T1, T2 AND T2* IN PATHOLOGY

How Pathology Changes T1 and T2

The main usefulness of T1, T2 and T2* in MRI comes not from their meaning – since they are not directly related to any physiological parameter – but from their sensitivity to microscopic pathological changes in tissue. This is a very interesting and important point:

T1, T2 and T2* can reveal microscopic pathologies on a much smaller scale than the voxel size (although these pathologies must permeate a macroscopic region on the order of the voxel size to be detected, due to MRI’s low sensitivity).

Pathologies can appear as either hypointense (dark) or hyperintense (bright) on T1 or T2 (or T2*) weighted images. Pathologies which are isointense (same as surroundings) are invisible, although a pathology might be isointense on a T1 weighted image but hyper/hypo intense on a T2 weighted image!

The following tables summarize some typical pathologies and their associated appearances:

<table>
<thead>
<tr>
<th>Hypointense (Shorter) T1</th>
<th>Hyperintense (Longer) T2</th>
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</thead>
<tbody>
<tr>
<td>Edema</td>
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<td>Tumor</td>
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<td>Infarction</td>
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<td>Inflammation</td>
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<td>Hyperacute hemorrhage</td>
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<td>Chronic hemorrhage</td>
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<td>Low proton density</td>
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<td>Calcification</td>
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<td>Flow void</td>
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<td>Tissue loss</td>
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The above are just rules of thumb and should never be used to make any sort of conclusive diagnosis. Leave those to the trained radiologists! We are not in the business of medical diagnosis, but rather in the business of understanding the reason for T1 and T2 contrast.

T1 Hyperintensity Usually Means A Shorter T1. T2 Hyperintensity Usually Means A Longer T2.

CSF, which has a long T1, appears dark on T1-weighted images. This is not a “law of nature” but has to do with the way T1 contrast is usually created in MRI images, via rapid pulsing or inversion recovery. For both, high T1 values appear darker, as discussed in the lecture dealing with creating T1 and T2 contrast.

On the other hand, T2-weighted sequences often rely on some form of spin-echo, which has a signal dependence of the form

$$s \propto e^{-TE/T2}$$

As T2 is increased, the signal decays more slowly, which results in hyperintensity (compared to normal, non-increased T2). This means that hyperintensity corresponds to longer T2s. It’s very important not to automatically assume that hyperintensity means there is “more” of something. It all depends on the signal equation and type of contrast!

A Brief Example: Multiple Sclerosis

Multiple Sclerosis (MS) is an inflammatory disease of the central nervous system which affects about 2 million people worldwide. In MS, prolonged inflammation leads to demyelination of neuronal
axons\(^1\), resulting in symptoms ranging from impaired vision and fatigue to depression and musculoskeletal weakness. There are two major theories for why inflammation occurs: either via an autoimmune response, or via failure of myelin producing cells. There is no cure for MS, but drugs can delay its onset and effects\(^2\).

The diagnosis of MS is often done by combining clinical evaluation with MRI imaging. The hallmark of MS is the appearance of lesions on the MRI scans. These are small round/oval structures that result from the underlying damage to brain tissue through the inflammatory processes. Most lesions appear hyperintense on T\(_2\)-weighted images and hypointense on T\(_1\)-weighted images. It is fairly common to see hyper-T\(_2\)/hypo-T\(_1\) pathologies in MRI, and we will explain why in a bit. This means that the T\(_1\) and T\(_2\) images sometimes contain the same information.

The problem with T\(_2\) images is that hyperintense lesions are hard to tell apart from the cerebrospinal fluid (CSF). A sequence known as FLAIR (FLuid Attenuated Inversion Recovery) precedes the T\(_2\)-weighting imaging with an inversion recovery designed to null the CSF signal based on its long T\(_1\).

In this Proton Density (PD) image, as little T\(_1\) and T\(_2\) contrast is created (e.g. by taking long TRs and short TEs). "Typical" MS lesions appear hyperintense.

In this T\(_2\)-weighted image, the same lesions also appear hyperintense. However, they are difficult to identify due to the bright CSF. This is why FLAIR is used (next).

The FLAIR image is T\(_2\)-weighted, but it uses the long T\(_1\) value of the CSF to null its signal with a special pulse sequence. This makes identifying the T\(_2\)-hyperintense lesions much easier.

