MEDICAL MAGNETIC RESONANCE (MR) PROCEDURES: PROTECTION OF PATIENTS

The International Commission on Non-Ionizing Radiation Protection*

INTRODUCTION

MAGNETIC RESONANCE imaging (MRI) has become an established diagnostic imaging modality. The clinical usefulness of in-vivo magnetic resonance spectroscopy (MRS) has been demonstrated in several clinical applications and is being explored further. These techniques involve exposure of the patient to static and time-varying magnetic fields, radiofrequency electromagnetic fields, and acoustic noise. In particular exposure conditions, these fields may pose a health hazard or increased risk.

The International Non-Ionizing Radiation Committee of the International Radiation Protection Association (IRPA/INIRC) has published a guideline on protection of the patient undergoing a magnetic resonance examination (IRPA/INIRC 1991). In recent years, the successor of IRPA/INIRC, the International Commission on Non-Ionizing Radiation Protection (ICNIRP) has performed reviews of the biological effects from exposure to static and time-varying electromagnetic fields (ICNIRP 1997a, 1997b, 2001). Guidelines on limits of exposure to static magnetic fields and guidelines for limiting exposure to time-varying, electric, magnetic, and electromagnetic fields (up to 300 GHz) have been published by ICNIRP respectively in 1994 and 1998 (ICNIRP 1994, 1998).

Recently, several reviews concerning safety aspects of MR procedures have been published (e.g., Ordidge et al. 2000; Shellock 2001a; Shellock 2003). These publications, in conjunction with other reviews and recent literature, form the basis for the review of research data on MRI procedures in this document.

PURPOSE AND SCOPE

The purpose of this document is to provide information on levels of exposure and health effects from magnetic and radiofrequency electromagnetic fields associated with the use of MR diagnostic devices, and on precautions to be taken to minimize health hazards and risks to patients and volunteers undergoing MR examinations.

The document is intended for use by international or national medical device regulatory authorities, MR users and health professionals, and those involved in the design and manufacture of MR equipment for clinical applications. Contraindications, precautions, and safety considerations for patients are given.

Guidelines on occupational and general public exposure limits to all ranges of electromagnetic fields (static, time-varying gradients, radiofrequency) have been published (ICNIRP 1994, 1998). However, these guidelines were written many years ago, and they are now under review.

RATIONALE

A review of the biological effects from exposure to magnetic fields is contained in UNEP/WHO/IRPA (1987) and ICNIRP (1997a and b, 1999). Additional data and references can be found in Magin et al. (1992), IEC (2001) and Shellock (2001a). Recommendations for radiofrequency exposure levels are based on the data contained in reports by the NCRP (1986), UNEP/WHO/IRPA (1993), ICNIRP (2001), WHO (2003) and on the rationale appended to ICNIRP (1998).

The following is a brief summary of conclusions drawn from the review of scientific literature.

Static magnetic fields

The possible health effects that might result from acute exposure to intense static magnetic fields have been recently reviewed by Schenk (2000, 2001). The basic actions of static magnetic fields are physical effects (translation and orientation), electrodynamic forces on moving electrolytes, and effects on electron spin states of chemical reaction intermediates. At a higher level of organization, biological effects in cells, tissues and living organisms have been studied.

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Translation and orientation of molecular and cellular substances such as retinal rods, and some living cells have been observed in vitro in experiments with fields at and above 1 tesla (T). This type of effect occurs on dia- and paramagnetic materials such as hemoglobin, collagen, fibrin, and also on ferrimagnetic particles such as magnetite. It is also now known that water distribution can be affected by high-intensity high-gradient magnetic fields (e.g., 8 T, 50 T m^{-1}; Ueno and Iwasaka 1994). Ueno and Iwasaka showed that in an 8 T magnetic field water can experience a force up to 30% the force of gravity. However, this force depends directly on the square of the magnetic field strength and inversely on the radius of the magnet. Consequently, in a whole-body 4 T magnet, the force is only about 1% of gravity.

Static magnetic fields exert electrodynamic forces on moving ions in blood vessels. These forces lead to the generation of electric potential across the blood vessels (Hall effect) and theoretically a reduction of blood flow velocity (Tenforde 1992). Such flow potentials caused by fields of more than 0.1 T can be detected during T-wave recording in the electrocardiogram (ECG) (Togawa et al. 1967; Tenforde et al. 1983). Kinouchi et al. (1996) calculated that the maximum flow potential induced by a field of 5 T would cause a current density of 100 mA m^{-2} at the location of the sinuatrial pacemaker mode (0.5 V m^{-1}, assuming a tissue conductivity of 0.2 S m^{-1}). This is below the estimated threshold for cardiac stimulation (Reilly 1998). The T-wave indicates the repolarization of ventricular heart muscle when electrical excitability gradually recovers following contraction (Antoni 1998). Fibrillation of the heart, potentially fatal asynchronous and irregular cardiac muscle contraction, can only be induced during this "vulnerable" period. However, the fibrillation threshold is about 10–20 times higher than that for cardiac muscle stimulation per se. Reilly (1998) estimates the 1- and 50-percentile ranks for cardiac stimulation in humans due to induced electric fields to be 5 and 10 V m^{-1}, respectively. In addition, a 5 and 10% reduction in blood flow in the aorta was predicted to occur in static fields of 10 and 15 T, respectively, due to magneto-hydrodynamic interactions (Kinouchi et al. 1996). However, Kangarlu et al. (1999) found that volunteers exposed to an 8 T field for 1 h showed no change in heart rate or diastolic or systolic blood pressure either during or after exposure. The ECG recorded during exposure was regarded as uninterpretable due to the superposition of the potential generated by aortic blood flow and smaller potentials generated by blood flow in other vessels. In addition, vertigo and other sensations were recorded during movement in this field.

More detailed studies by the same group have recently been published (Chakeres et al. 2003a, 2003b); both were approved by the U.S. FDA Investigational Review Board. The authors report that exposure of 25 healthy volunteers, aged between 18–65 y, to 8 T static fields (duration unspecified) had no effect on cognitive function, assessed during exposure using seven standard neuropsychological tests (Chakeres et al. 2003a). The second paper reports a lack of clinically significant effects of exposure to fields of up to 8 T on heart rate, respiratory rate, systolic and diastolic blood pressure, finger pulse oxygenation levels, and core body temperature (Chakeres et al. 2003b). There was a statistically significant trend for systolic pressure to increase with flux density, but at 8 T this was only 3.6 mm Hg, approximately half of the difference seen moving from a sitting to a supine body position. Interestingly, the volunteers were moved very slowly (one or two feet over a few seconds, followed by a 15–30 s pause, taking overall about 3–4 min) into the magnet bore in order to avoid the transient, movement-induced sensations described above (Schenck et al. 1992). Nevertheless, nine subjects reported sensations of dizziness, and two reported a metallic taste, assumed to be due to electrolysis of metallic chemicals in the subjects' teeth fillings.

The literature does not indicate any serious adverse health effects from the whole-body exposure of healthy human subjects up to 8 T. However, it should be noted that, to date, there have been no epidemiological studies performed to assess possible long term health effects in patients, workers, or volunteers. It is important that such research be carried out, particularly on individuals such as workers and volunteers with high levels of exposure.

Time-varying magnetic fields

The rapidly switched magnetic gradients used in magnetic resonance imaging produce time-varying magnetic fields in three orthogonal directions: normally, the z-axis corresponds to the longitudinal axis of the patient, the y-axis to the transverse one, and the x-axis to the antero-posterior one. These fields are characterized by the magnitude and duration of the change in magnetic field and are often described by the parameter, dB/dt, the time rate of change of the magnetic field. It induces electric fields in a subject in accordance with Faraday's law, which, if of sufficient magnitude, can produce nerve and muscle stimulation. The induced electric field is proportional to dB/dt and the size of the subject. In theory, the threshold for stimulation in terms of dB/dt should be lower in larger subjects. However, other factors also influence the nerve stimulation threshold of an individual and no correlation with subject size has been observed in volunteer studies.

