may be appropriate to ignore the effects of susceptibility differences in producing image distortion and regard the problem as one of detecting short T2 signals, whereas in other situations image distortion due to susceptibility is the primary problem that needs to be addressed. There has been considerable interest in these approaches and there are now solutions or partial solutions available to problems that have appeared intractable for many years.

2 TISSUE, FLUID AND MATERIAL PROPERTIES

The tissues of the human body can be divided into those that are "visible" in the sense that they provide detectable signal with clinical MR systems and those that are "invisible" because their mean T2s or T2*s are too short to provide a detectable signal. All tissues have multicomponent T2s. This means that they contain a mixture of short and long T2 components. The invisible tissues have a majority of short T2 components and a minority of long T2 components. The latter components typically do not provide enough signal to be detectable in relation to image noise levels. The "invisible" tissues of the body such as brain, liver and muscle have a majority of long T2 components which produce signal with conventional techniques. They also have a minority of short T2 components which do not contribute significantly to the detectable signal.

There is no agreement as to what constitutes a short TE and what is an ultrashort TE, and there is argument about how TE should be measured for tissues with short T2s (11-13), but for simplicity, a short TE is taken to be less than 10 ms and an ultrashort one to be less than 1 ms. It is also possible to define short T2/T2* as less than 10 ms and ultrashort as less that 1 ms. This reflects the fact that with older systems and SE sequences tissues with T2 or T2* less than 10 ms produced little or no signal and were "invisible". With more recent systems and gradient echo sequences the cut off is closer to 1 ms.

Within the invisible group of tissues (mean T2 < 10ms) it is possible to differentiate a first group including tendons, ligaments, and menisci with short mean T2s of about 1-10 ms, a second group including cortical bone and dentine with ultrashort mean T2s of 0.1-1 ms. There is also a third

group including dental enamel, protons in membranes, and molecules as well as crystalline bone with super short mean T2s of less than 0.1 ms. Materials can also be classified in a similar way.

An important factor in this context is the magic angle effect [14,15] since it can greatly increase the T2 of short T2 tissues such as tendons, ligaments and meniscii. When the orientation of tissues which contain highly ordered collagen is changed their T2 varies from a minimum at $\theta = 0°$ where dipolar interactions are greatest, to a maximum where $3 \cos^2 \theta - 1 \approx 0$ and $\theta = 55°$. θ is the orientation of the fibers to Bo. The increase can be large, for example from 0.6 ms to 21 ms [14] or from 7 to 23 ms [15] in the Achilles tendon.

Another phenomenon is directional susceptibility in tendons whereby their bulk magnetic susceptibility varies with orientation to Bo with signals at the water end of the proton spectrum when fibers are parallel to Bo and at the fat end of the spectrum (lower frequency) when fibers are perpendicular to Bo [16]. The difference is relatively large (of the order of three parts per million).

The ρ_m of tissues also varies markedly with bone having a ρ_m of 15-20% and semi-solid tissues such as tendons and ligaments values of 60-70%. ρ_m is generally a more important factor in generating contrast with short T2 tissues than it is with longer T2 tissues. The low ρ_m for bone places a limit on the maximum signal than can be obtained from it.
The mean T1s of some tissues with a majority of short T2 components are short with cortical bone having a particularly short T1, in fact less than that of fat [17]. The relative differences in

mean T2 or T2* between normal and abnormal tissue are generally much greater than those in mean T1.

Relative to air, soft tissues generally show a susceptibility difference of about -9 ppm (parts per million), and bone and calcified tissue about -11 ppm. By comparison the principal peak of fat resonates at about -12 ppm. Paramagnetic materials show small positive frequency shifts and superparamagnetic materials greater positive shifts. Metals including, for example, titanium, metal alloys and some types of stainless steel may show very large positive shifts of 10s to 1000s of ppm. These changes in field may be considerably greater than those of machine gradient fields used to encode MR signals and may therefore cause image distortion.

In disease, increases in T2 are frequently seen but decreases in T2 may be seen with increased iron content and in other disease processes. Loss of magic angle effect may be seen in degeneration and fibrosis.

3 ACQUISITION METHODS FOR SHORT T2/T2* COMPONENTS

Some of the techniques now being used to directly detect signal from tissues on clinical systems have been used in materials science and tissue studies using small bore high field spectrometers for many years. Methods now in use on lower performance clinical systems are summarized in Table 1. The prototype sequence for imaging short T2 tissues is Single Point Imaging (SPI) where a single point in k-space is acquired with an ultrashort TE. This is typically used with 3D phase encoding which unfortunately makes the technique time consuming even with optimized k space sampling [18].

