Chapter

20 But is it Safe? Bio-effects

20.1 Introduction

For centuries magnets have been attributed with alleged healing and hypnotic powers despite a lack of scientific evidence or plausible hypotheses on mechanisms. Magnets may not make you better, but are they harmful? In the course of undergoing a clinical MR examination, the patient will be exposed to the static field, time-varying gradient fields and RF fields as shown in Table 20.1. Staff normally will only be exposed to the fringe field from B_0. In 35 years of MR, there have been 16 documented fatalities related to magnet safety, 13 of these involving persons with cardiac pacemakers, one involving displacement of an aneurysm clip, one involving a projectile and the other from an unknown cause. Practical MR safety was considered in Chapter 2; you must thoroughly know your institution's safety practices and patient screening procedures, and carrying out a metal check on yourself and others will be second nature to you by now. The purpose of this chapter is to provide background on the underlying potential biological effects of magnetic fields, in particular:

- the main effect of RF exposure is tissue heating, restricted to less than 1 °C by monitoring and limiting the SAR (specific absorption rate);
- peripheral nerve stimulation (PNS) is the main bio-effect of the time-varying magnetic fields generated by the gradients, and may cause discomfort but it is not harmful;
- at high B_0 (i.e. 3 T and above) mild and transient sensory effects, associated with movement in the static field, may be experienced;
- caution is required for staff and patients who are pregnant, although there is no evidence of any deleterious effect on the fetus;
- occupation exposure limits for MR staff are low, and within sensible limits.

In addition we briefly review the safety of Gd-based contrast agents.

Table 20.1 The range of magnetic field exposures for patients in MRI; staff are normally only exposed to the B_0 fringe field and its spatial gradient

	Amplitude	Frequency/ slew rate	Typical duration
Static field B_0	0.2–7 T	0 Hz	Always present
Static fringe field spatial gradient	0–25 T m^{-1}	Movement acts as dB/dt < 1 Hz	Always present
Imaging gradients G_x, G_y, G_z	0–50 mT m^{-1}	0–10 kHz 0–200 T m^{-1} s^{-1}	0–10 ms
RF transmit field B_1	0–50 μT	8–300 MHz	0–1 ms

20.2 Radiofrequency Effects

RF effects arguably give the greatest cause for concern in terms of potential bio-effects, partly because they are under the operator's control. The principal physical effect is deposition of energy, leading to tissue heating with possible physiological effects including changes in cardiac output. Of particular concern are heat-sensitive organs such as the eyes and testes, although there is no evidence of any deleterious effect of MR on either. Caution is required where the patient has a metallic (but non-ferromagnetic) implant that may result in localized heating (see Figure 20.1). The use of inappropriate physiological monitoring leads can also result in heating of the electrodes and the possibility of skin burns. Other implant safety issues are addressed in Chapter 2 and elsewhere. See Further reading at the end of this chapter.

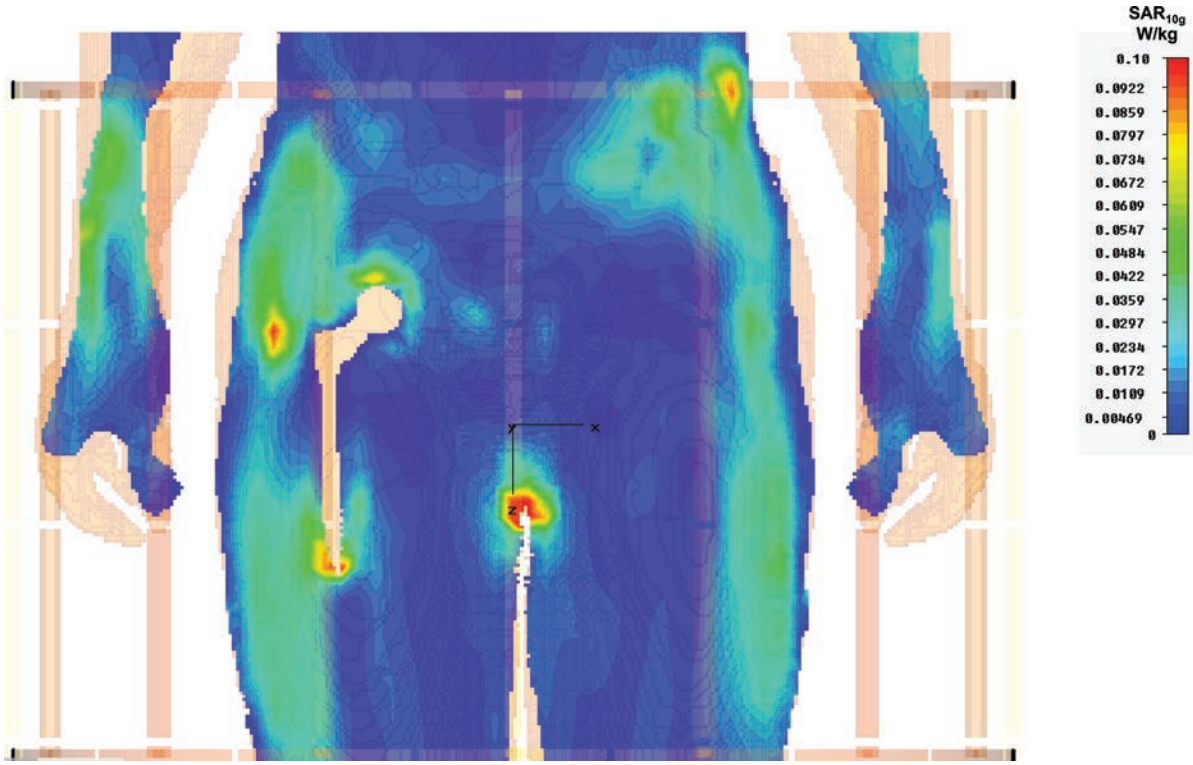

Figure 20.1 SAR hotspots occurring at the tip of non-ferromagnetic implants. Note that the groin region has higher SAR than the implant. Image courtesy of Prof J. Hand, King's College, London.