From a safety standpoint, the primary concern with regard to time-varying magnetic fields is cardiac fibrillation, because it is a life-threatening condition. The threshold for cardiac stimulation is lower than that for fibrillation (Reilly 1998). Peripheral nerve stimulation is a practical concern because, if sufficiently intense, it can be intolerable and result in termination of the examination.

Recommendations on limiting patient and volunteer exposure to time-varying magnetic fields are based primarily on stimulation of peripheral nerves and muscles, including the heart, by the induced electric fields.

Peripheral nerve stimulation. The most extensive work on peripheral nerve stimulation in humans was a study of 84 volunteers at Purdue University (Bourland et al. 1999; Schaefer et al. 2000; Nyenhuis et al. 2001). Data were obtained for the stimulation threshold, the threshold for uncomfortable stimulation, and the threshold for intolerable stimulation during exposure to ramped x- or y-gradient fields that induced pulsed electric fields and associated currents.

The thresholds varied with ramped gradient pulse width, increasing as pulse widths decreased in a manner that can be approximated by a hyperbolic relationship. Conventionally, the term rheobase describes the electrical stimulation threshold for long (infinite) pulse duration, and the term chronaxie is used to describe the pulse duration at which the stimulation threshold is twice the rheobase. Bourland et al. (1999) reported an average (dB/dt) rheobase and chronaxie for the sensation threshold of 15 T s^{-1} and 365 μs for the y-coil and 26 T s^{-1} and 378 μs for the z-coil. Significant motor contraction of either abdominal or thoracic skeletal muscles was observed for gradient field strengths approximately 50% greater than the sensation threshold. A dB/dt magnetic field rate of approximately twice the sensation threshold was described by the subjects in this study as intolerable. The dB/dt values for the z gradient are about 50% higher than the y gradient due to the fact that the induced electric field depends on the cross-sectional area, and the area of the coronal cross section of the human body is larger than that of the axial cross section.

The results were standardized by assuming a chronaxie for the responses of each volunteer of 380 μs; population median rheobases for perception without discomfort, uncomfortable sensation and intolerable sensation were calculated to be 18.8, 28.3, and 36.9 T s^{-1} for the y-axis, and 28.8, 44.0, and 59.8 T s^{-1} for the z-axis. These results for the y-axis are illustrated in Fig. 1, where, for comparison with the results of other authors, the values have been scaled by a factor of 1.48 for the y gradient to convert to maximum dB/dt values at 0.2 m off axis; the corresponding value for the z-gradient is 1.21 (Schaefer et al. 2000; Nyenhuis et al. 2001). Results consistent with these values have been reported in earlier studies (Ham et al. 1997; Abart et al. 1997).

A finite element calculation (Nyenhuis et al. 2001) indicated that the calculated rheobase electric fields for the y and z coils were about 2 V m^{-1}, somewhat lower

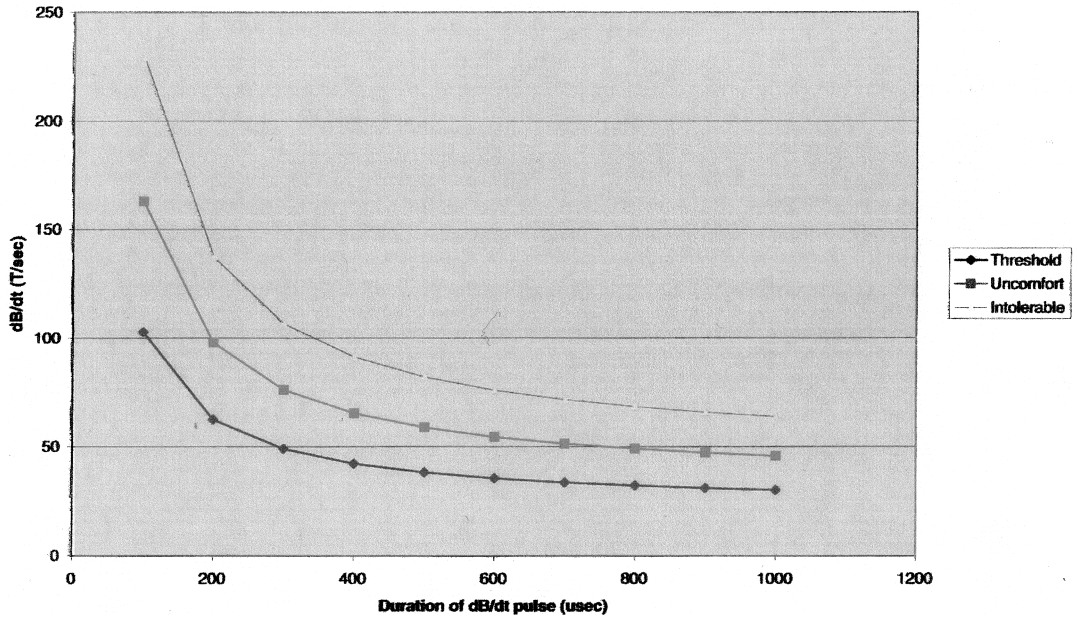

Fig. 1. Comparison of dB/dt values for threshold, uncomfortable and intolerable stimulation—Y gradient (from Bourland et al. 1999).

than previous theoretical estimates of 6 V m^{-1} for the excitation threshold of 20 μm diameter nerve fibers (Reilly 1990, 1992). The authors suggested local enhancement of electric field in the body might be due to the concentration of eddy currents by relatively high impedance structures such as bone, and that physiologic summation and local anatomical differences around nerves might also play a role.

When shapes of gradient pulses deviate from trapezoidal or sinusoidal, the biological effectiveness in causing stimulation changes. In such cases, the threshold must be evaluated on the basis of the shape and frequency of the pulse (Jokela 1997, 2000).

Fig. 2 shows stimulation data by Bourland's group (Nyenhuis et al. 2001) in terms of the number of subjects responding vs. dB/dt. Bourland found that the dB/dt needed for the lowest percentile for uncomfortable stimulation is approximately equal to the median threshold for perception. The lowest percentile for intolerable stimulation occurs at a dB/dt approximately 20% above the median perception threshold.

Cardiac stimulation data. Early in the development of fast-scan MR techniques, there was concern that the heart could be at risk with respect to stimulation by gradient pulses. Reilly (1990) noted that, for long durations of induced current, thresholds for peripheral nerve and cardiac stimulation are similar. However, Nyenhuis et al. (2001) observe that, with gradient pulse sequences presently used in MRI, cardiac stimulation thresholds are much higher than peripheral nerve stimulation thresholds.

Bourland et al. (1999) observed the mean threshold for magnetically stimulated respiration in dogs at approximately three times the mean peripheral nerve stimulation threshold. For cardiac stimulation (the induction of ectopic beats) in these animals, the threshold was reported to be nine times the peripheral nerve stimulation threshold at a pulse duration of 530 μs. The median cardiac stimulation threshold at this pulse width was found to be 2,700 T s^{-1}. When the threshold varies in a hyperbolic manner with stimulus pulse width, the threshold conditions can also be expressed by a constant equal to the product of the ramp time and the effective dB/dt, in this case equal to 1.43 T. By scaling the numbers to human geometry and assuming a chronaxie of 3 ms, a gradient field ramp of 0.43 T (a factor 0.3 lower) was