Another image type often used is a T\(_1\)-image after the injection of a contrast agent such as gadolinium (Gd-DTPA, or Gd for short). The effect of Gd is to shorten T\(_1\) substantially. As we have seen, rapid pulsing tends to saturate long T\(_1\), which is why CSF appears dark on T\(_1\) weighted images. Gd therefore causes hyperintensity wherever it reaches in the brain. Not all hyperintense T\(_2\) lesions are also hyperintense on T\(_1\) weighted contrast enhanced scans, but not always\(^3\).

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\(^1\) This means the myelin sheath that surrounds the neurons is somehow damaged or completely stripped. This, in turn, leaves the neuron vulnerable to damage, as well as impairs its ability to conduct electrical impulses.

\(^2\) Weizmann holds the patent rights for Copaxone, one of the most influential drugs on the market for treating MS.
The brain is special in having a **blood brain barrier** (BBB) which prevents contrast from entering the brain under normal circumstances. Lesions tend to "light up" whenever there is a breakdown of this barrier due to the inflammatory processes and the immune response at the site.

From a histopathological point of view, active lesions are a site of myelin breakdown. They are filled with macrophages, lymphocytes, and other cells, as well as myelin debris (taken up by the macrophages). Chronic (T₁-hypointense) inactive lesions have reduced cellular density, reduced inflammation and no active demyelination.

**T₂* Requires Extra Care**

We will defer discussion of T₂* to a later point in this lecture, for the simple reason that it is a very tricky parameter to measure. A large part of it comes from hardware imperfections which are obviously uninteresting and patient-independent. However, some T₂* decay is intrinsic to the tissue and is interesting. T₂* is created by field inhomogeneities, and these are induced on a microscopic scale whenever one magnetic material interfaces with another having a different magnetic susceptibility. The greatest inhomogeneity is created at air-tissue interfaces. These so-called **susceptibility artifacts** can be on either a macroscopic scale – as is near the air filled sinuses – in which case they are uninteresting and lead mainly to image artifacts; or they can be on a mesoscopic scale, much smaller than the voxel size, as can be at the interface between microscopic tissue in the brain. Such **mesoscopic susceptibility artifacts** can generate interesting and viable tissue contrast which is also sensitive to many changes. Extra care is needed to isolate the mesoscopic susceptibility effects from field imperfections and macroscopic susceptibility artifacts, since they all lead to a distortion in B₀.

**Outline of Relaxation Theory**

**Spins Are Subjected To Microscopic Fluctuating Magnetic Fields Due To Their Thermal Motion**

We’ve already remarked that spins are subjected to fluctuating fields due to their rotational thermal motion (see “Spin Dynamics” lecture). It is these fluctuating fields that lead to relaxation. The fluctuating fields B₀ felt by a spin can be composed into components transverse & longitudinal to the main B₀ field:

\[ B_D(t) = B_{D,\perp}(t) + B_{D,\parallel}(t). \]

It is instructive to assign some orders of magnitude to these fluctuations. We define the **rotational correlation time**, \( \tau_r \), in an informal manner as follows: imagine opening your eyes at \( t=0 \), then shutting your eyes and re-opening them at some time \( t>0 \). If we open the eyes "fast enough", you
can predict that the orientation of the molecule will remain close to its orientation at \( t=0 \). However, after a certain amount of time, you will not be able to predict the orientation of the molecule at all. The time-scale at which this happens is the rotational correlation time.

The correlation time of a molecule will depend on the temperature, its environment and its size. For a spherical molecule of hydrodynamic radius \( r \) in a liquid with viscosity \( \eta \), Stoke derived an expression for the rotational correlation time:

\[
\tau_c = \frac{4\pi \eta r^3}{3kT}.
\]

**Number time.** For water (\( \approx 18 \text{ Da} \)) at room temperature it is about one picosecond = \( 10^{-12} \) seconds. For ubiquitin (\( \approx 9 \text{ kDa} \)) in water, \( \tau_c \) is a few nanoseconds.

