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**Title Page:**

**How to understand it:**

**Magnetic Resonance Imaging**

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## ABSTRACT

MRI is a staple of the neurologist's armoury when facing diagnostic challenges. At times it can reveal or confirm the diagnosis with clarity, at others it brings us no further forwards, or even muddies the water. We rely on the expertise of neuroradiology colleagues to interpret MR images, but the choice of protocol for MR acquisition and its interpretation hinge crucially on the clinical information we provide. Having a degree of understanding about how MRI works, its limitations and pitfalls, can help to optimise what we learn from a scan.

### Abbreviations

ADC- apparent diffusion coefficient

BOLD- blood oxygen level dependent

CSF- cerebrospinal fluid

DWI- diffusion weighted imaging

FLAIR- Fluid attenuated inversion recovery

fMRI- functional MRI

SWI- susceptibility weighted imaging

MRI- magnetic resonance imaging

## INTRODUCTION

MR images are not direct 'pictures' of the brain, but approximations of particular tissue properties (and potentially uncontrollable influences). Understanding how the images are formed helps to understand the quirks and limitations that can apply.

One of the main components of an MR scanner is a very strong magnet- necessitating a thorough safety check for metallic items that may get forcefully pulled towards the scanner. The behaviour of hydrogen ions within the magnetic field is used to create MR images (figure 1).

When a magnetic field is applied, the spins of hydrogen ions become aligned, parallel to the axis of the field. Radiofrequency pulses are used to "flip" the orientation and direction of spin of some hydrogen ions. The signal measured corresponds to the speed of "relaxation", the return of these ions back into alignment with the main magnetic field. Relaxation, in a longitudinal (T1) and transverse (T2) direction, is influenced by the local tissue environment. This is why grey matter, white matter and CSF have different signal qualities.

## MR SEQUENCES

An MR scan produces several sequences, exploiting different tissue properties and useful in different ways. For each sequence, the parameters of the scan acquisition are varied to emphasise certain tissue features. It is important to note that these sequences are *weighted*, or biased, towards the

property of interest; they do not represent this property in isolation. We discuss commonly employed MR sequences below and Table 1 shows some presentation-specific uses for certain sequence combinations.

### **T1-weighted image**

A T1-weighted image is acquired in a way that is weighted towards the *T1 relaxation time*. This is a measure of the speed of return of the flipped hydrogen ions back to alignment with the main magnetic field (figure 2.A). The CSF is darkest and the white matter is brightest (Figure 2.B). This is because the CSF is slower to return to alignment than white matter.

### **T2-weighted image**

The T2-weighted image is weighted towards the *T2 relaxation time*. The radiofrequency pulse brings the spinning of hydrogen ions in time with each other (in phase). The T2 relaxation time is a measure of the time it takes for them to get out of sync (dephase). As the spins dephase, signal is lost (figure 3.A). CSF dephases relatively slowly, white matter much faster. The white matter, therefore, is much darker on a T2-weighted image than the CSF (figure 3.B).

### **FLAIR**

Fluid-attenuated inversion recovery (FLAIR) scans use a carefully timed extra radiofrequency pulse to null (cancel out) signal arising from free fluid (e.g. CSF spaces). They are generally weighted towards T2 signal (but can be applied to T1). This sequence is particularly useful for assessing periventricular lesions, because of the difficulty in evaluating areas of hyperintensity adjacent to hyperintense CSF on a standard T2 scan.

### **Diffusion weighted imaging (DWI)**

DWI looks at the diffusion properties of water by applying a “diffusion gradient”-using an additional magnetic field varying in strength across the imaging plane. Water molecules in CSF have relatively unrestricted diffusion, whereas cellular structures in grey and white matter impose constraints on water movement. Areas with more diffusion restriction have more signal retained at the point of the signal readout compared to areas with freer diffusion, causing brightness on DWI images (figure 5.A). Diffusion of water is particularly restricted in certain brain pathologies, e.g. in acute ischaemic stroke where there is cellular oedema (figure 6.A).

However, a DWI scan is essentially a T2-weighted image with an extra diffusion gradient applied. This can lead to “T2 shine through”, where an area of very high T2 signal intensity looks ‘bright’ in the absence of truly restricted diffusion (Figure 6.C&D). The apparent diffusion coefficient (ADC) map is useful for ascertaining whether brightness on DWI reflects true restricted diffusion. The ADC map is generated by calculating the difference in signal between images with different amounts diffusion weighting; areas of true diffusion restriction will show little difference and therefore appear dark on the ADC map (figure 6.B).