20.2.1 Specific Absorption Rate

The RF exposure is measured in terms of the specific absorption rate (SAR), defined as the total transmitted power in watts (W) per kilogram of tissue. This is why you need to enter the patient's weight when registering them. The scanner will estimate the SAR for each sequence before scanning begins. During the scan the scanner may monitor its RF transmitter output and compute an average SAR (see also 'SAR Maths'). Normally two levels of RF exposure are accessible. The lower (Normal Mode) level can be applied without restriction. Exposure to the First Level (Controlled Mode) requires positive confirmation from the operator. The Second Level is only available in research mode operating under research governance guidelines.

SAR Maths

For a uniform conducting medium of conductivity σ the SAR can be calculated as follows. The energy deposition is given by the product of induced current density J and induced electric field E (this is just 'power = voltage times current', but for a volume conductor)

$$P = \mathbf{J} \cdot \mathbf{E} = \sigma E^2$$

and then

$$\mathrm{SAR} = 0.5\sigma \frac{E^2}{\rho}$$

where ρ is the density of tissue and the factor 0.5 comes from time-averaging the alternating electric field (just as in AC power calculations). Thus SAR has units of W kg^{-1}.

From Faraday's law (see Box 'Faraday Induction') and allowing for a sinusoidal B_1 (and for simplicity assuming rectangular, i.e. hard, pulses) we get an average SAR

$$\mathrm{SAR} = 0.5\sigma \frac{\pi^2 r^2 f^2 B_1^2 D}{\rho}$$

where D, the duty cycle, is the fraction of total scan time for which the RF is present. This shows that:

- SAR increases with the square of Larmor frequency or B_0;

- SAR increases with the square of flip angle;
- SAR increases with the patient size;
- SAR increases with the number of RF pulses in a given time.

Of course, this calculation is a huge simplification. The details of anatomical geometry can change the power levels. The occurrence of local hotspots has led to the development of localized SAR limits for partial body exposure. At 3 T local SAR is often the limiting factor.

Some scanners also compute the total energy imparted in joules.

20.2.2 Staying Cool: Reducing SAR

SAR is under the control of the MR operator. Some factors that help to reduce the SAR are:

- using quadrature transmit coils (this is standard) or parallel transmission, if available, on high-field systems;
- using a localized transmit coil for certain examinations, e.g. using a transmit–receive head or extremity coil if available;
- increasing TR;
- using fewer slices;
- reducing echo train length (ETL, turbo factor) in TSE sequences;
- reducing the refocusing pulse flip angle, especially in TSE sequences and also fully rewound gradient-echo sequences (bFFE, True-FISP, FIESTA).

Reducing the refocusing pulse is by far the most effective as SAR depends upon B_1^2 which determines the flip angle – a reduction to 150° reduces SAR by 30% but barely affects image quality. Scanning at lower field, e.g. 1.5 T rather than 3 T, also results in lower heating, as SAR is proportional to the Larmor frequency squared, i.e. proportional to B_0^2 (see Box 'Standing Waves'). Using parallel imaging may also help in some instances by reducing the number of RF pulses used. Alternating between higher and lower SAR sequences can help to spread the thermal load.

Standing Waves

The wavelength λ for a medium of dielectric constant ε_r is

$$\lambda = \frac{c}{\sqrt{\varepsilon_r} f}$$

where c is the speed of light, 3×10^8 m s^{-1}. This gives the nominal 'wavelength' of the B_1 field in air as 4.8 m at 63 MHz (1.5 T), or 2.4 m at 126 MHz (3 T) – remember we are dealing with fields not waves – strictly the 'near' field zone. However, the dielectric constant of tissue (basically water) of 80 gives wavelengths of 0.52 m and 0.26 m at 1.5 T and 3 T. If the dimension of the patient or a metallic implant is equal to half a wavelength then standing waves can be established. These will lead to B_1 non-uniformities (signal non-uniformity) and increased RF heating.

20.2.3 RF Exposure Standards

The IEC 60601-2-33 standard is based upon limiting RF-induced core temperature rises to 0.5 °C or 1 °C for normal and first-level controlled operations respectively. This translates into whole-body SAR limits of 2 and 4 W kg^{-1} averaged over 6 min. The IEC 60601-2-33 standard gives the following limits for the temperature rise (Table 20.2) and SAR limits (Table 20.3) for the first and second-level controlled modes.

20.3 Gradient Effects

The time-varying fields generated by the gradients fall in a part of the frequency spectrum known as extremely low frequency (ELF). There is much controversy about the effect of chronic exposure to ELF fields from high-voltage power lines and household appliances. However, in MRI we are concerned with acute effects. There is no evidence of MR switched gradient fields causing carcinogenic or teratogenic (literally, the production of monsters!) effects.