How about the size of the fluctuations? In a water molecule the sources of fluctuations are dipolar and can be divided into intra- and inter-molecular. Because the dipolar field goes as \( r^3 \), the intermolecular contributions are only a second order effect, and we are left with the intramolecular ones, exerted by one hydrogen in H\(_2\)O on the other. First, we must examine the geometry of the water molecule:

The dipolar field created by one spin at the position of the other is:

\[
B = \frac{\mu_0}{4\pi} \frac{3\hat{r} (\mathbf{m} \cdot \hat{r}) - \mathbf{m}}{r^3}
\]

where \( \mathbf{r} \) is the vector connecting both hydrogen atoms. We see that the maximal and minimal values of \( B \) occur when \( \mathbf{m} \) and \( \mathbf{r} \) are either parallel or antiparallel, leading to the values:

\[
|B_{\text{max}}| = \frac{\mu_0 |m|}{2\pi r^3}
\]

Hence the magnitude of the fluctuations vary between \( \pm |B_{\text{max}}| \). Fixing \( |r| = 1.52 \text{Å} \) and \( |m| = 1.4 \times 10^{-26} \text{ J/T} \) (\( ^1\text{H} \) magnetic moment), this amounts to

\[
|B_{\text{max}}| \approx 8 \times 10^{-3} \text{ T} = 8 \text{ Gauss}.
\]

To a first approximation, as we will argue next, the longitudinal fluctuating field causes transverse relaxation and the transverse fluctuating field causes the longitudinal relaxation.

**The Longitudinal Fluctuating Field Leads to \( T_2 \) Relaxation**

We start by showing how a fluctuating longitudinal field leads to transverse \( T_2 \) decay. Imagine exciting a spin onto the \( xy \) plane. Without the fluctuating field, it would just execute precession and make a phase \( f = gB_0t \) after precessing for a time \( t \). With the fluctuating field along \( z \) the precessing frequency fluctuates as well, with the end result being a slightly different precessing frequency at the end, \( f + \Delta f \), where \( \Delta f \) depends on the exact nature of the fluctuations (imagine turning a wheel with a shaking hand):

No fluctuations

("Firm hand")

With fluctuations

("Shaky hand")

Note here \( \Delta f < 0 \)

Now imagine a number of spins. In the absence of fluctuations they would all make the same angle. In the presence of fluctuations, they would fan out (remember, each spin feels a different fluctuation):
Many spins, no fluctuations. (microscopic view)

This is what happens microscopically. Now, the macroscopic magnetization is the (vector) sum of the microscopic magnetization. What happens when you sum vectors that don’t point in the same direction? They (partially) cancel out. Example:

Adding up slightly “out-of-phase” magnetization vectors leads to signal loss (smaller vector sum).

When all vectors are in-phase there is no signal loss.

You can now see why the magnetization in the plane decays:

The fluctuating z-field causes the spins to spread out (dephase), and hence add up destructively, leading to a decay of the macroscopic magnetization vector, M.

How fast does M decay – what determines T₂? Quite simply: the rate of fluctuations. Fast fluctuations will result in lesser dephasing and hence slower decay.

An analogy from physics might help you see this: think of diffusion. An ink is injected into two cups containing two fluids, one denser than the other. In which cup will the ink spread further? In the less dense fluid. The idea is that the additional collisions it undergoes per unit time in the dense fluid slow the ink down and minimize the distance it can diffuse to at a given amount of time. A similar process occurs when discussing T₂: you can think of the spin’s phase as “diffusing” under the action of the fluctuating field – slower fluctuations mean “fewer collisions” and hence a “less dense” environment, leading to greater “diffusion” (dephasing, in our case).

This directly relates to molecule sizes, because:

Large molecules
  → Tumble slowly
  → Slow fluctuations
  → Short T₂ (fast decay)

Small molecules
  → Tumble fast
  → Fast fluctuations
  → Long T₂ (slow decay)

Hence, large molecules such as proteins have short T₂s, and as a result suffer from both broad linewidths (leading to a lack of spectral resolution) and smaller signal intensities (leading to lesser SNR). This is one of the reasons why the study of large proteins can be very challenging.

We can draw this graph:

In tissue, water can be free (A) or in the vicinity of large macromolecules (B), which slow it down and lengthens its T₂:

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We can draw this graph:
In solids, where motion is greatly reduced, $T_1$ can be extremely short.

**The Transverse Fluctuating Field Leads to $T_1$ Relaxation**

Remember one of our earliest questions when discussing relaxation: how can it be that a tiny RF component compared to $B_0$ can excite the spins? The answer we found is that the RF field can excite the spins if it is on resonance. We can reverse the reasoning and state that a transverse fluctuation will appreciably affect the $z$-component of the spins if it is resonant.

If we think of the transverse fluctuating field in terms of its frequency components, we might imagine that when $\tau_c \approx 1/(\gamma B_0)$ – that is, when the fluctuations are on resonance – the longitudinal relaxation will be most effective, leading to the shortest possible $T_1$. Conversely, as $\tau_c$ becomes slower or faster than $1/(\gamma B_0)$, we can predict that it will be less effective at inducing longitudinal relaxation, leading to longer $T_1$.