### **Susceptibility based sequences (e.g. SWI)**

Certain substances (including blood breakdown products, deoxygenated haemoglobin, calcium and copper) have paramagnetic qualities. They exert a small local magnetic field, inducing more rapid T1 and T2 relaxation in local hydrogen ions (figure 7). This effect can be a source of unwanted image artefact. Susceptibility weighting amplifies this effect, enhancing sensitivity to certain features that are undetectable on standard T1-/T2-weighted sequences, such as helping to identify (i) old intracerebral haemorrhage e.g. delayed presentations of subarachnoid haemorrhage, (ii)

microhaemorrhages e.g. hypertension, amyloid angiopathy or diffuse axonal injury, (iii) cavernous malformations, (iv) calcium deposition, e.g. Fahr syndrome. SWI is also being studied for the ability to detect the presence of small veins in demyelinating (versus vascular) white matter lesions(1) and in the assessment of progressive iron deposition in the basal ganglia in Parkinson’s disease.(2)

**Functional MRI (fMRI)**

fMRI utilises the diamagnetic properties of oxygenated blood and the paramagnetic properties of deoxygenated blood to produce signal by measuring their relative ability to induce local magnetic field distortions. This so-called ‘blood oxygen level dependent’ (BOLD) response alters in response to an increase in local neuronal activity. In fMRI, changes in the BOLD response are measured and are regarded as a proxy for local neuronal activity. While fMRI remains largely a research tool, it can be utilised clinically in situations such as pre-surgical planning for resection of tumours or epileptogenic foci that are in close proximity to eloquent brain regions such as motor cortex, whose location can be identified and mapped by performing fMRI while the patient undertakes a relevant task.

*Table 1: Useful MR sequences in common neurological conditions*

<b>Condition</b>	<b>Helpful MR sequences</b>
<i>Epilepsy</i>	An epilepsy MRI protocol is particularly geared towards identifying structural abnormalities that may predispose to epileptic activity, such as hippocampal sclerosis or focal cortical dysplasia. Ideally 3T MRI should be used, with lower field strength scanning potentially missing subtle lesions. Important sequences include volumetric T1 (high resolution 3D acquisition that allows reconstruction in all imaging planes), and high-resolution axial and coronal FLAIR (or 3D FLAIR if available). Patients with suspected temporal lobe epilepsy require T2/FLAIR coronal sequences perpendicular to the hippocampal long axis. Double inversion recovery (with a second inversion pulse to null signal from normal white matter as well as CSF) is used as an adjunct to identify epileptogenic foci.
<i>Demyelination</i>	Sequences that help in the new diagnosis of neuroinflammation include T2W for detecting white matter lesions (especially infratentorial lesions) and T2W FLAIR (for periventricular and juxtacortical lesions). T1W sequence allows detection of T1 black holes and contrast enhanced assesses for the presence of active inflammation. In addition, if the T1W sequence is volumetric, a better assessment of volume loss can be made. DWI is required for monitoring for progressive multifocal leukoencephalopathy in patients taking immunotherapy.
<i>Dementia</i>	In young onset or unusual dementia presentations, volumetric T1W can help to assess for particular patterns of atrophy; T2W FLAIR to assess for vascular pathology; and DWI to look for the typical cortical ribboning in Creutzfeldt–Jakob disease. SWI can also help in assessing for microhaemorrhages.
<i>Tumour</i>	In assessing potential tumours on MRI, DWI can help in distinguishing patterns of diffusion restriction, and contrast-enhanced scans are particularly useful in assessing the likely cause of a lesion. SWI can identify microhaemorrhages and neovascularisation in high-grade gliomas. Advanced imaging techniques such as MR spectroscopy (assessing metabolite peaks based on their differing frequencies of spinning hydrogen ions) and arterial spin labelling (a form of perfusion imaging) are sometimes applied in diagnostically challenging cases.

**BUSTING TERMINOLOGY**

**Voxels**

When you take a photo and store it on a computer, that photo is stored as a grid of 'blocks' of different colours and intensities, called pixels. The image produced by MRI is represented using 3-dimensional 'blocks' called voxels. Larger voxels tend to mean faster imaging, but with lower resolution and less contrast.

### **T2 versus T2\***

T2\* refers to the weighting that uncovers paramagnetic qualities of a tissue. Some sequences (such as SWI) specifically seek to measure T2\*-weighting, whereas in other situations T2\*-weighting of a sequence can result in artifact.