Table 20.2 RF temperature limits

Operating mode	Core temperature rise (°C)	Maximum temperature limits (°C)	
		Core	Local
Normal	0.5	39	39
First-level controlled	1	40	40
Second-level controlled	>1	>40	>40

Table 20.3 SAR limits

Operating mode	SAR (W kg^{-1})					
	Whole body	Partial body		Local transmit coils		
		Any	Head	Head	Trunk	Extremities
Normal	2	2–10	3.2	10	10	20
First-level controlled	4	4–10	3.2	20	20	40
Second-level controlled	>4	>4–10	>3.2	>20	>20	>40
Short-term SAR	The SAR limits over any 10 s period should not exceed three times the stated SAR average					

Note: The averaging time is 6 min for all except the short term SAR limit.

20.3.1 Stimulation Effects

The switching of the gradients induces electrical fields and currents in conducting tissues according to Faraday's law (see Box 'Faraday Induction') which may exceed the nerve depolarization threshold and cause peripheral nerve stimulation (PNS). The possibility also exists, at least theoretically, of stimulating cardiac muscle, thus presenting a hazard. Stimulation of motor nerves and skeletal muscle may be disconcerting to the patient (discomfort being reported for levels 50–100% greater than the sensation threshold) but is not itself hazardous and will not normally occur in routine clinical scans. Animal research (with dogs) has shown that respiratory stimulation occurs at exposure levels of the order of three times that required for PNS, while cardiac stimulation requires about 100 times the PNS threshold. In addition to the strength of the stimulus, the rate of change of the gradient fields (dB/dt), the likelihood of stimulation is related to the membrane time constant of the tissue, requiring a stronger stimulus for shorter pulse durations. See Box 'The Strength–Duration Curve'.

Faraday Induction

Faraday's law gives the EMF (or voltage) induced in a conducting loop of area A from a uniform time-varying field as

$$\text{EMF} = A\frac{dB}{dt} = \pi r^2 \frac{dB}{dt}$$

for a circular loop (see Figure 20.2).

The induced electric field round a circular loop is given by volts/distance (strictly $\int E.dl$ for the mathematically unchallenged) or

$$E = \frac{1}{2} r \frac{dB}{dt}$$

around the circumference of the circle. We can work out the maximum induced E by assuming a loop radius (r) of 0.25 m around the torso at the point of peak value of the gradient, where the field generated by the gradient is highest:

$$E_{max} = \frac{1}{2} r^2 SR_{max}$$

where SR_{max} is the maximum slew rate in T m^{-1} s^{-1}.

$$E_{max} = 0.03125 \times SR_{max}$$

A slew rate of 64 T m^{-1} s^{-1} (or mT m^{-1} ms^{-1}) is required to give an electric field on the order of 2 V m^{-1}, the lower limit for stimulation. This is well within the capabilities of modern gradients. In practice the stimulating slew rate is also determined by the pulse duration, as in Box 'The Strength–Duration Curve'.

In older publications current density (J) in A m^{-2} is considered. This is given by

$$J = \sigma E$$

('Ohm's law' for volume conductors) and σ is the electrical conductivity measured in siemens per metre (S m^{-1}).

PNS is most likely to occur in echo planar imaging. In particular we have to be careful when oblique slices are used and it is possible to have a greater slew rate by summing the contributions from two or three sets of gradient coils. In all cases the scanner will calculate dB/dt and advise on the likelihood of stimulation, requiring positive confirmation to proceed to the first-level controlled mode.

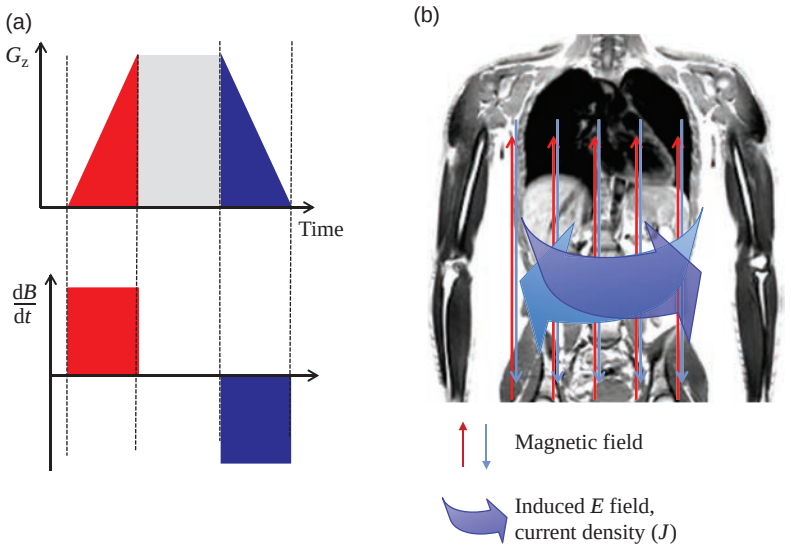

Figure 20.2 Faraday induction in a time-varying magnetic field. (a) With a trapezoidal gradient waveform dB/dt only exists during the ramp-up and ramp-down periods. (b) An electric field is induced in loops around the patient, with circulating currents in conductive tissues. The direction of these reverses for the down-ramp periods.

Another well-documented effect is magneto-phosphenes, or experiencing the harmless sensation of flashes of light. This is thought to originate from retinal stimulation by the induced electric field. Phosphenes occur most readily in the frequency range 10–100 Hz and are not commonly encountered in MRI.