This general analysis turns out to be quite true, and we can draw a general curve relating the correlation time and $T_1$:

An important question now arises: on which “side” of this curve are we in biological tissue? A typical MRI magnet is ~3T and has a frequency of ~127 MHz for protons. The correlation time for free water is ~1 picosecond, so $1/\tau_c$~THz=10^{12}$ Hz, and we are well to the right of the “dip”.

**$T_1$ Increases With Increasing $B_0$; $T_2$ Is Largely Unaffected by $B_0$**

Our $T_1$ curve also shows us that $T_1$ is expected to increase with $B_0$. Since we are to the right of the dip, we see that increasing $B_0$ will “push” the curve to the right and decrease $1/T_1$, or increase $T_1$. This is indeed consistent with what we see in actual experiments. This is illustrated in the following schematic graph:

$T_2$ tends to slightly decrease with increasing field strength. This seems not to be indicated by our diagram, which does not depend on $B_0$. However, our theory was incomplete and omits more complicated effects (e.g., the transverse field can also contribute to $T_2$ relaxation by transferring magnetization from longitudinal to transverse states). These corrections tend to be small to negligible in fluid tissue. In semi-fluid/solid tissue such as bone and cartilage this approximation is somewhat less valid. We will not treat these more complicated cases here.

The increases in $T_1$ are usually sub-linear and lead to better $T_1$ contrast. To see why this is so, consider the steady state signal in a spoiled GRE sequence:

$$S \propto \frac{1 - e^{-TR/T_1}}{1 - \cos(\alpha)e^{-TR/T_1}} \sin(\alpha).$$

Plotting this as a function of $TR/T_1$ for, say, $\alpha=90^\circ$, we get:

For a fixed TR, the signal from two tissue types having two $T_1$ values would be represented by two points on that graph. For concreteness, let’s take $TR=1$ sec, $T_1^{\text{GM}}=1.5$ sec, $T_1^{\text{PL}}=1.0$ sec. The
two signal intensities correspond to the two red
points on this graph:

When we climb to 7T both increase. Taking values
from the Table in Lecture 3, we have
\( T_1^{\text{WM}} = 1.2 \text{ sec}, \quad T_1^{\text{GM}} = 2.0 \text{ sec}. \) Adjusting the
TR to 1.25 we get the two green points on the
graph, which are farther apart, implying increased
contrast at 7T. Numerically,

\[
\begin{align*}
S_{T1}^{\text{WM}} &= 0.632 \\
S_{T1}^{\text{GM}} &= 0.487 \\
\Delta S_{T1} &= 0.145
\end{align*}
\]

The signal difference is about 25% larger at 7T.
This is only half the story, thought, because SNR
also improves at higher fields approximately
linearly with \( B_0 \), effectively leading to lower noise
levels and therefore even greater CNR.

Had we kept the same \( \text{TR}=1.0 \text{ sec} \) in the above
example we would have obtained

\[
\begin{align*}
S_{T1}^{\text{WM}} &= 0.565 \\
S_{T1}^{\text{GM}} &= 0.393 \\
\Delta S_{T1} &= 0.172
\end{align*}
\]

This is still an increase in contrast, but a milder
one. It is also interesting to note the signals
themselves have diminished because of the longer

\( T_1 \)s (which imply that, for the same TR, we
saturate our magnetization more).

**Note.** \( T_1 \) does not always become longer with
increasing \( B_0 \). One notable exception is
phosphorous \((^{31}\text{P})\) imaging, in which \( T_1 \)
actually becomes shorter, leading to better
SNR but worse CNR. This comes about
because of additional, more complicated effects
we have not discussed here, such as chemical shift anisotropy, which creates field fluctuations
originating from the way electrons are
distributed around the nucleus. For protons
\((^{1}\text{H})\), however, the above discussion is fairly
accurate.