### **Spin echo versus gradient echo**

Different MRI sequences are generated using different "pulse sequences". The term "echo" is used to describe the signal, or read-out, of the MRI. Spin echo and gradient echo are commonly used pulse sequences. A spin echo sequence uses a second radiofrequency pulse to refocus the spins and produce the read-out, cancelling out the effects of magnetic field inhomogeneities. A gradient echo sequence only uses one radiofrequency pulse, instead using a reversal of the magnetic gradient to refocus and create the echo. Gradient echo sequences do not cancel out the effects of susceptibility or field inhomogeneities, so they feature some T2\*-weighting.

### **1.5T versus 3T**

The T stands for Tesla, a measure of magnetic field strength. The higher the preceding number, the stronger the field. For context, the Earth's natural magnetic field is 0.00005T (and it is possible to create a basic low-resolution image using this field!). As the strength of the field goes up, the image's spatial resolution increases, allowing finer details to be visualised. Higher field strengths can be used to enhance susceptibility weighting.

### **Partial volume effects**

This phenomenon occurs when a single voxel contains two different tissues (commonly grey matter and CSF) with different signal intensities. The voxel itself represents the average intensity only, not truly representative of either substance.

## **FRAMING OUR CLINICAL QUESTION**

One of the most compelling reasons for neurologists to understand a little about MRI, is to frame the question better that we pose to our neuroradiology colleagues. The clinical question helps tailor the sequences that the radiologists choose to acquire; it would be too time consuming to perform every possible sequence for each patient.

### **Case study 1: Amyloid spell**

*A 68-year-old woman presented with recurrent, transient left arm shaking, with spreading paraesthesia, lasting a few minutes at a time.*

The classical appearance of superficial siderosis and blooming on susceptibility-weighted MR (figure 8), suggests a likely diagnosis of cerebral amyloid angiopathy. The diagnosis may be missed in the absence of a SWI sequence. In the context of stereotyped episodes of neurological dysfunction, the neuroradiologist may choose an epilepsy MRI protocol, which does not routinely include SWI. As a neurologist reviewing the case and the results, it is important to check whether SWI was performed.

### **Case study 2: Delayed presentation of subarachnoid haemorrhage**

*A 30-year-old woman presented with a history of thunderclap headache 3 weeks earlier.*

CT scanning is highly sensitive to the presence of acute haemorrhage, but its sensitivity wanes over time. MRI is the most useful investigation in a delayed presentation. However, as the blood products gradually break down, the appearances of T1- and T2-weighted sequences change (figure 9).

### **Case study 3: Acute cerebral infarct**

*An 88-year-old man attended the emergency unit following a fall. Two weeks previously he had developed sudden onset left-sided weakness, for which he did not seek medical help, but his mobility had remained poor since.*

After ischaemic stroke, in the subacute phase, a phenomenon called *pseudonormalisation* of ADC can occur. Acutely, restricted diffusion causes brightness on DWI, and decreased ADC. However, diffusion within the acutely infarcted tissue gradually increases as tissue destruction evolves, and at around 1–2 weeks, ADC can appear normalised (figure 10).<sup>(3)</sup> After this point, as the infarct enters a chronic phase, diffusion often becomes less restricted than in healthy tissue. A similar phenomenon occurs on T2-weighted images, where between 6 and 36 days after an infarction the signal intensity becomes close to that of healthy surrounding tissue.

Cases 2 and 3 emphasise the importance of providing information regarding the timing of the clinical event relative to scan. A neuroradiologist may otherwise be falsely reassured that the ADC or T2 sequences are normal, resulting in a falsely negative report.

## **TRADE OFFS AND DOWNFALLS IN MRI**

Many parameters can be altered when acquiring MR images, but there is generally a trade-off to consider. For example, increasing the length of time between applying a radiofrequency pulse and measuring signal can improve differentiation between tissues, but also results in decay of the overall signal. Reducing voxel size (resulting in higher resolution and fewer partial volume effects), providing contrast, and undertaking more sequences, all offer additional information, but at the cost of increasing the time that patients spend in the scanner. The consequences of long scan times include increased likelihood of movement artefact as patients become restless, and a potential reduction in overall scanner efficiency (fewer patients scanned per day, longer waiting lists).

Additionally, signal collected in an MR scan is not limited to the properties of interest. There is significant 'noise' in the signal produced (such as from table vibrations, flow of blood and CSF, the presence of metallic implants), that can cause image degradation, distortion and artifact (figure 11). These can limit image interpretation, sometimes even leading to false conclusions about tissue properties.