The Strength–Duration Curve

Both the gradients and the RF are examples of time-varying magnetic fields and both induce electrical currents in tissue. So why are their associated bio-effects so different? The reason lies in the strength–duration (SD) curve, a plot of the threshold for stimulation against the duration of the stimulating pulse. In MRI terms, the duration of the pulse refers to the duration of the leading and trailing slopes of the gradient pulses, the part during which tissue currents are produced (Figure 20.2a).

Each type of muscle fibre or nerve may have a different time constant that determines the shape of the SD curve. For MRI the following hyperbolic relationship is considered to apply

$$\left(\frac{dB}{dt}\right)_{\text{threshold}} = C \cdot rb \cdot \left[1 + \frac{\tau_{\text{chron}}}{\tau}\right]$$

where $(dB/dt)_{\text{threshold}}$ is the threshold for peripheral nerve stimulation (about 20 T s^{-1}), τ is the duration of the gradient field change (i.e. the time to ramp from maximum negative to maximum positive) and τ_{chron} (the chronaxie) is a type of tissue electrical time constant. Typical values for τ_{chron} are 0.5 ms for a peripheral nerve and 3.0 ms for cardiac muscle. *rb* is known as the 'rheobase', the lowest threshold for long stimulus durations. The constant *C* accounts for the tissue radius and the gradient orientation. Theoretical hyperbolic SD curves for cardiac stimulation and the PNS limits for the IEC Normal level and first-level controlled operating modes are illustrated in Figure 20.3. The lowest thresholds occur for the longest ramp times and therefore gradients that switch faster, i.e. have very short rise times, actually allow much greater amplitude changes as well. Cardiac stimulation requires a lengthy duration of switching, and is not possible on any real MR system. In any event, owing to the different likely conduction paths or loops, the patient would almost always experience severe peripheral muscular stimulation first, which would serve as adequate warning.

In an alternative formulation of the SD curve, the step-size change in *B*, ΔB, is considered as the stimulus (this is analogous to electrical charge) giving

$$\Delta B_{\text{stim}} = \Delta B_{\text{min}}\left(1 + \frac{\Delta t}{\tau_{\text{chron}}}\right)$$

where ΔB and Δt are the maximum change in *B* (including negative portions) and the duration of the change. This gives a linear SD relationship and also shows that there is a minimum value of ΔB below which no stimulation can occur. In whole-body MR gradient systems this value is around 9 mT.

20.3.2 Gradient Noise

The characteristic knocking or drilling noise heard when an MRI sequence is in progress arises from the Lorentz force generated by the coils when a current is pulsed through them in the presence of the static magnetic field. The noise is caused by the movement of the coils against their mountings, and can be in excess of 100 dB(A) for some manufacturers' sequences. This is why hearing protection is recommended for patients during MRI scanning. The reduction of gradient noise is an active area of development for system manufacturers, with various approaches including acoustic shielding or the use of non-Cartesian spiral or radial acquisitions that minimize gradient switching (see Chapter 14).

20.3.3 Gradient Exposure Standards

The principle behind the IEC 60601-2-33 standard gradient exposure limits is to prevent cardiac stimulation and minimize PNS at any operating mode. IEC standard thresholds for normal and the first-level controlled operating mode for PNS and for cardiac stimulation are shown in Figure 20.3. The limit of the normal mode is set as the 80% median perception threshold for PNS, while the first-level limits at 100%. Further details are considered in Box 'Crossing the Threshold'.

The risk to hearing is also addressed by the IEC, which states that the system manufacturer must issue a warning on the system console if a particular pulse sequence is likely to exceed 99 dB(A). The FDA advice is effectively the same. Note that the threshold for instantaneous acoustic trauma is 140 dB and that properly fitting ear-plugs offer about 20 dB(A) attenuation. dB(A) is a unit of sound pressure level which takes into account the normal hearing curve for most people.

Crossing the Threshold

In IEC 60601-2-33, cardiac stimulation is assumed to be avoided when the combined gradient output of all gradient units of the gradient system satisfies

$$\frac{dB}{dt} < 20/1 - \exp\left(\frac{-ts}{3}\right)$$

where dB/dt is in T s^{-1} and ts is the duration of the gradient field change (i.e. the time to ramp from maximum negative to maximum positive) in ms.

PNS limits for the normal operating mode (L01) and the first-level controlled operating mode (L12) are

$$L01 = 0.8 \cdot rb \cdot \left(1 + \frac{0.36}{ts}\right)$$
$$L12 = 1.0 \cdot rb \cdot \left(1 + \frac{0.36}{ts}\right)$$

where again ts is the effective stimulus duration and rb is the rheobase, the threshold below which no further excitation is possible, independent of the stimulus duration. Manufacturers may choose to derive experimental threshold limits to use for L01