**\( T_1 \) and \( T_2 \) Both Increase in Edema**

Let’s take the relatively simple case of edema. In
edema, water accumulates in the interstitium,
which constitutes about 25% of the body’s total
fluids (cells contain another two thirds, and the
remainder is allocated to blood vessels and
cerebrospinal fluid).

\[
\begin{array}{c}
\text{Blood vessels} \\
\text{Interstitial fluid} \\
\text{Cells}
\end{array}
\]

We’ve remarked that \( T_1 \) appears hypointense and
\( T_2 \) appears hyperintense. This actually means that
both \( T_1 \) and \( T_2 \) tend to increase. When you think
of edema, the additional water tends to reduce the
viscosity in the interstitial space, leading to a
shorter correlation time, which – looking at the
graphs of \( T_1 \) and \( T_2 \) – leads to an increase in both:

\[3\text{ By “effectively” I mean that both noise and signal change as the field increases, but when we normalize things back it appears as if the noise has decreased. For example, assume } S=1.0, \text{ and } n=0.1 \text{ is the noise SD at } 3\text{T, so } \text{SNR}=S/n=1.0. \text{ At } 7\text{T we might get } S=3.0, \text{ n}=0.15, \text{ so } \text{SNR}=2.0. \text{ Normalizing the } 7\text{T result by dividing by 3, we get } S=1.0, n=0.05, \text{ yielding the same SNR=2.0. Thus a higher SNR is equivalent to effectively reducing the noise while keeping the signal constant.}

\[4\text{ In Hebrew: נKeyName.} \]
Multi-Compartment Relaxation Models

A more realistic look at relaxation in biological tissue must take into account their multi-compartmental nature. Water in tissue exists in pools, or compartments, which might exchange. For example, the intracellular and extracellular spaces have different viscosity and therefore different $T_1$, $T_2$ values.

Even within cells different pools may exist. For example, in neurons, water trapped within the myelin sheath has a shorter $T_2$ compared to water diffusing around inside the cell, because of their restricted motion (as remarked earlier, solid/semi-solid phases tend to have longer correlation times and therefore shorter $T_2$s).

Exchange effects, in which water crosses from one pool to another one, cause further complications. If a water molecule jumps from intra- to extra-cellular space very rapidly$^5$, it will average out their respective $T_2$s and $T_1$s and we will only observe an average tissue $T_1$ and $T_2$.

Different microscopic environments can also be considered as different compartments. For example, water can chemically bind and unbind with macromolecules in their environment. This can be a single-bond, meaning the water molecule is still free to rotate, or a double-bond, meaning the water is irrotationally bound:

These processes usually happen on fast timescales, meaning we only get to see an average of them. If we denote by $f_f, f_{rb}$ and $f_{irb}$ the fraction of free, rotationally bound and irrotationally bound water molecules, we get

$$\frac{1}{T_1} = \frac{f_f}{T_{1,f}} + \frac{f_{rb}}{T_{1,rb}} + \frac{f_{irb}}{T_{1,irb}}.$$  

Usually, $T_{1,f} >> T_{1,rb} >> T_{1,irb}$. However, note that even small fractions can cause significant differences. For example, putting $T_{1,f}=1$ sec, $T_{1,rb}=1$ ms and $T_{1,irb}=0.1$ ms, and setting $f_f=0.9$, $f_{rb}=0.09$ and $f_{irb}=0.01$, we get

$$\frac{1}{T_{1,free}} = \frac{0.9}{1000} + \frac{0.09}{1} + \frac{0.01}{0.1} \approx 10 \text{ ms}$$

which is a far cry from the 1000 ms of free water, even though 90% of the spins are in the free water phase!

We conclude with a concrete example. It is possible to separate the different compartments and prepare a histogram of $T_1$ and $T_2$ values in a given tissue, through methods we will not discuss here. This was done for excised pork muscle at low fields (0.47 T), giving a histogram of the form$^6$:

The histogram showed little variation when the muscle was minced or homogenized, indicating the different $T_2$ pools did not originate from extra/intracellular compartments. Following further experiments, the authors show that the fastest component (~ few percent) originates from water bound to macromolecules; the largest peak corresponds to water located within organized protein structures; and the fastest peak (longest $T_2$)

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$^5$ The definition of “rapid” is a fine point we will not tackle here. We will only remark at this point that exchange is rapid.

$^6$ Taken from Bertman et. al., J. Agric. Food Chem. 49:3092-3100 (2001)
reflects extra-myofibrillar water (i.e. between the fibers of the muscle).