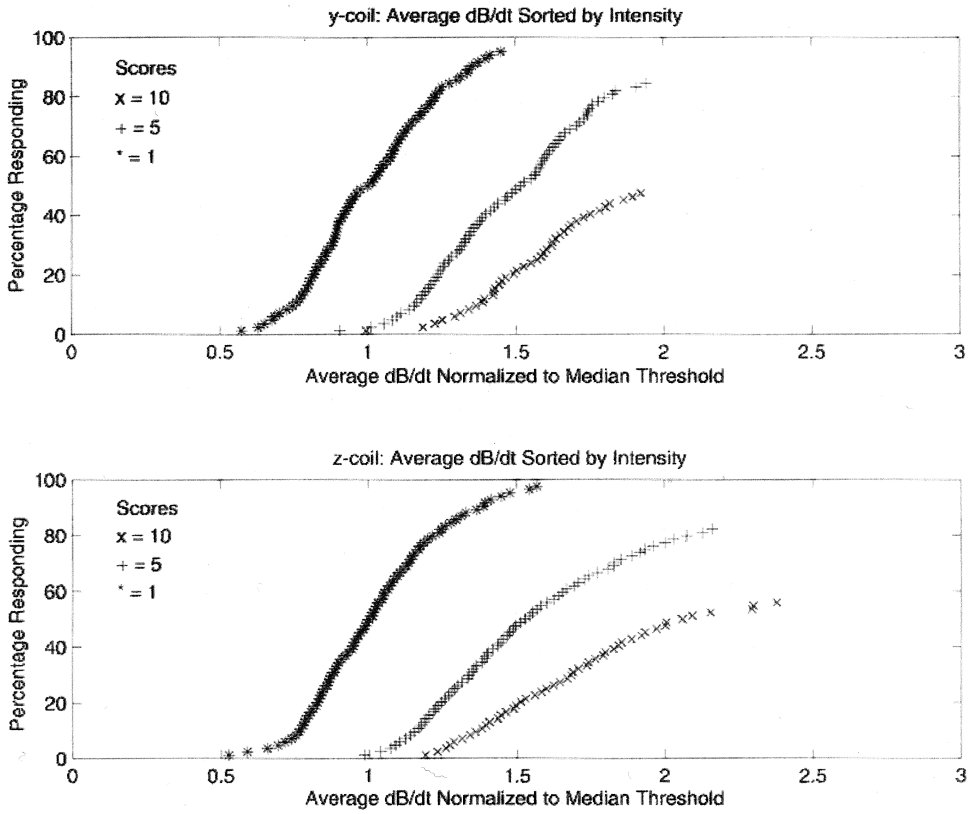

Fig. 2. Percentage thresholds for perception (1), uncomfortable stimulation (5) and intolerable stimulation (10) in a group of 84 volunteers. Data are presented as normalized values to the median threshold of perception (from Nyenhuis et al. 2001).

estimated to be the cardiac stimulation threshold for humans. Using Reilly's observation that the 1-percentile level in the population is half the median stimulation threshold, Bourland estimated a value of 0.215 T for this 1-percentile level, which is in good agreement with Reilly's estimate of 0.19 T. The corresponding value of dB/dt would be 405 T s^{-1} at a current pulse width of 530 μs, which is a factor of ten above the threshold for peripheral nerve stimulation and a factor of five above the median for intolerable peripheral nerve stimulation.

Nyenhuis et al. (2001) conclude that because there is essentially "zero risk" of cardiac stimulation in present day MRI gradient fields, the practical physiological limit of exposure to such fields can be based on avoiding uncomfortable or intolerable sensations caused by the very strong perception of the field.

Brain stimulation data. Neural tissue of the brain can be stimulated by time-varying magnetic fields, as demonstrated by transcranial magnetic stimulation (TMS) studies. Reilly (1998) calculated induced electric field rheobase thresholds to be of the order of 20 V m^{-1}, about an order of magnitude greater than the thresholds cited above for peripheral nerve stimulation. Similar values derived from volunteer studies have been recently reported by Kowalski et al. (2002). These TMS studies show some people to be more susceptible. Such people include those with epilepsy, a family history of seizure, and users of tricyclic anti-depressants, neuroleptic agents and other drugs that lower seizure threshold (Wassermann 1998). Serious heart disease and increased intracranial pressure have also been suggested as contraindications due to the potential complications that would be introduced by seizure.

Such potential complications may be borne in mind when contemplating experimental investigations of very high rates of change of gradient field. However, studies of volunteers following MRI exposure have found no effects on cognitive function (Sweetland et al. 1987; Brockway and Bream 1992; Chakeres et al. 2003a).

For long durations of dB/dt pulses, stimulation thresholds may be lower. From the work of Jefferys et al. (2003) and Durand (2003), it looks as though fields of the order of 1 to a few V m^{-1} can have effects on the excitability of neurons in the brain. However, these effects have time constants that mean that induced currents will need to be maintained for several ms, probably $>$10 ms.

Radiofrequency fields

Radiofrequency energy at frequencies above 10 MHz deposited in the body during an MR examination will be converted to heat, which will be distributed largely by convective heat transfer through blood flow. Since temperature changes in the various organs and tissues of the body during an MR procedure are difficult to measure in clinical routine, RF exposure of patients is usually characterized by means of the "specific energy absorption rate" (SAR), which is defined as the average energy dissipated in the body per unit of mass and time. In general, only parts of the patient's body are exposed simultaneously during an MR procedure. Therefore, not only the whole-body SAR but also partial-body SARs for the head, the trunk, and the extremities should be considered.

It is important to restrict the rise of tissue and body temperature to levels below which local thermal injury or systemic thermal overload may occur. These can be derived from experimental, clinical, and dosimetric modeling studies of the thermal effects of MR exposure (Adair and Berglund 1986, 1989; Athey and Czerski 1988; Shellock et al. 1989; Grandolfo et al. 1990; Shellock et al. 1994; Hand et al. 1999, 2000; Gandhi and Chen 1999; Shellock 2000; Gandhi 2001; Shellock 2001a; Shellock and Schaefer 2001) and from experimental and clinical studies of the effects of hyperthermia (WHO 2003).

The prime consideration in limiting radiofrequency exposure is elevation of temperature in the skin, body core, or in spatially limited volumes of tissues where local temperature increases ("hot spots") may occur under conditions of MR exposure. Non-uniformity in RF energy deposition, especially in tissues particularly sensitive to heat such as the hypothalamus or poorly perfused such as the lens of the eye were considered in the recommendations that follow. In addition, heat loss from the embryo and fetus across the placental barrier is less efficient than heat dissipation in other well-vascularized tissues.

Whole-body physiological responses in healthy adults. Cardiovascular responses to heat are central to body temperature regulation in humans (Donaldson et al. 2003). Except in various pathological conditions or overwhelming heat stress, the body "core" temperature is maintained under a wide range of environmental conditions at a "set-point" value showing a circadian fluctuation of about $\pm$0.5°C around a mean value of about 37°C. Heat gained during exposure to RF radiation has to be compensated by heat loss and is often accompanied by a small increase in heat storage.

Humans possess comparatively effective heat loss mechanisms, the principal effectors are the sweat glands and cutaneous blood vessels (Rowell 1983; Nadel 1984). In addition to a well developed ability to sweat, which in humans can be produced over most of the body surface,

the dynamic range of blood flow rates in the skin is much higher than in other species. Skin blood flow can increase from approximately 0.2–0.5 L min^{-1} in thermally neutral conditions, to values exceeding 7–8 L min^{-1} during severe hyperthermia, an increase of about twenty-fold (Fig. 3).

Prolonged rates of increase in heat storage, however, will lead to unacceptable rises in body temperature. Generally, organizations responsible for safety during work in hot environments advise restricting body temperature rise to 38°C in order to protect individuals from heat-related disorders such as heat exhaustion (e.g., NIOSH 1986).

Similar, less marked, physiological responses have been seen in resting, healthy volunteers exposed to MR under controlled environmental conditions. Two such studies by Shellock et al. (1989, 1994) of the effects of acute abdominal exposure at 64 MHz electromagnetic fields indicate that volunteers will accommodate whole-body RF heat loads of between approximately 1 W kg^{-1} for 45 min at environmental temperatures of up to 31°C to 6 W kg^{-1} for at least 15 min at ambient temperatures with increased skin blood flow and profuse localized sweating but with minimal changes in core temperature.

Generally, these studies are supported by mathematical modeling of human thermoregulatory responses to MR exposure. For example, Adair and Berglund (1986) calculated that, during exposure at a whole-body SAR of 4 W kg^{-1}, the body temperature of a lightly clothed patient whose thermoregulatory ability was unimpaired would rise by up to a maximum of 0.6°C, depending on environmental conditions. Skin blood flow was estimated to rise to maximum values at higher SARs, requiring increased cardiac output. In these circumstances, however, they noted that the health of patients with impaired cardiac function could be compromised. Further calculation (Adair and Berglund 1989) predicted that patients with reduced skin blood flow (up to about 70% normal) would still experience body temperature increases of less than 1°C at 4 W kg^{-1} (for 40 min or less) under normal ambient conditions but noted that patients with greater degrees of impairment might be compromised under these circumstances.