It is possible to acquire several points at a time which makes the sequences more time efficient but results in longer TEs for the additional points [19]. There are also Free Induction Decay (FID) based techniques where a radial line of k-space is acquired from the center out [20]. This can be coupled with long T2 water and fat suppression to selectively image short T2 components [21]. Other trajectories in k-space are possible including a Stack of Spirals [22, 23].

A particularly innovative method of imaging short T2 components is to divide the excitation pulse into subpulses and acquire data after each of these pulses. This is known as Swift Imaging with Fourier Transformation (SWIFT) or Simultaneous Excitation and Acquisition (SEA). The acquired data needs to be deconvolved with the excitation pulse, but the end result is a much more time efficient acquisition than with typical 3D acquisitions [24-33]. Other techniques which have only been used in the pre-clinical phase include methods in which radiofrequency (rf) absorption is assessed rather than signal detection [34]. The methods borrow from continuous wave spectroscopy and electron spin resonance where electronic T2s are extremely short and may be of the order of a microsecond.

4 MAGNETIZATION PREPARATION AND PULSE SEQUENCES SIGNAL SUPPRESSION TECHNIQUES

Traditional contrast mechanisms exploiting differences in ρ_m, chemical shift and other tissue properties can be used in ways that are well known from conventional imaging.

There are also numerous old contrast mechanisms operating in new ways as well as new contrast mechanisms that are of interest in imaging short/ultrashort T2/T2* components in tissue. Some of these are listed in Table 2. They are typically used in conjunction with the acquisition

techniques mentioned in the previous section. These provide a wide range of possible ways of effecting magnetization. For example, 90°, 180°, fat saturation and magnetization transfer pulses can all be used to suppress unwanted long T2 signals and to produce T2 contrast in the short T2 range. There are also new potential mechanisms (as far as clinical imaging is concerned) involving reductions in dipolar coupling [35, 36] and double quantum filters [37, 38]. These techniques are usually used in conjunction with one of the acquisition methods described in the previous section.

5 MAGNETIZATION TRANSFER (MT)

This differs for clinical approaches in that use of short TE acquisitions makes it possible to study MT in tendons, ligaments, menisci and cortical bone [39]. The definition of the bound (short T2) and free (long T2) pools may change because previously undetected signals are included in the free (detectable) pool. Direct saturation is a greater problem. There may also be a greater degree of magnetization exchange present in short mean T2 tissues. The technique provides indirect access to ultrashort and even supershort T2 relaxation components in tissues with super short T2s of about 5-15 μs which are not directly accessible with most UTE techniques.

6 SUSCEPTIBILITY WEIGHTED IMAGING

Susceptibility weighted imaging has been in use for a considerable time. It usually exploits reductions in T2* to develop contrast and imaging may utilize both magnitude and phase data [40, 41]. The T2* may be so short that this becomes in effect an indirect form of imaging utilizing the reduction in signal of adjacent longer T2 components. The applicability of the technique and related methods can be expanded by utilizing forms of data collection with short

or ultrashort TEs that can detect signal from very short T2* components [42, 43]. Quantitative methods of imaging susceptibility changes need to account for errors in spatial encoding which may require solutions to a complex inverse problem [44, 45]. To date it has mainly been applied to brain imaging. Phase and frequency changes can be detected in fibrous structures even with UTE sequences [43].

7 POSITIVE CONTRAST AND WHITE MARKER IMAGING

These forms of imaging have been used to describe the particular situation with MIOPs which may not only reduce T2 and T2* but produce local field distortions. A variety of different methods are available. It is possible to selectively excite only off resonance spins. It is also possible to apply an additional gradient so that only the magnetization of spins in regions affected by MIOPs is refocused. The inhomogeneities from the particles induce echo shifts and these can be used to calculate and correct for the field distortion. The images reflect both tissue MIOP concentration and deviations of the local magnetic field produced by the particles [46-50]. Techniques using SWIFT [51] and UTE [52, 53] have also been successful for imaging MIOPs.