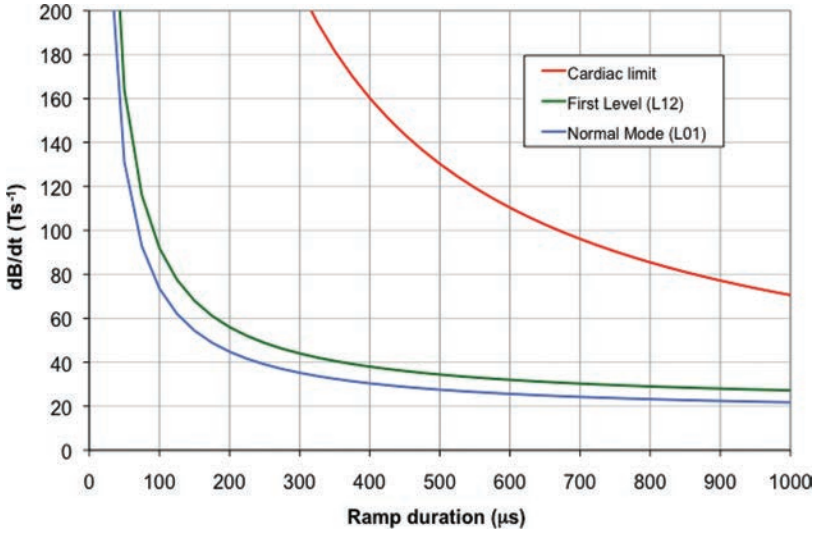

Figure 20.3 Derived strength–duration (SD) curves for the IEC 60601-2-33 limits for cardiac stimulation and the normal (L01) and first-level controlled (L12) operating modes for peripheral nerve stimulation (PNS).

Table 20.4 Rheobase values for different types of gradient system

Type of gradient system	*rb* expressed as d*B*/d*t*	*rb* expressed as *E*
Whole-body gradient system (cylindrical magnet)	2.2 V m^{-1}	20 T s^{-1}
Special-purpose gradient system	2.2 V m^{-1}	(not applicable)

and L12, setting them at 80% and 100% of the median threshold experienced by a cohort of volunteers. These are shown in Figure 20.3.

The IEC 60601-2-33 rheobase values are given in Table 20.4 and may be expressed either as the electric field E (V m^{-1}) induced in the patient or as the time rate of change of the magnetic field in the patient dB/dt (T s^{-1}).

20.4 Static Field Effects

There is evidence for some mild sensory effects of static magnetic fields, including vertigo (sometimes called 'magnet sickness'), nystagmus (involuntary eye movement) and taste sensations, with the suggestion of a dose–effect relationship for 1.5, 3 and 7 T whole-body magnets. Other effects, namely headache, tinnitus, vomiting and numbness, have not been substantiated, with some subjects claiming the effect with the magnet switched off! Recently mild transient neuro-cognitive effects in humans have been reported, although in some psychometric tests the participants did better when the field was present. At very high fields the possibilities exist of altering nerve conduction characteristics at least theoretically (e.g. for a field of 450 T), of changing the rate of ion transport across cell membranes and of altering chemical reactivities. None of these hypothetical effects has been demonstrated experimentally.

Published animal-based experiments have been beset by contradictory evidence, failure to be reproduced, poor control and lack of exposure details. For example, prolonged exposure to 9.4 T fields had no effect on numbers of offspring, growth rates, feeding patterns, blood and urine biochemistry and behavioural development for male and female adult and fetal rats. In another study on mice at 4 T (although with combined RF and switched fields and ultrasound) small changes in fetal weight, birth rates, delayed motor skill learning and adult sperm production rates were reported. At 10 T some behavioural changes in laboratory animals have been noted. Whatever the final conclusions of these experiments, any acute physiological effects of static field exposure from MRI are extremely subtle or of a mild nature.

Remember that the exposure of human subjects in MRI is for short periods only and that these effects cease with the exposure. Epidemiological studies on female magnet workers have shown no deleterious effects on fertility, pregnancies or children. A cautious approach should nevertheless be adopted for both patients and staff who are pregnant.

So what about 'mag lag', the idea that cognitive function or memory is affected by exposure to fringe fields? There is no evidence for it. It simply doesn't exist. (That loss of short-term memory you are experiencing is simply old age!)

20.4.1 Flow Effects

One well-established bio-effect is the generation of electric potentials in moving, conducting tissue, e.g. across blood flowing in vessels, particularly the aorta (the magneto-hydrodynamic effect was covered in Chapter 16). Although this is not known to be hazardous, the possibility exists, at least theoretically, of the induced potential exceeding the threshold for depolarization of cardiac muscle (about 40 mV).

Magneto-Hydrodynamic Effect

The magneto-hydrodynamic effect is illustrated in Figure 20.4, where charged particles moving at velocity v within and at an angle θ to a magnetic field B generate an electric field E

$$E = vB \sin\theta$$

Flow along the field direction will produce no effect, the maximum occurring for flow perpendicular to the field. In an idealized case, the voltage across a vessel of diameter d containing conducting fluid (e.g. blood) will be

$$V = dvB \sin\theta$$

The above expression estimated for aortic flow gives a voltage of about 40 mV at 2.5 T. Although these voltages have been demonstrated in vivo, there is no evidence of any consequent ill-effects.

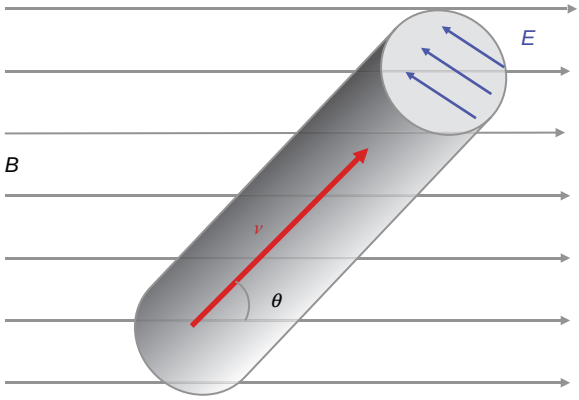

Figure 20.4 Magneto-hydrodynamic effect. An electric field *E* is induced across the moving conducting fluid, giving an EMF (voltage) across the vessel. *v* is velocity.