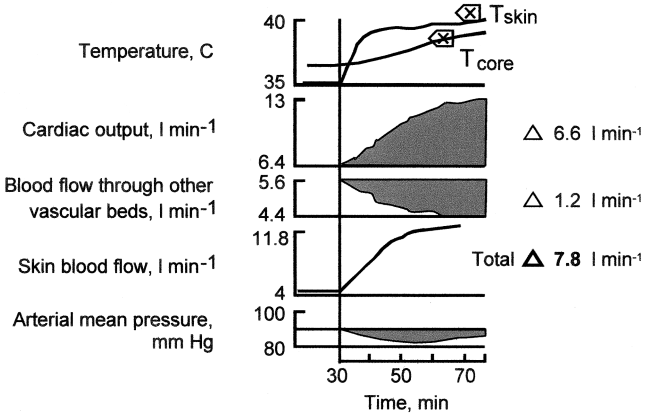

Fig. 3. Cardiovascular adjustment in supine resting volunteers heated through the skin and peripheral tissues via a "hot water jacket" to the limits of thermal tolerance of around 39°C body temperature (from Rowell 1983).

Possible complications resulting from disease and medication. Cardiovascular diseases that compromise the circulation, such as peripheral vascular disease, which may be caused by atherosclerosis or heart failure, are highly prevalent in the elderly (Corti et al. 2001; De Sanctis 2001; Lakatta 2002). In addition, dehydration makes the blood more prone to clot, and this increases the incidence of coronary and cerebral thrombosis in people with pre-existing roughening of the arteries due to atheroma. This is commonly present in middle-aged and older people and accounts for the fact that most of the heat-related mortality from arterial thrombosis occurs in people of this age group (Donaldson et al. 2003). Older people also appear less effective at maintaining normal body temperature compared to the young due to declines in sweating and blood flow responses as well as from a decline in the neural control of these responses (Rooke et al. 1994; Anderson et al. 1996).

Otherwise, heat-related disorders in sedentary people are usually associated with impairment of sweating and vasodilatation, either by drugs or disease. They are most commonly seen in psychiatric patients receiving drugs such as barbiturates or phenothiazines which depress reflex regulation of body temperature generally, or anticholinergic drugs which specifically suppress sweating and vasodilatation (Donaldson et al. 2003; Shellock 2001a). General autonomic hypofunction due to diabetes also increases susceptibility in sedentary people. Generally, however, the interactions between drugs and temperature regulating mechanisms are complex and depend on a number of factors.

Fever is also generally assumed to increase susceptibility to exogenous sources of heat such as RF radiation (e.g., NCRP 1986). Adair et al. (1997) have investigated the effect of exposure to RF radiation on experimentally-induced fever in a non-human primate (the squirrel monkey). Fevers are generated by an increased metabolic rate and by peripheral vasoconstriction, the opposite response to hyperthermia induced by RF radiation or exercise. The authors reported that RF energy absorbed during a febrile episode may have a sparing effect on endogenous energy production but may augment the fever if deposited deep within the body, as occurred during exposure at a resonant frequency (450 MHz in the

squirrel monkey). In addition, the fever may also be exacerbated if exposure occurs later in the febrile episode, during defervescence when active heat loss mechanisms are required.

Clearly, it is important to assess the responses of patients of varying degrees of susceptibility to imposed heat loads. Information regarding patient responses has been collected and is summarized in Shellock and Schaefer (2001). Unfortunately, few records have been made; the data are highly variable and mostly clustered around responses at whole-body SARs of 0.3–0.6 W kg^{-1} with no indication of duration of exposure. Further, there was no indication as to the disease status of the patient or their potential susceptibility to hyperthermia.

Exposure during childhood. The main physical difference between children and adults affecting thermoregulation is the much higher surface-area-to-mass index of children. In a warm environment this allows them to rely more on increased skin blood flow and heat loss through convection and radiation, and less on evaporative cooling (Falk 1998). Nevertheless, during exercise in thermally neutral or warm environments, children thermoregulate as effectively as adults. However, dehydration from excessive sweating may have a more detrimental effect on children because of their greater reliance on elevated skin blood flow to dissipate heat.

Localized heating. The extent to which RF absorption in tissues or organs of the body results in localized peaks of temperature rise compared to the average rise in core body temperature depends not only on the local SAR but also on the vascularity and flow of blood through the tissue or organ in question. Whilst the former is an intrinsic property of the tissue, that latter can be varied considerably, particularly through the skin and musculature, by metabolic, endocrine and neural control mechanisms (e.g., Sukkar et al. 2000). The distribution of blood flow through organs and tissues is also likely to be compromised in the older people. Whilst cardiac output is maintained in healthy older people, total peripheral resistance is increased (Ferrari 2002); cardiovascular diseases which will further compromise the circulation, such as atherosclerosis, peripheral vascular disease or chronic heart failure, are also highly prevalent (Corti et al. 2001; De Sanctis 2001; Lakatta 2002). In addition, people taking medications such as beta-blockers that affect the peripheral distribution of blood flow may also be compromised in this respect.

Hyperthermia is being used increasingly as an adjunct to radio- or chemotherapy in the treatment of tumors (Dahl et al. 1999; Falk and Issels 2001). A considerable number of acute studies have been carried out both in vitro and in vivo, investigating "dose"-response relationships for tissue damage resulting from localized tissue or whole-body heating. Temperatures have usually ranged between 40–45°C, sometimes up to 50°C or more, for periods lasting from a few minutes to several hours. The results of such studies have been summarized recently by Dewhirst et al. (2003).

In animal studies and in a very small number of human studies (mostly of skin damage), cell loss and/or tissue lesions have been induced in a variety of tissues following whole-body or localized heating. The results from different studies are variable but in many cases lesions occurred when temperatures exceeded 42°C or so for periods of more than about 1 h (Dewhirst et al. 2003). This occurred with increasing rapidity as temperatures rose further so that at around 45°C, lesions could occur within 10–30 min in many tissues. With regard to the susceptibility of different animal tissues, the central nervous system, including the blood-brain barrier, and the testes seemed the most sensitive to heat; significant changes were reported occurring after exposure to temperatures of only 40–41°C for periods of around 1 h (Dewhirst et al. 2003). However, human and pig skin seemed less susceptible to raised temperature than the skin of some other animals such as mice.

It can generally be assumed that adverse effects will be avoided with a margin of safety if temperatures in the head are less than 38°C, temperatures in the trunk less than 39°C and temperatures in the limbs less than 40°C (Athey and Czerski 1988).

Simple calculation (Athey 1989) relating localized heating in the eye to SAR in the head suggests that exposure resulting in an SAR to the head of 3 W kg^{-1} is unlikely to raise the temperature of the eye by more than 1.6°C; brain temperatures are unlikely to rise by more than 1°C under these conditions.

Gandhi and Chen (1999) and Gandhi (2001) have applied the finite-difference time-domain method to a millimeter resolution model of the human body developed from MRI scans to estimate SAR distribution in the body. To this end, the electrical properties of 30 different tissue types were prescribed in the model. Their calculations, which were performed for different RF coils operated at 64, 128, and 170 MHz, indicate that the maximum SAR for 100 g of tissue can be ten times greater than the whole-body average when exposed in a 64 MHz body coil.

For RF decoupling coils operated at frequencies between 64 and 213 MHz, electromagnetic and thermal modeling of SAR and temperature fields in the human leg have been performed by Hand et al. based on a three-dimensional bio-heat transfer model (Hand et al. 1999, 2000). The predicted SAR distributions were

strongly dependent on the spatial distribution of muscle and fat/bone within the leg. Since currents induced in the tissue tend to pass through the more conducting muscle, it was in this tissue that the higher SARs occurred.