Patient factors must also be considered. Some patients struggle to tolerate a scan either due to claustrophobia, or due to an inability to lie still resulting from a movement disorder or confusion. Monitoring patients is more challenging during MRI than CT, so MR imaging of medically unwell patients poses a particular challenge, and there are a number of risks, contraindications and special circumstances to consider in MRI (tables 2 and 3).

*Table 2: Risks of MRI*

<b>Risk</b>	<b>What's the problem?</b>
<i>Translational and torque forces</i>	The magnetic field exerts force on ferromagnetic materials to rotate or move them, risking dislodging implanted devices and damage to local structures.
<i>Specific absorption rate (SAR)</i>	The radiofrequency pulse causes energy deposition in tissues, which can lead to excessive heating. This is exacerbated at higher field strengths.
<i>Projectile injuries</i>	The magnetic field can cause magnetic materials to act as projectiles.
<i>Burns</i>	From coils and cables coming too close in contact with the patient's skin, or from rapidly switching gradients causing electromagnetic induction. Jewellery, ECG cables, medicinal patches, clothing and occasionally even tattoos can contain substances that can result in skin burns.
<i>Peripheral neurostimulation</i>	The rapid changing of magnetic field gradients can cause peripheral nerve stimulation, which can be painful.
<i>Noise</i>	The rapidly switching gradients produces huge noise levels, with the potential to damage hearing without appropriate measures.
<i>Contrast agents</i>	There is a rare risk of anaphylactic reactions, and of nephrogenic systemic fibrosis in patients with renal failure. Additionally, studies have identified high T1-weighted signal intensity in the dentate nucleus and globus pallidus in patients who have undergone serial contrasted scans; whether there are clinical implications is not firmly known. Caution is needed in people with renal failure, and consideration of benefits made before serial contrast scanning.

Table 3: Special considerations

<b>Consideration</b>	<b>Explanation</b>	
<i>The unconscious or unstable patient</i>	Inability to screen fully for contraindications poses a risk; consulting relatives, reviewing previous imaging and reviewing medical records can help. Unexplained scars may require CT imaging before considering MRI.	
<i>Paediatrics</i>	Caution is taken with the use of gadolinium-based contrast agents in neonates and infants due to renal immaturity and potential lower renal clearance.	
<i>Pregnancy</i>	There are no known adverse effects of MRI in pregnancy; however data are lacking, and there is theoretical potential for teratogenicity or acoustic damage. Gadolinium crosses into fetal bloodstream, but with no documented adverse outcomes.	
<i>Breastfeeding</i>	Generally considered safe. Small quantities of gadolinium are excreted in breastmilk; these concentrations are felt to be safe, but some people opt to stop breastfeeding for 12–24 hours after contrast administration.	
<i>Implanted devices</i>	<i><u>Examples of potentially contraindicated devices</u></i>	Aneurysm clips
		Cardiac pacemakers- most modern pacemakers are MR compatible, but it is important always to check with cardiac physiology before scanning, and get the device checked after the scan.
		Cardiac/vascular stents soon after implantation
		Gastrointestinal endoscopic clips- generally a time limited and relative contraindication
		Shrapnel and bullets- depends on location and knowledge of composition. CT imaging may be necessary before considering MRI.
		Metal implants (e.g. cochlear implants)



		Intrauterine devices- non-metallic devices are generally safe; copper devices are generally fine at a maximum 3T field strength. Stainless steel devices are contraindicated.
		Programmable ventriculo-peritoneal shunts
		Vagus nerve stimulators are often compatible, but require checking before and after MR imaging
		Baclofen pump. Some are compatible but generally need testing and turning off before MR imaging
		Some dental work (fillings are safe)
	<u>Examples of generally safe devices- but always check!</u>	Surgical sutures
		Vascular and biliary stents
		Plates and screws

## The spine

It is possible to image the whole spine in one go, with a very long field of view. If lesion localisation is unclear from the history and examination, a long field of view whole spine scan can be useful for a relatively time efficient overview. A trade-off is that this reduces spatial resolution, particularly relevant in spinal imaging where partial volume effects substantially degrade the scan quality. Localising the lesion using the clinical symptoms and signs can facilitate a higher quality, shorter segment scan, and/or ensure that axial slices are captured at the relevant level.

Additionally, worth noting if the clinical question relates to the spinal cord, do request 'whole cord' rather than 'whole spine' imaging; the latter encompasses lumbar-sacral segments which may unnecessarily increase scan time or reduce scan quality.