20.4.2 Force Fields

Static fields also pose hazards through the displacement of ferromagnetic implants (clips, coils, stents, etc.). The field will exert both a translational force and a torque (twisting force) on magnetic objects (see Box 'Of Frogs and Forces'). The field may disrupt the function of cardiac pacemakers. Of the sixteen reported deaths in MR incidents, thirteen resulted from the inadvertent scanning of persons with pacemakers. In specialist centres, under strict protocols, it has become possible to scan patients with certain newer kinds of MR conditional pacemakers. However, we strongly recommend that you don't do this unless you happen to be working in one of those centres and have appropriate local policies and procedures.

Of Frogs and Forces

Biological tissue is diamagnetic, which means it is essentially, but not entirely, non-magnetic. A diamagnetic material responds to an applied magnetic field by generating fields that oppose the applied field, i.e. generating a repulsive force. This effect has been demonstrated dramatically by magnetically levitating frogs in the spatial gradient of the fringe field of a 16 T magnet (we always thought frogs were repulsive).

Forces and torques were examined in Section 2.3.1. Aside from floating frogs, the theoretical effect of these forces on biological tissues in vivo is negligible compared with the normal mechanical and haemodynamic forces involved with life. Although red blood cells in sickle cell anaemia have shown displacement in vitro in a 0.5 T field, this has not been replicated in patients, or for normal blood cells.

20.4.3 Static Field Exposure Standards

The IEC 60601-2-33 standard gives the following static magnetic field limits:

- normal operating mode: equal or lower than 3 T;
- first-level controlled operating mode: higher than 3 T and equal to or lower than 8 T;
- second-level controlled operating mode: higher than 8 T.

20.5 MR Exposures and Pregnancy

Although there is no convincing biological, physiological or epidemiological evidence that the magnetic field exposures encountered in MRI are harmful to the fetus, it is usual to practice caution for patients in the first trimester, delaying the scan if feasible, or using alternative (but not ionizing) investigations. There is now so little concern that one organization (the HPA) forgot to advise on magnetic field exposure during pregnancy in their current guidelines! There is a call for caution (again without direct evidence) concerning the sensitivity of fetal hearing, so quieter sequences should be used if possible. Scanning should be restricted to the normal mode. Gadolinium contrast should only be used if clinically justified.

For staff who may be pregnant, there is no need to specifically alter their duties. The **A**merican **C**ollege of **R**adiology (ACR), and the UK **S**ociety and **C**ollege **o**f **R**adiographers (SCoR) guidelines recommend that, on account of the theoretical risk to fetal hearing, pregnant staff should not enter the scanner room during scanning, but all other routine activities are okay.

20.6 Occupational Exposure

The patient exposure limits are very well controlled in MRI, but what about the staff? This has been a major focus recently on account of the **E**uropean **U**nion (EU) Physical Agents Directive (Electromagnetic fields) of 2004 which has generated a decade's worth of controversy.

Studies of static field exposure have shown that, in general, the peak B field exposure to staff is around 40% of B_0 (unless you crawl into the magnet), with a time-averaged exposure (over an eight-hour working day) of around 5 mT. In most instances this is the only magnetic field exposure staff will experience. Exposure to RF and dB/dt time-varying fields will only occur in close proximity to the bore entrance during scanning – for example, when monitoring an anaesthetized patient or comforting an anxious or vulnerable patient, or during interventional procedures. Studies, including those commissioned by the EU, have shown that the exposure limits set by ICNIRP in 2010 and adopted in the 2012 EU Directive are unlikely to be exceeded. Indeed the Directive allows for its own limits to be exceeded in the special