As an alternative to these time-consuming computer simulations, the temperature rise in a partial-body region during RF exposure can roughly be assessed by means of analytical solutions to an appropriate bio-heat transfer model. This approach has been employed to assess temperature changes in a homogeneous tissue region due to localized RF heating from interventional MR devices (Yeung and Atalar 2001) and to roughly predict the maximum temperature rise during an MR procedure with varying SAR levels at the center of a larger homogeneous tissue region (Brix et al. 2002).

Summary. For whole-body exposures, no adverse health effects are expected if the increase in body core temperature does not exceed 1°C. In the case of infants and persons with cardiocirculatory impairment, the temperature increase should not exceed 0.5°C. With regard to localized heating, it seems reasonable to assume that adverse effects will be avoided with a reasonable certainty if temperatures in localized regions of the head are less than 38°C, of the trunk less than 39°C, and in the limbs less than 40°C.

MR procedures and pregnant patients

In pregnancy, there is both the safety of the mother and that of the unborn child to consider. In particular, the developing embryo and fetus is susceptible to a variety of teratogens, including heat. Potentially susceptible processes include the highly ordered sequences of cell proliferation and differentiation, cellular migration and programmed cell death (apoptosis). Sensitivity varies during gestation and is usually greatest during organogenesis when the main structures of the body are formed. This period occurs during the first trimester of human pregnancy. The fetal stage is largely characterized by the growth of these structures and is generally considered less sensitive to the effect of teratogens, although the central nervous system continues to develop during this period and postnatally and can be adversely affected by some agents.

General health and safety issues relating to MR procedures and pregnancy have been discussed by, for example, Kanal (1994) and Colletti (2001). The possible developmental effects of exposure to static and extremely low frequency magnetic fields, often in an occupational or environmental context, have been reviewed recently by IARC (2002) and ICNIRP (2003). The effects of maternal hyperthermia, including RF-induced hyperthermia, have been reviewed recently, for example by Edwards et al. (1995, 2003).

Static magnetic fields. Generally, no consistent effects of static magnetic field exposure on reproduction and development have been seen using mammalian species (IARC 2002; ICNIRP 2003); however, few comprehensive studies have been carried out. Several studies indicate that implantation and prenatal and postnatal development of the embryo and fetus are not affected by exposure for varying periods during gestation to fields of between 1 and 9.4 T (Sikov et al. 1979; Konermann and Monig 1986; Murakami et al. 1992; Okazaki et al. 2001). However, Mevissen et al. (1994) reported continuous exposure to a 30 mT field slightly decreased the numbers of viable fetuses per litter. As a probable consequence of these smaller litter sizes, prenatal development as measured by skeletal ossification was accelerated, and postnatal growth up to day 50 was increased. IARC (2002) note that two somewhat dated studies (Neurath 1968; Ueno et al. 1984) report that exposure to 1 T fields with high spatial gradients (10–1,000 T m^{-1}) can adversely effect the development of frogs and toads, but note that most studies indicate a lack of effect of static field exposure.

Low frequency magnetic fields. The possibility that exposure to low frequency electromagnetic fields, mostly at levels encountered occupationally or in the environment, may affect fertility, reproduction, or pre- and postnatal growth and development has been widely investigated (AGNIR 1994; NIEHS 1988; IARC 2002; ICNIRP 2003). This issue has been addressed using both mammals and birds, although the results of studies using mammals are most relevant to possible effects on humans (Brent 1999). However, it should be noted that the coupling of low frequency magnetic fields to small mammals will be different to that in humans because of the differences in body size and shape.

In summary, several well designed studies noted an increase in the incidence of minor skeletal variants following in utero exposure to power frequency (50–60 Hz) fields up to 30 mT (e.g., Kowalczuk et al. 1994; Mevissen et al. 1994; Juutilainen et al. 1997; Huuskonen et al. 1998a) or VLF fields (mostly 10–20 kHz) up to 15 μT (peak-to-peak) (e.g., Juutilainen et al. 1997; Huuskonen et al. 1998a, 1998b) although other studies have not reported this effect (e.g., Rommereim et al. 1996; Ryan et al. 1996; Dawson et al. 1998). The effects of exposure of three generations of rats to 60 Hz magnetic fields of up to 1 mT had no effect on fertility and reproductive performance in rats (Ryan et al. 1999). Generally, the prolonged exposure of rodents to low

frequency magnetic fields of up to 30 mT has had no adverse effect on reproductive outcome.

Only one very preliminary study has investigated the effect of pulsed gradient fields on pregnancy outcome in mice (McRobbie and Foster 1985); rates of change of flux density (several kT s^{-1}) were sufficient to cause muscle contraction in some experimental runs. No adverse effects were seen, but the results are not informative. Variable but small numbers of mice were used, few teratological end-points were examined (litter size and weight) and the animal husbandry was poor (in at least two of the four experimental runs, the mice had parasitic infections resulting in post-natal deaths).

RF-induced hyperthermia. Generally, pregnant women maintain their heat balance as well as non-pregnant women during exercise in warm environments (Donaldson et al. 2003). Fetal temperature is "clamped" to the temperature of the mother, but is usually about 0.5°C higher because of counter-current heat exchange in the vessels of the umbilical cord (Schröder and Power 1997) and may be affected not only by changes to maternal body temperature per se but also by changes to placental blood flow, during heat stress for example. However, excessive hyperthermia has a direct effect on the growth of the embryo and fetus in utero. Neural tube and facial defects have been found in children whose mothers had experienced prolonged or repeated hyperthermia (39°C or more for longer than 1 d) during the first trimester of pregnancy (Milunsky et al. 1992; Chambers et al. 1998). Similar effects have been seen in experimental studies; the threshold in many species occurs when maternal body temperature is raised by about 1.5–2.0°C above normal core body temperature for tens of minutes up to an hour or so (reviewed by, e.g., Graham et al. 1998; Edwards et al. 1995, 2003). Higher elevations, up to about 5°C, were required for shorter durations. RF-induced hyperthermia has similar effects to those induced by more conventional heating (e.g., Verschaeve and Maes 1998; O'Connor 1999). However, the effects of hyperthermia on the developing nervous system, and by implication RF-induced heating, have not been fully characterized and should be further investigated.

MRI exposure—animal and human studies. Several studies have examined the effects of exposure of animals to the fields generated by MRI systems. Whilst such exposure is clearly realistic, the coupling of MRI fields to small mammals will differ from the way in which they couple to humans.

Tyndall (1993) reported that the exposure of pregnant mice to MRI significantly increased the percentage of affected fetuses with regard to both cranio-facial perimeter and crown-rump length. Heinrichs et al. (1988) had previously reported decreased crown-rump length following prolonged (16 h) exposure during gestation. These latter authors suggested that noise-induced stress may have contributed to the outcome. In addition, both studies based their analyses on individual fetuses which ignores litter effects resulting from interactions with the mother and tends to overestimate statistical significance (AGNIR 1994). Further, many experimental parameters, such as SAR, were unspecified. More recently, Carnes and Magin (1996) and Magin et al. (2000) report decreased post-natal survival, fetal weight and crown-rump length in some groups of mice exposed to MRI fields but not in other groups. The authors note a general lack of consensus concerning possible MRI effects on reproduction and development and suggest that exposure thresholds and mechanisms of such effects be further evaluated before the associated safety risks can be determined.

There are two studies of pregnancy outcome in humans following exposure in utero to echo-planar MRI, discussed by Coletti (2001). Baker et al. (1994) carried out a 3-y follow-up of 20 children examined in utero with echo planar MRI during the second or third trimester. All the fetuses imaged were from pregnancies deemed to be abnormal, with congenital abnormalities diagnosed on ultrasonography, suspected growth retardation, or problems with the placental site. Pregnancy outcome was briefly summarized, no unexpected abnormalities were found that the authors considered could reasonably be attributed to the MRI exposure. With such an uncommon number of subjects, however, it would be difficult to assess any comparatively small effects of MRI exposure.