**T²* CONTRAST**

B₀-Inhomogeneity Leads to Both Signal Loss and Phase Shifts In Gradient Echo Images

We now forget about T²* for a moment and assume we only have microscopic T² effects and B₀ inhomogeneity. If our inhomogeneities are time-independent, \( \Delta B(r) \), then spins at \( r \) will have an offset \( \gamma \Delta B(r) \) and accumulate a phase \( \phi (r,t) = \gamma \Delta B(r)t \) after a time \( t \). Our transverse magnetization will behave as:

\[
M_y (r,t) = M_y (r,0) e^{-i\phi (r,t)}
\]

This means that if all of our spins start out in-phase at time \( t=0 \), then end up dephasing at later times:

\[
s(r,t) \approx \int_{\text{voxel}} M_y (r',0) e^{-i\phi (r',t)} dr'
\]

Without knowing the exact form of \( \Delta B(r') \) we cannot make any exact claims, but we can see that overall two effects will occur:

1. **Dephasing**: The spins will go out of phase, leading to a loss of signal.
2. **Net phase accumulation**: The spins might accumulate some average non-zero phase which would create a non-zero phase for the signal \( s(r,t) \).

For example, if the inhomogeneity only varies weakly in the voxel, we can use a Taylor expansion, keeping things in 1D and assuming the voxel’s center coincides with \( x=0 \) for simplicity:

\[
\Delta B(x) \approx \Delta B(0) + \left( \frac{d\Delta B(x)}{dx} \right)_{x=0} x
\]

Substituting this into the signal, and assuming we have a homogeneous voxel (again, for simplicity):

\[
s(r,t) \approx \int_{\text{voxel}} M_y (r',0) e^{-i\Delta B(r') x} dr'
\]

We see that for a linear inhomogeneity the signal does not decay exponentially with time but rather as a sinc function.

While a linear approximation over a voxel might be a good approximation for the macroscopic fields, that is not the case for the microscopic ones. In a macroscopic ~ 1 mm³ voxel there is significant heterogeneity and the microscopic fields are very complicated. Their average effect is not a linear gradient over the voxel, but some statistical distribution of fields, leading to a statistical distribution of spin phases inside the voxel. This statistical distribution leads more naturally (although not always!) to a more exponential decay.
Phase Imaging Reveals Microstructure Due To Microscopic Susceptibility

As seen before, susceptibility artifacts can lead to the signal being a complex quantity. Instead of looking at magnitude images, we can try looking at phase images, that is plot the phase of the signal as each point. This might tell us something about the microstructure that created it.

When acquiring phase images, one usually gets something that looks like this (images taken from Haacke et. al., AJNR 30:19-30 (2009)):

The gross variations are due to macroscopic inhomogeneity effects such as the main field’s imperfections. They can be addressed by unwrapping the phase (canceling out its discontinuities). Once this is done, we assume that the slowly changing components of the inhomogeneity are caused by macroscopic fields, and we can get rid of them by applying a high pass filter which assures us we remain only with the fast changing – hopefully microscopic – parts of the phase:

We can indeed see some contrast here between the different tissue types and also some vessel-related contrast, as will be discussed below. Indeed, by multiplying the phase and magnitude images we can get what’s known as a susceptibility weighted image. Such images usually show better contrast for some structures, such as blood vessels, or iron-containing structures, which are known to create microscopic susceptibility artifacts around them. For example, Shmueli et. al. have examined the cerebellum in a marmoset brain at 11.7 Tesla. In humans, the cerebellum appears almost as a separate structure attached to the base of the brain, which is involved in coordinating a great deal of our motor activity. Shmueli et. al. have been able to delineate the purkinje cell layers in the marmoset brain (Magn. Reson. Med., 62:1510-1522 (2009)):

The contrast between the different cell layers in the cerebellum is highly correlated to their iron content (iron particles have a large electronic magnetic moment and induce significant field distortions on a microscopic scale).

From $T_2^*$ To $T_2$

We’ve presented $T_2$ are stemming from microscopic temporal field fluctuations, and $T_2'$ as stemming from static spatial inhomogeneities. What would happen if we created a static inhomogeneity but let a water molecule diffuse (translationally, not rotationally!) through it? The field the molecule would “see” would fluctuate as it would move around. If the molecule moves around fast enough, $T_2'$ would “become” $T_2$!

This is not a hypothetical situation and it happens often in tissue. For example, water can diffuse around a blood vessel (venous blood has deoxygenated hemoglobin which is paramagnetic).
These effects play a big role in understanding hemodynamic effects in functional imaging.

One way to think about $T_2^*$ vs $T_2$ is as follows: imagine running a spin-echo experiment. Whatever the spin-echo keeps is $T_2$, and whatever goes away is $T_2^*$. 