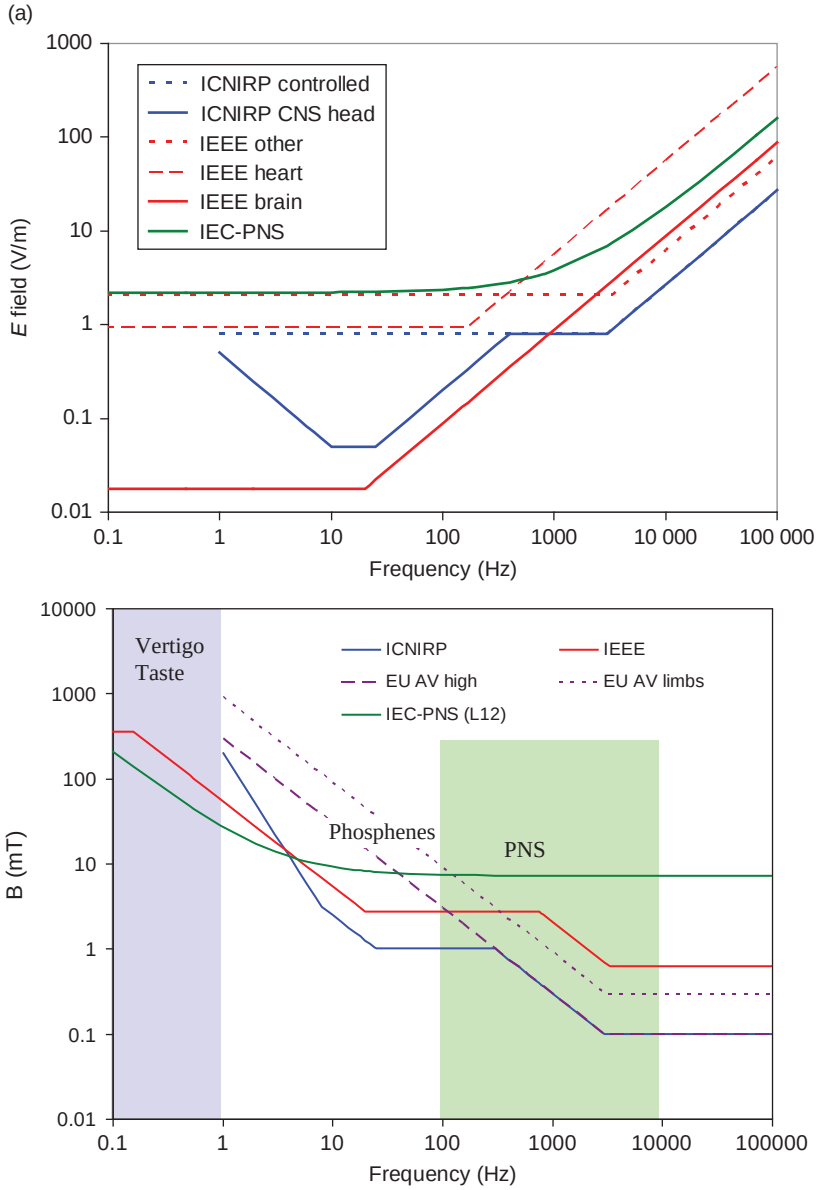

Figure 20.5 (a) Basic restrictions for occupational exposure for 1 Hz to 100 kHz and (b) corresponding Reference Levels. The blue shaded area represents the frequency range relevant to the static field (and movement within it), while green represents the imaging gradient region. These are defined as RMS values. The approximate regions of known bio-effects are also indicated.

case of clinical or research MR and MR engineering. More details are contained in Box 'Occupational Exposure Limits'.

Occupational Exposure Limits

Outside of the EU, we are not aware of any legislated occupational limits affecting MRI. Instead most countries apply guidelines set by international bodies such as ICNIRP (the International Commission on Non-Ionising Radiation Protection). There is no shortage of organizations wishing to protect you from the 'harmful' effects of electromagnetic fields. In our opinion (and that of the MR community) their definition of 'harmful' seems overly cautious, and some limits lack scientific basis.

The structure of these guidelines usually encompasses two limits shown in Figure 20.5. The Basic Restriction (BR) or Exposure Limit Value (ELV) is most often expressed in terms of the electric field induced in a tissue which is related to the physiological effect of the exposure. As the internal induced field is very difficult (i.e. impossible) to measure, Reference Levels (RL), Maximum Permissible Exposures (MPE) or Action Values (AV) are derived in terms of the incident field, usually *B*, which can be readily measured. Compliance with the RL (MPE, AV, etc.) is sufficient to ensure compliance with the Basic Restriction or equivalent. Tables 20.5 and 20.6 contain static field and RF occupational exposure limits relevant to MRI. Relevant references are listed in Further reading at the end of the chapter.

The IEC occupational limits (which apply only for MRI) are the same as the patient exposure values, except for RF, where the limit is 0.4 W kg^{-1}.

Table 20.5 Occupational exposure limits for static magnetic fields

	Trunk and head instantaneous ceiling (T)	Limbs (T)
IEC[a]	8	8
ICNIRP[b]	2	8
IEEE[c]	0.5	0.5

[a] International Electrotechnical Commission (2013) *Medical Electrical Equipment – Part 2-33: Particular Requirements for the Safety of Magnetic Resonance Equipment for Medical Diagnosis*, 3rd edition. Geneva: IEC.
[b] International Commission on Non-Ionising Radiation Protection (2009) 'Guidelines on limits to exposure from static magnetic field'. *Health Physics* 96:504–514.
[c] The Institute of Electrical and Electronics Engineers (IEEE) (2002) *IEEE Standard for Safety Levels with Respect to Human Exposure to Radio Frequency Electromagnetic Fields. 0–3 kHz*. New York: IEEE.

20.7 Contrast Agent Safety

There are several different formulations available commercially with various osmolalities and safety profiles (Table 20.7). In general, gadolinium is a safe drug well tolerated by subjects, and apart from NSF (see Box 'Gadolinium and NSF Case History') there are only a handful of serious adverse effects noted in the literature. In 2010 the European Medicines Agency (EMA) published definitive advice

Table 20.6 Occupational exposure limits for RF magnetic fields

	Frequency (MHz)	Basic restriction	Reference Level, Limit or Maximum Permissible Exposure		
		SAR (W kg^{-1})	*E* (V m^{-1})	*H* (A m^{-1})	*B* (μT)
IEC[a]	Any	4			
ICNIRP[b]	10 to 400	0.4	61	0.16	0.2
IEEE[c]	0.1 to 100	0.4	61.4	0.163	
	127.7		61.4	0.128	
	298.0		61.4	0.0547	

[a] International Electrotechnical Commission (2013) *Medical Electrical Equipment – Part 2-33: Particular Requirements for the Safety of Magnetic Resonance Equipment for Medical Diagnosis*, 3rd edition. Geneva: IEC.
[b] International Commission on Non-Ionising Radiation Protection (2010) 'Guidelines for limiting exposure to time-varying electric, magnetic, and electromagnetic fields (up to 100 kHz)'. *Health Physics* 99:818–836 and Erratum: *Health Physics* (2011) 100:112.
[c] The Institute of Electrical and Electronics Engineers (2005) *IEEE Standard for Safety Levels with Respect to Human Exposure to Radio Frequency Electromagnetic Fields, 3 kHz to 300 GHz*. New York: The Institute of Electrical and Electronics Engineers.