Subsequently, the same group (Myers et al. 1998) carried out a prospective study of pregnancy outcome in which 74 pregnant women were exposed to up to five serial scans of echo planar imaging (0.5 T static field and 500 Hz gradient fields) between 20 and 40 weeks gestation compared with a control group of 148 pregnant women receiving only ultrasound scans. The controls were matched closely by maternal age, parity, ethnic origin, smoking history and postcode; however, no information was given on alcohol consumption, diet, socio-economic status, etc. The results were again briefly summarized: infant birth weight was significantly lower in the MRI group compared to the control group, although this disappeared if corrected for gestational age. The authors note the lack of "blinding" in this study; the MRI group was closely monitored, which may have resulted in the significantly higher induction rate seen in the MRI group and in a lower gestational age.

Summary. Excessive hyperthermia, including hyperthermia induced by exposure to RF radiation, is teratogenic in animals and would possibly be so in humans if the temperature excursions were sufficiently large. It seems reasonable to assume that adverse developmental effects will be avoided with a margin of safety if the body temperature of pregnant women does not rise by more than 0.5°C and the temperature of the fetus is less than 38°C.

There is no clear evidence that exposure to static or low frequency magnetic fields can adversely affect pregnancy outcome. Few studies of static field effects have been carried out. A greater number of low frequency studies have been conducted but the interpretation and relevance of some of these studies is obscured by the differences in exposure level and duration, and in the coupling of such fields to small mammals compared to humans.

Whilst there is no evidence of any adverse effect, the two studies of pregnancy outcome in women exposed to MRI during pregnancy were small and lacked rigor.

Delayed effects of acute and repeated MRI exposure

There is virtually no information about any delayed or long-term effects of single or repeated exposure to the electromagnetic fields used for MRI procedures, as long as excess heating is avoided, and no guidance can be derived in this area other than that concerning the benefits to the patients.

Acoustic noise

The gradient magnetic field is the primary source of acoustic noise associated with MR procedures (McJury and Shellock 2000; McJury 2001; Shellock et al. 1998; Shellock 2001a). This noise occurs during the rapid alterations of currents within the gradient coils. The currents, in the strong static magnetic field of the MR system, produce significant Lorentz forces at the wires of the gradient coils that induce vibrational modes in the coil structures generating substantial noise. The situation is exacerbated in ultra-high speed imaging because of the very high switching rates used in these techniques. Noise levels can be as high as 140 dB, which is well above generally accepted safety level permitted in the workplace (Mansfield et al. 2001).

Acoustic noise is characterized in terms of frequency spectrum (in Hz), intensity (in dB), and duration. Since the ear is not equally sensitive to all frequencies, data are normally weighted using the dB(A) measurement scale, which responds similarly to the human ear. Quantitative data about physiological effects of noise can be found in the review of Jansen (1991). Temporary noise levels of 60–70 dB(A) start activation processes in the central nervous system. Transient hearing loss may occur following loud noise exceeding 100 dB(A), resulting in a temporary threshold shift in audible threshold. Noise levels above 100 dB(A) may result in disturbances of the micro-circulation in the cortical organ and short term impulse levels above 120–130 dB(A) produce primary mechanical damage in this organ. If the noise insult is severe, full recovery can take up to several weeks. If the noise is sufficiently injurious, this may result in a permanent hearing loss. 85 dB(A) is the threshold for permanent hearing loss following long term noise.

The problems associated with acoustic noise for patients and health care workers include simple annoyance, difficulties in verbal communication, heightened anxiety, temporary hearing loss, and potential permanent hearing impairment (McJury and Shellock 2000; Shellock 2001a). Acoustic noise may pose a particular hazard to specific patient groups who may be at increased risk (e.g., patients with psychiatric disorders, elderly, pediatric and sedated patients, newly born children) (McJury and Shellock 2000). Noise exposure for the fetus could be of concern for both patients and interventional MRI staff (Academy of Pediatrics 1997). For dangerously ill patients a maximum level of 67 dB(A) can be considered as the hazardous threshold (Jansen 1991).

Occupational exposure

Routine MR procedures. The exposure of medical staff to static magnetic fields while positioning the patient can be as high as the main field in the system, although locally and for limited periods of time. The trend towards the routine use of high field MR systems (3–4 T) peak static magnetic field exposures is an increasing concern that people are exceeding the existing recommended guidelines. Static field exposure levels must be quantified and controlled for medical staff safety. In the near future, ICNIRP is going to review its guidelines on limiting exposure to static magnetic fields.

Medical or paramedical staff may be exposed at low magnetic and electromagnetic fields around the device or outside the room for hours daily.

An analysis of the RF fields outside of a cylindrical bore type MR scanner with a birdcage body coil indicates that they are more than a hundred times smaller at the entrance to the magnet than at isocenter. The power deposition is more than a factor of 10,000 smaller at the entrance to the magnet than that received by the patient. Thus, the exposure of the operator to RF fields is well below existing recommended limits (Elder et al. 1989).

Open MR devices. Concerning open or interventional MR devices with magnetic field strength below 1.0

T, staff operating such devices are not exposed at levels higher than the currently recommended limits for occupational exposure. However, there are only limited data on the exposure of surgeons at open MR devices.

Pregnant operators. Kanal et al. (1993) conducted a comprehensive postal questionnaire survey of the reproductive outcomes in pregnant female workers in clinical MR facilities in the U.S. Almost 2,000 responses were received from MR workers (technologists or nurses) and various controls groups, principally "other" workers, from which data concerning about 1,400 pregnancies could be analyzed. The authors found no large or statistically significant difference in pregnancy outcome between 280 MR workers compared to 'other' workers for a variety of outcomes such as premature delivery, infertility, low birth weight or spontaneous abortion. Whilst acknowledging weaknesses in the data, namely a low response rate (20–50%) and a subjective assessment of pregnancy outcome, the authors note that bias introduced by these factors typically tends to elevate rather than decrease any positive outcome. They concluded that the data do not suggest a substantial increase in common adverse reproductive outcomes in women working in the MR environment. However, as the response rates were below 50%, it is difficult to draw any meaningful conclusion from the study.

The key issue with regard to occupational exposure and pregnancy is to obtain far more complete data than were obtained in the study by Kanal et al. (1993). Further study is required with much higher participation rates based on an objective assessment of pregnancy outcome. For outcomes such as birth weight, a cohort of moderate size would probably give reasonable information, whereas for individual congenital malformations, which are comparatively uncommon in the general population, the size of cohort needed would be much larger. A case-control approach might be suitable if it was in a population in which a reasonably high proportion of pregnancies had MRI exposure.

RECOMMENDATIONS

General

There are many gaps in knowledge of biological effects and interaction mechanisms of MRI-related electromagnetic fields with tissues. ICNIRP emphasizes the following in the medical application of MR:

1. The need for a MRI examination and the safety of the patient undergoing such an examination is the responsibility of the medical practitioner;
2. Where MR examinations form part of a research project, the project shall be guided by rules of human ethics; informed consent of the patient shall be obtained;
3. MR equipment users must be adequately trained in the principles and operation of the equipment, indications and contraindications for use, record keeping requirements, safety aspects, and precautions; and
4. MR system manufacturers should supply complete documentation about patient and staff exposure levels for their equipment, and these safety guidelines should be considered in the design of equipment and facility layout so that exposures to magnetic and radiofrequency fields are within the levels recommended for patients and staff.

Exposure levels for patients

Clinical experience currently indicates that adequate diagnostic information can be obtained while examining a patient for periods ranging from 5 min to over 1 hour and may be repeated several times over the course of the disease or abnormal condition. In some cases, due to the use of MR spectroscopy or interventional MR procedures, examinations can last several hours.

Because of the uncertainty over identified deleterious effects, it is recommended that exposure limits be divided into three tiers:

- routine MR examinations for all patients (normal operating mode);
- specific MR examinations outside the normal operating range where discomfort and/or adverse effects for some patients may occur. A clinical decision must be taken to balance such effects against foreseen benefits; exposure must be carried out under medical supervision (controlled operating mode);
- experimental MR procedures, at levels outside the controlled operating range, for which special ethical approval is required in view of the potential risks (experimental operating mode).