## THE VALUE OF A SECOND READ

Commonly, additional clinical information becomes available after the scan is undertaken, or review by a neurologist poses new questions. Multidisciplinary team meetings or re-evaluating scans with neuroradiology colleagues often provides valuable additional insights, particularly informing on whether the MR investigation undertaken was sufficient to address the clinical questions.

### Case study 4: Todd's paresis

*A 30-year-old man presented with acute right arm weakness, MR imaging excluded an acute cerebral infarct. He was later thought to be experiencing seizures with Todd's paresis.*

In this example, the patient was investigated for the presence of acute stroke, but evidence to suggest seizure only emerged later. In this example, the MR imaging protocol is likely to include diffusion-weighted imaging, but probably lacked key sequences required to detect a subtle epileptogenic focus, e.g. hippocampal sclerosis (figure 12). In this context, it is important to re-evaluate and return to a discussion regarding whether further imaging is necessary, given this new information.

## KEY POINTS

- **Much of how MR images are acquired requires some form of 'trade off'.**
- **The way we frame our clinical question, and the contextual clinical information we provide, can help to guide both the image acquisition protocol and the neuroradiologist's ability to interpret the images accurately.**
- **MRI is not just a direct picture of the brain; as such it is vulnerable to numerous difficult to control influences and artefacts.**
- **If in doubt, it is always worth a direct conversation with neuroradiology, with further review of the imaging in light of new information.**

## **SUGGESTED READINGS**

Mriquestions.com

Radiopedia.org

Tsai LL, Grant AK, Mortelet KJ, Kung JW, Smith MP. A Practical Guide to MR Imaging Safety: What Radiologists Need to Know. *Radiographics*. 2015 Oct;35(6):1722-37. doi: 10.1148/rg.2015150108. PMID: 26466181.

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Consent: the manuscript contains fictionalised case studies, which do not correspond to real patients, therefore there are no patients to get consent from.

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## Figure legends:

Figure 1: Generation of an MR signal. A) Hydrogen ions in water molecules are randomly orientated in the absence of a magnetic field. B) applying a magnetic field causes the hydrogen ions to align. C) Applying a radiofrequency pulse flips them out of alignment. D) Over time, the hydrogen ions return to alignment with the magnetic field. E) This gives us a measurable signal, which can be converted into an image.

Figure 2: A) Schematic of T1 relaxation B) T1-weighted brain image

Figure 3: A) Schematic of T2 relaxation B) T2-weighted brain image

Figure 4: A) FLAIR image of healthy brain. B) T2-weighted image with subtle periventricular lesions. C) corresponding FLAIR image showing periventricular lesions.

Figure 5: Degree of diffusion with varying constraints. A) Starting positions of hydrogen ions. B–D) new positions of hydrogen ions after a set time; B) in a highly restricted environment (such as an area of acute infarction); C) in a moderately restricted environment (such as in healthy grey matter) and D) in a relatively unrestricted environment (such as CSF in ventricular system).

Figure 6: A) DWI in acute infarct. B) ADC map in acute infarct. C and D) T2-shinethrough-appearance on DWI (C) and ADC map (D).

Figure 7: A: Typical central microhaemorrhages in hypertension. B: multiple cavernomas on SWI.

Figure 8: Examples of typical imaging findings in cerebral amyloid angiopathy on susceptibility weighted imaging. A) Right hemisphere superficial siderosis B and C) peripheral microhaemorrhages.

Figure 9: Haematomas of different ages, showing different MRI appearances. A and B) A left frontal intraparenchymal haematoma and left convexity subdural 10 days following trauma. This is becoming hyperintense from the outside on T1W (A) and becoming hyperintense on T2W (B). C and D) An extra-axial haematoma 5 weeks after resection of a left frontal cavernoma. C) This has become hypointense on T1W. D) Hyperintense on T2W.

Figure 10: Imaging example of pseudonormalisation of ADC. A) Small region of hyperintensity on T2W in the region of the right posterior pontine/middle cerebellar peduncle. B) Subtle corresponding hyperintensity on DWI. C) no corresponding hypointensity on the ADC map.

Figure 11: Examples of classic MR artefacts. A) Highly-degraded image quality due to movement artefact B) Susceptibility artefact caused by a metallic foreign body.

Figure 12: Left-sided hippocampal sclerosis shown on coronal slices with the left hippocampus being smaller and with increased signal intensity on A) T2-weighted image and B) T2-weighted FLAIR.