Table 20.7 Commercially available Gd-based contrast agents, ordered by Gd concentration. The European Medicines Agency (EMA) classified all available agents according to their risk profile for NSF in 2010; Ablavar was subsequently withdrawn from all EU countries in 2011. All trade names are registered trademarks of their respective manufacturers

Active ingredient	Ligand structure	Trade name	EMA risk class	Gd conc'n (mmol mL^{-1})	Indications for use								
					Adults	Children >2yo	Lesions with abnormal vascularity				Evaluate vessels		
							Brain, spine, associated tissues	Head and neck	Body/liver	Heart	Aorto-iliac	Iliac-femoral	CNS
Gadoxetate disodium	Linear, ionic	Eovist, Primovist	Medium	0.25	X				X				
Gadofosveset trisodium	Linear, ionic	Ablavar (US) previously Vasovist	N/A	0.25	X						X	X	
Gadoterate meglumine	Cyclic, ionic	Dotarem	Low	0.5	X	X	X						X
Gadoteridol	Cyclic, non-ionic	Prohance	Low	0.5	X	X	X	X					
Gadobenate dimeglumine	Linear, ionic	Multihance	Medium	0.5	X	X	X		X		X	X	
Gadopentetate dimeglumine	Linear, ionic	Magnevist	High	0.5	X	X	X	X	X				
Gadobenate dimeglumine	Linear, ionic	Magnegita (some EU countries)	High	0.5	X		X	X	X	X	X	X	
Gadobenate dimeglumine	Linear, ionic	Gado-MRT, RatioPharm (Germany only)	High	0.5	X		X	X	X	X	X	X	
Gadoversetamide	Linear, non-ionic	Optimark	High	0.5	X		X		X				X
Gadodiamide	Linear, non-ionic	Omniscan	High	0.5	X		X		X				
Gadobutrol	Cyclic, non-ionic	Gadavist (US), Gadovist (EU)	Low	1	X	X	X						X

Source: FDA website.

concerning NSF and Gd, classifying all Gd agents as either high, medium or low risk. In the USA, the FDA published new guidelines for manufacturers of Gd agents, requiring the information label to include warnings about NSF. The FDA requires the same warning for all formulations, even though there is good scientific evidence that some agents are much higher risk than others.

The main contraindications are poor renal function (with glomerular filtration rate <30 ml min^{-1}) and pregnancy. The gadolinium complex crosses the placenta into the fetal circulation and there is insufficient safety data about fetal exposure to gadolinium. Gadolinium also crosses into breast milk, so lactating mothers should not breastfeed for 24 h following gadolinium administration. Full details of contraindications and clinical applications can be found on the information insert in any preparation of gadolinium.

Starting in 2014 there have been reports that gadolinium may be deposited in the brain following repeated Gd contrast agent administration. It is not yet clear whether it is free Gd or still chelated, but it is well known that unbound Gd is toxic. Although Gd-based contrast agents still have a better safety profile than X-ray contrast media and radioisotope tracers, companies and radiologists should be aware of the potential risk and stay abreast of the latest research.

Gadolinium and NSF Case History

The first reports of Nephrogenic Systemic Fibrosis (NSF) appeared in 1997. In patients with severe kidney dysfunction, NSF may develop over a period of days to several weeks. The first symptoms are red or dark patches or papules that develop on the skin. The skin thickens and feels 'woody', and the skin surface can have an orange-peel texture. In addition patients may experience pain in the affected areas. In many cases, skin thickening prevents joint movements, and other organs might be affected. About 5% of patients have very rapid and progressive disease development, and some patients may die.

In 2006 a pivotal study reported that five of nine patients with NSF had received a gadolinium-based contrast agent 2–4 weeks before reporting symptoms. Shortly after, several more studies confirmed the link between Gd and NSF; higher risk was shown with high-dose administration (e.g. double-dose or bolus injection for contrast-enhanced MRA), and with one particular formulation, gadodiamide. By 2010 around 250 cases had been reported linking NSF in patients with renal failure with administration of Gd agents. (Note that NSF has never been reported in patients with normal renal function.)

20.8 So is MRI Safe?

With hundreds of millions of people having been scanned over the last four decades, it seems unlikely that some unthought-of detrimental effect from the field exposures should appear now. Caution is required concerning the use of gadolinium-based contrast agents. Aside from the NSF issue, there is some evidence that gadolinium ions may accumulate in very small concentrations in the brain. However, that is an issue for pharmaceutical safety, not magnetic fields. Ultimately the everyday dangers arise from the magnetic attractive and twisting forces and from implant heating or malfunction. Unfortunately accidents are usually caused by people, not machines. MRI is only as safe as you are in your practice.

See also:

- Safety first: Section 2.3

Further Reading

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