8 IMAGING IN THE PRESENCE OF METAL

When forms of metal are implanted in the body an extreme situation may arise in which there is very marked T2* shortening but the image distortion is so great that images of regions adjacent to the metal are uninterpretable. This has been a longstanding problem. A variety of solutions have been proposed in the past, but these have had relatively little clinical impact. The development of Multi-Acquisition Variable-Resonance Image Combination (MAVRIC) [54], and Slice Encoding for Metal Artefact Correction (SEMAC) [55] has resulted in a remarkable

degree of restoration of images which are grossly degraded by metallic artefact when imaged using conventional approaches. With MAVRIC irradiation at a range of different off resonance frequencies is used to detect signals whose resonant frequency has been shifted by metal, and these are then combined. With SEMAC, phase encoding is used during slice selection to reallocate signals that are improperly located by the slice selection process. View angle tilting (VAT) [56] is also used with this technique to correct for errors with in plane spatial encoding. Faster versions [57] and a MAVRIC -SEMAC hybrid [58] have also been implemented. UTE alone shows some improvement over conventional techniques but this may be less than that available with SEMAC and/or MAVRIC [59].

9 IMAGING OF BOUNDARIES INVOLVING SHORT T2/T2* TISSUES

Structures of interest in the short T2 range include thin layers such as those in entheses, periosteum and the deep layers of articular cartilage where there are short T2 tissues, susceptibility effects between the soft (or semi-solid) tissues and bone, as well as partial volume effects between these tissues which are present over curved surfaces. In this situation high resolution 3D isotropic UTE imaging often has a distinct advantage since it can detect short T2/T2* signals as well as reduce the impact of susceptibility differences and partial volume effects. Imaging of ordered fibrous structures such as tendons and ligaments include some of the above issues, but in addition loss of contrast of the fiber structure or "blurred" appearance may arise from obliquity of the fibers relative to the imaging slice. This effect may simulate changes due to disease. There are also distinctive artefacts at boundaries from chemical shift effects including those associated with radial acquisitions.

10. FUTURE

The future of this area is of course uncertain, but obvious developments include perfusion, diffusion for short T_2 species for example using a stimulated echo approach greater emphasis on quantitative including bicomponent approaches.

There is also likely to be a shift towards applications outside the musculoskeletal system. These are likely to include the brain and cancer. Direct imaging of the protons in myelin is possible using dinical systems. This may be more specific than indirectly imaging the water associated with it. Imaging of short T_2 comgonents in fibroglandular tissues such as the breast and prostate may add useful information in cancer imaging.

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Table 1 - Short and Ultrashort TE Imaging Techniques		
Technique	Radiofrequency pulses and gradient	k-space trajectory
Single point (18)	Non selective hard pulse with gradient applied	3D point by point
Multipoint (19)	Hard pulse with gradient applied	3D partial lines Several points
UTE (20)	2D two half pulses 3D hard pulse No gradient applied during rf	Radial from center out FID acquisition
WASPI (21)	3D hard pulse with gradient on. Preparation pulses with water and fat signal suppression	Radial from center out, FID acquisition
Gradient echo	2D, 3D	Radial rephasing gradients
Cones Spiral [60] Stack of spirals (22-23) Echo Planar Imaging (61) bSSFP PETRA (77) ZTE [78-80]	3D	Spiral, from center out, FID data collection
SWIFT, SEA (23-33)	3D rf sub-pulses	Radial, center out

Table 2 – Magnetization Preparation, Pulse Signal Suppression Techniques and Pulse Sequences	
Mechanism	Effect
90° pulse [62-66]	Selective excitation of short T2/T2* components with or without subsequent long T2 signal suppression
180° pulse [62-66]	Selective excitation of short T2/T2 components and inversion of long T2 components
180° pulse and nulling [66]	Selective inversion of long T2/T2* components with nulling
Off resonance saturation [67-68]	Selective reduction of short T2 components
Magnetization transfer (MT) [39]	Selective reduction of short T2 components with MT to detectable T2 components
Fat saturation and water excitation [69]	Selective reduction of fat signal
Later image subtraction from first image [70, 71]	Selective reduction of long T2/T2* components
Susceptibility and spectral mapping UTESI [42, 43]	Direct mapping of field and frequency change as well as susceptibility differences
R* – IDEAL – UTE [72]	Combination of fat suppression and R2* measurement of short T2/T2 components
Double quantum filter [37, 38]	Comparison of spin echo and magic sandwich echo imaging
Dipolar imaging [35]	Selective imaging of protons with strong unaveraged dipolar coupling
Dipolar Anisotropy Fiber Imaging [73]	Systematic exploration of signal at different orientations of fibers to B_0 application in short T2 tissues
$T_1\rho$ imaging [74-75]	Applicable to short T2 tissues
$T_2\rho$ imaging [74]	T2 in the rotating frame
Phase shift due to flow can be specifically targeted [76]	Detection and measurement of high velocity flow