SYLLABUS

CONTRAST MECHANISMS FOR MR IMAGING OF TISSUES AND FLUIDS
WITH SHORT T2s AND/OR T2* s

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 and fluids in the short T2 or T2* range which can provide visualization of anatomy which has not previously been seen. Particular methods have been developed to target susceptibility effects, allow accurate quantitation by compensating for anatomical distortion produced by these effects. Specific methods have been developed to image the effects of magnetic iron oxide particles with positive contrast and to correct for loss of signal and image distortion near to metal due to gross susceptibility effects. These methods are likely to provide interesting options and increase the range of applications of MR imaging.

1 INTRODUCTION

To image short or ultrashort 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 this 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 of their difference in susceptibility from that of the surrounding longer T2 tissues 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 [1]. A third indirect method 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 detectable longer T2 components [2] and so inferences can be made about the short T2 tissue and/or the exchange between the shorter and longer T2 components.

An alternative to using conventional sequences to study short T2 tissues in these ways is to employ methods which directly detect signal from them. These usually involve the use of short or ultrashort echo time (UTE) sequences to detect MR signals 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 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 difference approaches to imaging of short T2/T2* components in relation to underlying susceptibility differences.

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

(ii) The second is Susceptibility Weighted Imaging (SWI), where magnitude and phase data are used to recognize loss of signal from tissue due to susceptibility effects. It can be direct and/or indirect (where T2* become too short to detect) and is qualitative [3,4].
(iii) Quantitative Susceptibility Imaging (QSI) is the third approach. This technique recognizes the fact that susceptibility differences effect the spatial encoding of MR signals and endeavours to correct for this, and to calculate values of T2* which accurately reflect T2 and susceptibility effects [5,6].

(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 [7,8].

(v) The fifth group of techniques is targeted at imaging in the presence of metal. Metals can produce very large susceptibility effects with loss of signal due to T2* effects 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 for the images to be clinically useful [9,10].

There is some overlap between these approaches. 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. Over the last year there has been considerable interest in these approaches with solutions now appearing to some problems that have appeared intractable for many years.

2 TISSUE 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* 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 comparison 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 the signals seen 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], but for simplicity, a short TE is taken to be less than 10 ms and an ultrashort less than 1 ms. It is also possible to define short T2/T2* as less than 10 ms and ultrashort as less than 1 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 large molecules as well as crystalline bone with mean T2s less than 0.1 ms.

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

A recently described 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 [12]. The difference is relatively large (of the order of three parts per million).

The \(\rho_m\) of tissues also varies markedly with bone having a \(\rho_m\) of 15-20% and semi-solid tissues such as tendons and ligaments values of 60-70%. \(\rho_m\) is generally a more important factor in generating contrast with short T2 tissues.
than it is with longer T2 tissues. The low $\rho_m$ 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 (15). 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. By comparison paramagnetic materials may show small positive chemical shifts and superparamagnetic materials greater positive shifts again. Metals including, for example, titanium and some types of stainless steel may show large positive shifts of 10s to 100s (or more) ppm. These changes in field may be considerably greater than those used by applied machine gradients to encode MR signals and may therefore cause image distortions.

3 ACQUISITION METHODS FOR SHORT T2/T2* COMPONENTS OF TISSUE
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 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 very time consuming [13].

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 [14]. There are also Free Induction Decay (FID) based techniques where a radial line of k-space is acquired from the centre out [15]. This can be coupled with long T2 water and fat suppression to selectively image short T2 components [16]. Other trajectories in k-space are possible including a Stack of Spirals [17].

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. 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 [18-21]. 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 [22]. The methods borrow from older forms of spectroscopy and electron spin resonance where electronic T2s are extremely short and may be of the order of a microsecond.

4 MAGNETIZATION PREPARATION, CONTRAST MECHANISMS AND SIGNAL SUPPRESSION TECHNIQUES
Traditional contrast mechanisms exploiting differences in $\rho_m$, chemical shift and other tissue properties can be used in ways that are well known from conventional imaging. There are also numerous new contrast mechanisms, or old contrast mechanisms operating in new ways 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 detailed 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 quite new potential mechanisms involving double quantum filters [23] and reduction in dipolar coupling [24, 25]. These techniques are usually used in conjunction with one of the acquisition methods described in the previous section.

5 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 “Filler effect” may simulate changes due to disease. There are also distinctive artefacts at boundaries from chemical shift effects including those associated with radial acquisitions.

6 CLINICAL APPLICATIONS
There are now 2D and 3D UTE sequences available with imaging times of 5-6 minutes and clinically acceptable spatial resolution. In general the difficulty of acquiring short/ultrashort T2/T2* signals means that invisible tissues are imaged at lower spatial resolution, but with signal levels and contrast that are not attainable with conventional techniques. There is a balance necessary to obtain qualitative and/or quantitative information which is novel at spatial resolutions that are sufficient to show anatomical features with acceptable clarity.

Cortical Bone
Cortical bone can be demonstrated with high signal [26]. Its T2 is about 0.4 ms and T1 250-350 ms at 1.5T which is shorter than typical values for fat. Its mobile proton density is about 15-20%. This data can be used both for quantitative [27] and qualitative studies.

Tendons, Ligaments, and Entheses
With conventional sequences the signal from tendons, ligaments and entheses is very low or zero. Entheses are the attachment sites of tendons, ligaments and capsules to bone. They typically contain calcified and uncalcified fibrocartilage (which both have short T2s). These tissues have a major role in dispersing mechanical stress at the junction between flexible tendons or ligaments and rigid bone.