Static magnetic fields. Until now, most MRI or MRS examinations have been made using static magnetic fields up to and including 3 T, although devices with static magnetic fields up to 7 T are already used in clinical tests. Higher magnetic flux densities offer potential diagnostic advantages, particularly for MRS. Because exposure to magnetic fields above 2 T can produce nausea and vertigo due to static field gradients, it is recommended that examinations above flux density be conducted under especially careful medical supervision. The recommended upper limit for clinical routine whole-body exposure to static magnetic fields is 4 T, due to the limited information concerning possible effects above this static field strength (U.S. FDA 1997; IEC 2001). At higher field strengths applications should be made based

on critical risk/benefit analyses and informed consent of the subject. Additionally, more careful monitoring of subjects is required, although physiological monitoring in an MR scanner does itself increase the risk of RF burns, which is however an avoidable risk. Recently, the FDA deems magnetic resonance devices to be a significant risk when the main static magnetic field is greater than 8 T for adults, children and infants aged >1 month, and greater than 4 T for neonates, i.e., infants aged 1 month or less (U.S. FDA 2003).

Time-varying magnetic fields. The threshold for cardiac stimulation is well above the level for intolerable stimulation, except at very long pulse durations which are not clinically useful. The trend in clinical MRI is toward shorter gradient pulses to reduce imaging time.

The study on nerve stimulation (Nyenhuis et al. 2001) is the largest study to date, and because it distinguishes between varying levels of stimulation (i.e., threshold, uncomfortable, intolerable) it provides a basis for recommended exposure levels for time-varying magnetic fields. Many medical procedures are uncomfortable or painful, but are tolerated by patients for the medical benefit. However, intolerable stimulation would interfere with an examination and the patient would receive no benefit. Consequently, this is to be avoided. Bourland's data indicate that the lowest percentile for intolerable stimulation is approximately 20% above the median threshold for peripheral nerve stimulation (Fig. 2 above). Consequently, it is recommended that the maximum exposure level for time-varying magnetic fields be set equal to a dB/dt of 80% of the median perception threshold for normal operation, and 100% of the median for controlled operation. This median perception threshold is described by the following equation, which is an empirical description:

$$dB/dt = 20(1 + 0.36/\tau)T\,\mathrm{s}^{-1}, \quad (1)$$

where τ is the effective stimulus duration in ms. The effective stimulus duration is the duration of the period of monotonic increasing or decreasing gradient. It is defined as the ratio of the peak-to-peak variation in B and the maximum value of the time derivative of B during that period.

Radiofrequency fields

For whole-body exposures, no adverse health effects are expected if the increase in body core temperature does not exceed 1°C. In the case of infants, pregnant women, and persons with cardiocirculatory impairment, it is desirable to limit body core temperature increases to 0.5°C. Similarly, local temperature under exposure to the head, trunk, and/or extremities should also be limited to the values given in Table 1. It is important when significant whole-body heating occurs, particularly in the elderly, to ensure that patients drink adequate amounts of liquid prior to investigations.

As only parts of the patient's body are exposed simultaneously during an MR procedure, not only the whole-body SAR but also partial-body SARs for the head, the trunk, and the extremities should be estimated on the basis of suitable patient models (e.g., Brix et al. 2001). It should be noted that there are no dosimetric models of pregnant women. Based on the published experimental studies concerning temperature rise and theoretical simulations, the SAR levels summarized in Table 2 should not be exceeded in order to limit temperature rise to the values given in Table 1.

With respect to the application of the SAR levels defined in Table 2, the following points should be taken into account:

- Partial-body SARs scale dynamically with the ratio r between the patient mass exposed and the total patient mass. For $r \rightarrow 1$ they converge against the corresponding whole-body values, for $r \rightarrow 0$ against the localized SAR level of 10 W kg^{-1} defined by ICNIRP for occupational exposure of head and trunk (ICNIRP 1998);
- The recommended SAR restrictions do not relate to an individual MR sequence, but rather to running SAR averages computed over each 6-min-period, which is assumed to be a typical thermal equilibration time of smaller masses of tissue (Brix et al. 2002);
- Whole-body SARs are valid at environmental temperatures below 24 °C. At higher temperatures, they should be reduced depending on actual environmental temperature and humidity.

Users of diagnostic MR devices usually do not have adequate resources to determine energy deposition within the patient's body. Such information should be supplied by the manufacturer, and it is recommended that the user requests detailed data from the manufacturer. In addition, real-time temperature monitoring may be performed during MR procedures in the controlled operating

Table 1. Basic restrictions for body temperature rise and partial-body temperatures.

Operating mode	Rise of body core temperature (°C)	Spatially localized temperature limits		
		Head (°C)	Trunk (°C)	Extremities (°C)
Normal	0.5	38	39	40
Controlled	1	38	39	40
Restricted	>1	>38	>39	>40

Table 2. SAR levels valid at environmental temperatures below 24°C.

	Averaging time: 6 min					
	Whole body SAR (W kg^{-1})	Partial-body SAR (W kg^{-1})		Local SAR (averaged over 10 g tissue) (W kg^{-1})		
Body region → Operating mode ↓	Whole-body	Any, except head	Head	Head	Trunk	Extremities
Normal	2	2–10[a]	3	10[b]	10	20
Controlled	4	4–10[a]	3	10[b]	10	20
Restricted	>4	>(4–10)[a]	>3	10[b]	>10	>20
Short term SAR	The SAR limit over any 10 s period should not exceed 3 times the corresponding average SAR limit.					

[a] Partial-body SARs scale dynamically with the ratio r between the patient mass exposed and the total patient mass:
– normal operating mode: SAR = $(10-8 \cdot r)$ W kg^{-1}
– controlled operating mode: SAR = $(10-6 \cdot r)$ W kg^{-1}
The exposed patient mass and the actual SAR levels are calculated by the SAR monitor implemented in the MR system for each sequence and compared to the SAR limits.
[b] In cases where the eye is in the field of a small local coil used for RF transmission, care should be taken to ensure that the temperature rise is limited to 1°C.

mode for patients at risk and should be performed in all cases in the experimental operating mode.

Acoustic noise. Generally, the acoustic noise produced during the MR procedures represents a potential risk to patients undergoing examinations on MR systems operating above 0.5 Tesla (McJury and Shellock 2000; Shellock 2001a). Internationally recommended limits for acoustic noise produced during MR procedures are based on recommendations for occupational exposures that are inherently chronic; comparable recommendations do not exist for non-occupational exposure to relatively short term noise produced by medical devices. For the safe use of medical equipment the acoustic noise must be restricted. Technical standards recommend that hearing protection shall be required for the safety of the patient if the maximum A-weighted r.m.s. sound pressure level of the MR equipment can exceed 99 dB A (IEC 2001). However, this noise level may not be appropriate for individuals with underlying health problems, who may have problems with noise at certain levels or at particular frequencies. Other guidelines recommend to limit the noise level at the ear of the patient for exposure times up to 2 h to 91 dB A (SSK 2003).

It is recommended to offer hearing protection to the patients, when a noise level of 80 dB(A) is exceeded; hearing protection should always be worn by patients undergoing MR procedures at levels exceeding 85 dB A, at best by headphones allowing verbal communication. Other devices such as earplugs hamper verbal communication with patients during the operation of the MR system and offer non-uniform noise attenuation over the hearing range; however, earplugs are often used to prevent problems from acoustic noise associated with MR procedures. For adolescents and infants, smaller earplugs are required to attenuate acoustic noise associated with MR procedures.

The exposure of staff and other health workers near the MR system is also a concern. This includes particularly those persons who are involved in interventional procedures or who remain in the room for patient management reasons (McJury and Shellock 2000; Shellock et al. 1998). Several national guidelines recommend that hearing protection be worn by staff exposed to an average of 85 dB A over an 8-h day (SSK 2003). In view of the inherently chronic nature of occupational exposure and the comparably small inconvenience, it is recommended that staff follow the same rules for wearing hearing protection that is recommended for patients.

Because of the different problems mentioned above, ICNIRP strongly recommends the design of "quiet" gradient coils. Gradient coils windings can be designed such that all Lorentz forces generated by the pulsing of current are balanced (Mansfield et al. 2001). Greater coil stiffness and damping the coil should reduce mechanical vibration and associated noise.