Tendons and ligaments contain endotenon and endoligament which have longer T2s than the fibrous components (although they are still in the short T2 range) and less magic angle effect. Uncalcified fibrocartilage has a longer T2 than the tensile components of tendons as well as an increase in T2 due to the magic angle effect although this may be present over a wider range of angles reflecting the more dispersed arrangement of the fibers within it. Magic angle effects may result in a pronounced longer T2 line adjacent to bone from fibers which change in direction from parallel to the bone surface to perpendicular to it as they insert into bone.

Tendons and ligaments can readily be seen with UTE sequences and entheses have been studied in detail [28,29]. Off resonance fat suppression pulses reduce the signal from short T2 fibers (which have a broad line width) more than endotenon, or enthesis fibrocartilage (which have longer T2s and narrower line widths) and this can be an effective contrast mechanism. Inversion pulses may be used to selectively invert and null enthesis fibrocartilage (exploiting its longer T2) and so visualize this tissue with high contrast. It is also possible to visualize oblique and transverse fibres in tendons using a combination of fat suppressed UTE sequences to reduce short T2 tissue water components and magic angle imaging to lengthen the T2 of the fibers at particular angles to Bo.

Entheses are selectively involved in the seronegative spondyloarthropathies such as ankylosing spondylitis and psoriatic arthropathy. The differential diagnosis is of a loss or reduction in fascicular pattern and includes normal sesamoid fibrocartilage, partial volume effects with a loss of fascicular pattern due to the Filler effect, magic angle effects and disease.

The Menisci of the Knee
The central region of the adult meniscus has no blood supply (the white zone) while the more peripheral region (the red zone) has a blood supply. Healing of tears in the white zone is generally unsatisfactory and the preferred surgical strategy is usually resection of the torn tissue. Suture and repair is more successful in the red zone. Distinction between the two zones has not previously been possible with MR imaging using conventional sequences in spite of repeated attempts. Using UTE sequence and gadolinium based contrast enhancement the two zones can be distinguished [30] and provide a basis for surgical planning.

Anatomical descriptions of the meniscus include circumferential, radial, lamella, vertical and meshwork fibre groups. With conventional imaging some radial fibres may be distinguishable from the majority of circumferential fibres but with UTE and magic angle imaging each of these fibre groups can be identified. It is also possible to distinguish the internal structure of the meniscus from that of the root ligaments, and the more central cartilaginous region from the peripheral more fibrous region of the meniscus.
The fibre structure provides a basis for understanding the biomechanics of the knee and the various patterns of tear in the meniscus. It also helps in distinguishing magic angle effects within fibre groups from degenerative changes.

The temporomandibular joint disc
This shows some of the characteristics of the meniscus of the knee. Fibre structure can be seen. These are lamella, circumferential antero-posterior and superior-inferior fibres identifiable.

Articular Cartilage
Articular cartilage has a range of T2s from about 1 to 30-40 ms from deep to superficial. With conventional imaging the deep radial and calcified layers as well as the adjacent subchondrial bone are invisible. With UTE imaging signal is detectable from the deeper layers of cartilage allowing more superficial cartilage and subchondral bone to be distinguished [31]. This provides a basis for study of the junction between cartilage and bone which may be of importance in the pathogenesis of osteoarthritis. Complex magic angle effects are seen because of the fibrous architecture of articular cartilage.
In disease there may be both loss of signal from the deep layer and increased extent of the short T2 associated with deep layers. There is electron microscope evidence of thinning of the deep layers in osteoarthritis but preservation in osteomalacia.

The Spine
Imaging of the spine includes many visible tissues so that attention to date has focused on invisible structures such as (i) entheses (ii) the end plate of the disc, and (iii) short T2 components in the intervertebral discs and red bone marrow. Fibrocartilage has also been demonstrated in the functional entheses of the transverse ligament of the Atlas and the alar ligament. The dorsal capsule of the facet joints of the lumbar spine are also subject to cartilagenous metaplasia. Evidence of iron deposition can be seen in intervertebral discs in thalassemia.

7 QUANTITATIVE APPROACHES
Quantitation may include specific MR properties including in particular T2 and T2*, the properties of the remaining signal after long T2 components are suppressed, and the ratio of short T2 to long T2 components. There are also other features such as the magic angle effect and dipolar contrast that can be characterized.

There are issues about measuring T2 and T2* in the correct range, characterizing different T2 components (e.g., long and short) including their relative proportions and dealing with artefacts from various sources. However quantitation may be confounded by slice selection and eddy current problems and by contamination of short T2 components with long T2 components which are present in higher concentration.

8 CONCLUSION
Imaging of short T2 and T2* components is a rapidly expanding area which has seen a convergence of methods targeted at tissues with short T2 components, susceptibility effects, MIOP imaging and metal artefact control. The methods have borrowed from solid state imaging, spectroscopy including continuous wave methods, electron spin resonance and MR microscopy. The much lower technical performance of clinical systems compared with small bore spectrometers is a major limitation, but innovative methods for overcoming this problem are now being developed.

The tissues of interest have mainly been in the musculoskeletal system but all tissues of the body have some short T2 components and study of these may prove to be of diagnostic interest. Some techniques such as imaging in the presence of metal are likely to be immediately useful in the clinical domain while others may require validation and comparative assessment to establish their role. Sodium and phosphorous studies may also be of interest. Quantitative approaches may be particularly useful given the large fractional changes in T2 and T2* that are frequently seen in disease. The techniques used for imaging often require high gradient performance with control of short term eddy currents to a level not previously necessary in clinical MR systems. In spite of these and other technical difficulties, application to the study of short T2 and T2* tissues appears likely to be an area of MR imaging of considerable importance in the near future.
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   [Distinction of red and white zones.]