Pregnant patients

There is at present insufficient knowledge to establish unequivocal guidance for the use of MRI procedures on pregnant patients. In these circumstances, it is advised that MR procedures may be used for pregnant patients only after critical risk/benefit analysis, in particular in the first trimester, to investigate important clinical problems or to manage potential complications for the patient or fetus. The procedure should be conducted using a verbal and written informed consent procedure. The pregnant patient should be informed on the potential risks, also

compared with those of other alternatives. Excessive heating is a potential teratogen; because of uncertainties in the RF dosimetry during pregnancy, it is recommended that exposure duration should be reduced to the minimum and that only the normal operation level is used. In addition, large doses of MRI gadolinium-based contrast agents have been shown to cause post-implantation fetal loss, retarded development, increased locomotive activity, and skeletal and visceral abnormalities in experimental animals. Such agents should only be used during pregnancy if the potential benefit justifies the risk to the fetus.

The few studies on pregnancy outcome in humans following MRI have not revealed any adverse effects, but are very limited because of the small numbers of patients involved and difficulties in the interpretation of the study outcomes.

In 1991, the Safety Committee of the Society for Magnetic Resonance Imaging (Shellock and Kanal 1991) recommended that "MR imaging may be used in pregnant women if other non-ionizing forms of diagnostic imaging are inadequate or if the examination provides important information that would be otherwise require exposure to ionizing radiation (e.g., fluoroscopy, CT, etc.)."

Recommendations on research with volunteers

Where MR examinations are performed within the framework of a research project, the project should be guided by rules of human ethics. According to the "Declaration of Helsinki for ethical principles on medical research on human beings," the leading principles should include that

- the expected scientific result justify the performance of studies on volunteers;
- the schedule of the study contain the aim of the research, the methods of examination including technical details;
- criteria of inclusion and exclusion of volunteers are justified.

The research project should be reviewed and approved by a local Ethics Committee according to local requirements or national regulations.

Prior to the study, the volunteer should be instructed about type and significance of the planned examination and should give his or her written consent. The parameters of the examination and the results should be kept in the minutes.

Special care must be taken in experimental MR procedures at levels outside the controlled operating mode, for which special ethical approval is required in view of the potential risks. Depending on national regulations, a special insurance for investigations with volunteers may be required.

Special requirements for the experimental operating mode should include that

- specific security measures are provided to prevent unauthorized operation in the experimental operating mode (IEC 2001);
- the specific security measures involve a key-lock, a software password or other protective devices (IEC 2001);
- the experimental operating mode may be assessed only under the authorization of the responsible medical person;
- appropriate supervision is guaranteed to avoid possible detriments caused by the well known interaction mechanisms. In addition, a permanent supervision of the state of health of the volunteers in general (subjective state of health, circulation, respiration, etc.) must be put in safe keeping;
- a permanent optical and acoustical contact is provided between investigator and volunteer;
- specific emergency medical procedures are defined in order to provide medical treatment if necessary.

Contraindications and further considerations

Contraindications. Examinations of patients who have electrically, magnetically, or mechanically activated implants (e.g., cardiac pacemakers), or who rely on electrically, magnetically, or mechanically activated life-support systems, may be contraindicated for certain devices. Examinations of patients with ferromagnetic aneurysm clips or certain metallic implants are also contraindicated. Lists of implants and materials tested for safety or compatibility in association with MR systems have been established and identified. Objects in patients should be checked against those lists (Shellock 2001b; Shellock 2002a; Shellock 2003). This information is readily available on-line at www.MRIsafety.com.

Considerations related to patient's condition. Communication with the patient and/or monitoring (e.g., of the anesthetized patient) must be assured throughout the examination.

Certain patients may experience claustrophobia. The possibility of claustrophobic reactions should be explored before an examination is undertaken.

Because some individuals may exhibit an increased sensitivity to heating, it is advisable to ascertain if the patient's history comprises incidents indicative of sensitivity to heat and, if necessary, limit the duration of the examination.

Special requirements apply to the equipment and methods used for the monitoring of the patient under MR

exposure conditions. Cardiorespiratory function may be monitored using non-ferromagnetic transducers to register the heart beat rate, blood pressure, and respiratory rate. The ECG may be subject to distortion because of electrohydrodynamic interactions and may not yield useful information. Non-perturbing fiber-optic probes for measurement of body temperature are available. Under MR exposure conditions, oral temperature and the temperature of the skin of exposed body parts are suitable for patient monitoring. Detailed information on body temperature measurements may be found in a review by Shellock (2001c).

Ferromagnetic objects are attracted by magnetic fields. Depending on size, composition, and location of metallic implants or inclusions, serious injuries may result because of motions and displacement of such objects. Moreover, the presence of such objects results in artifacts in diagnostic information. The presence or absence of such objects in the body has to be ascertained and the consequences evaluated before an examination is undertaken. Additionally, adjustments with regard to the MR safety information may be required in consideration of the field strength of the MR system that is being used for the patient. For example, magnetic field interactions are different using a 0.2-T vs. a 3.0-T MR system (Shellock 2002a; 2002b; Shellock et al. 2003a; 2003b).

Projectile/missile effects. The magnetic fringe field near the MR system's magnet may be strong enough to attract ferromagnetic objects and to cause them to fly towards the magnet. Thus, metallic objects, particularly with sharp edges, may become dangerous projectiles. All such objects have to be eliminated from the examination room and proper danger or warning signs must be posted. Details are presented in the IEC standard (IEC 2001). Guidelines to prevent projectile or missile effect accidents have been presented (Shellock 2001b; 2003).

The manufacturer should provide information regarding the extent of the zone in which collision hazards and danger of uncontrolled movements of objects exist (e.g., uncontrolled movement of hospital carts, trolleys, loose tools, medical instruments, etc.).

Record keeping and patient follow-up. Examination records should be kept and patients should be monitored according to standard requirements of good medical practice. Observations on adverse reactions should be collected, reported according to national requirements, and published in the medical literature.

Electromagnetic interference. There are numerous reports of failures of electronic and mechanical medical devices due to electromagnetic interference (EMI) generated by the intense pulsed and static fields emitted by MRI systems. EMI involves the induction of deleterious voltages and currents into the circuitry of medical electronics, causing temporary or permanent failures of critical components. Damage of mechanical components due to forces induced by static magnetic fields also can be considered EMI. Non-fatal problems were experienced by several patients during MRI treatment involving each of the following devices: totally implanted and external infusion pumps delivering large drug overdoses, pulse oximeters for cardiac monitoring failing or providing erroneous data, and a ventilator malfunctioning during an MRI examination.

In addition, more than several dozen reports of burns exist for patients who were connected to external monitoring devices while receiving MRI imaging procedures. Most of these problems occurred when using ECG electrodes mounted on the chest, or pulse oximeter sensors on the finger tip. Heating is caused by RF power that is coupled into the metallic leads that connect an external monitoring instrument to objects mounted on the surface of the body.

The use of "MRI compatible" devices can prevent associated patient burns and the electronic and mechanical failure of such devices. MRI compatible devices are being designed using appropriate materials and wires or fiber optics to minimize coupling of the RF fields to medical devices.

Research needs

While the data cited herein provide a good foundation for safety guidelines, there are several areas in which additional knowledge could be used. ICNIRP therefore recommends:

- Monitoring of occupational exposure;
- Epidemiological studies of possible long-term health effects in patients, volunteers, and staff with occupational exposure, particularly those with high levels of cumulative exposure, and carefully conducted epidemiological studies on pregnancy outcome. Especially, there is a need for monitoring workers above 4 T, suitable to allow epidemiological studies in the future. Vibration can also be an issue for long term studies;
- More studies should be performed on biological effects of strong static magnetic fields, especially of chronic exposure on reproduction and development;
- Further investigation to define more precisely the spatial deposition of RF energy during an MR procedure and the corresponding temperature fields in the human body using a three-dimensional bio-heat transfer model, including modeling of the pregnant woman

and fetus. Based on these studies, more detailed and realistic patient models for SAR monitoring should be developed; and

- Body core temperature should be investigated during MR examinations using high SARs, particularly in patients suffering from impaired thermoregulatory ability.

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