Review

Invited

Review of Patient Safety in Time-Varying Gradient Fields

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In magnetic resonance, time-varying gradient magnetic fields (dB/dt) may stimulate nerves or muscles by inducing electric fields in patients. Models predicted mean peripheral nerve and cardiac stimulation thresholds. For gradient ramp durations of less than a few milliseconds, mean peripheral nerve stimulation is a safe indicator of high dB/dt. At sufficient amplitudes, peripheral nerve stimulation is perceptible (ie, tingling or tapping sensations). Magnetic fields from simultaneous gradient axes combine almost as a vector sum to produce stimulation. Patients may become uncomfortable at amplitudes 50%–100% above perception thresholds. In dogs, respiratory stimulation has been induced at about 300% of mean peripheral nerve thresholds. Cardiac stimulation has been induced in dogs by small gradient coils at thresholds near Reilly's predictions. Cardiac stimulation required nearly 80 times the energy needed to produce nerve stimulation in dogs. Nerve and cardiac stimulation thresholds for dogs were unaffected by 1.5-T magnetic fields. J. Magn. Reson. Imaging 2000;12:20–29. © 2000 Wiley-Liss, Inc.

Index terms: dB/dt; stimulation; gradient; safety; cardiac; nerve; pain

NUCLEI WITH MAGNET moments precess about magnetic fields at resonant frequencies proportional to local magnetic field strengths (1). In MR imaging, gradient magnetic fields (aligned with the static field) produce resonant frequencies corresponding with spatial position (1). Gradient magnetic fields (B) typically vary with time (t) at some rate, dB/dt. Time-varying magnetic fields induce electric fields in patients(2–7) (Fig. 1). At sufficiently high amplitudes, gradient-induced electric fields could stimulate nerves or muscles (4,6–23). At extremely high levels, cardiac stimulation or even ventricular fibrillation are of concern (24–29). However, the induction of ventricular fibrillation or even cardiac stimulation would require exceeding large gradient fields more than an order of magnitude greater than those now available.

Safety standards (6,30–32) have been devised to protect patients against potential hazards. Early standards limited dB/dt to 20 T/sec for typical applications. The development and wide use of echoplanar imaging (EPI) techniques led to a need for larger gradients, switched more rapidly. These needs resulted in more research on gradient-induced safety and to updated safety standards. This paper reviews gradient hardware, theoretical stimulation models, and animal and human stimulation data.

GRADIENT HARDWARE

Gradient coils used in MR add approximately linear variations to "static" magnetic fields. Gradient coil sets generate magnetic field variations for the three Cartesian coordinates. Both static magnetic fields and the desired gradient fields are in the same direction (typically, the Z direction). Only gradient field components in the Z direction matter for MR imaging physics. Since magnetic fields close on themselves, physics dictates that those gradient coils also produce components other than Z. *All* gradient magnetic field components contribute to electric field induction (and safety concerns) in patients (20,23,33,34).

Most MR scanners use cylindrical magnets and whole-body, cylindrical gradient coils (35–37). Experimental stimulation data, reviewed below, was all from cylindrical gradient coils. Most local gradient coils (ie, head gradient coils) are also cylindrical. However, typical "open" MR scanners have biplanar magnets and biplanar gradient coils (38,39). Currently, gradients used with open magnets have slew rates too low to cause nerve stimulation. Patient cross-sectional areas seen by biplanar gradients are likely to differ from those seen by cylindrical gradients. Biplanar gradient stimulation thresholds expressed as dB/dt may deviate from those produced by cylindrical gradient sets. However, electric field stimulation thresholds should be relatively independent of gradient coil geometry. Admittedly, electric field models themselves may be complicated by conductivity interfaces and patient to patient variation. How-
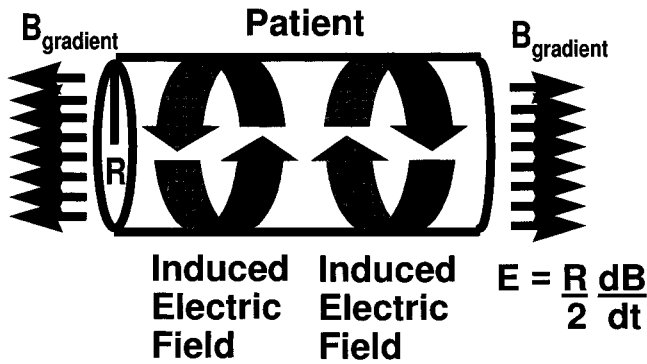
Figure 1. Cylindrical human model used by Reilly to estimate dB/dt stimulation thresholds. The patient is oriented along the static magnetic field and assumed to have a radius of 0.2 m. Peak electric fields are induced on the cylinder surface.

Table 1
Comparison of Hyperbolic Fit with Reilly SENN Model Nerve Stimulation Threshold Estimates

Ramp time (μsec)	Reilly-SENN nerve (T/sec)	Fit to Reilly nerve (T/sec)
2.5	2903.9	3034.8
5.0	1482.0	1544.4
10.0	772.7	799.2
20.0	416.1	426.6
50.0	200.0	203.0
100.0	129.3	128.5
200.0	90.7	91.3
500.0	68.3	68.9
1000.0	62.0	61.5
2000.0	60.0	57.7

ever, these same variations also further confound dB/dt models.

THEORETICAL STIMULATION MODELS

Peripheral nerve stimulation was proposed by John Bergeon (40) as a safe physiological indicator of high gradient-induced electric fields. In this way, patients could be protected from gradient-induced ventricular fibrillation by not exceeding peripheral nerve stimulation thresholds. Pat Reilly applied his electrode numerical stimulation models to determine gradient-induced nerve (4) and cardiac stimulation thresholds (7,24,41). The models predicted electric field amplitudes required for stimulation as functions of waveform (pulse duration, waveshape, and pulse train length). Reilly simulated patients as uniform cylinders with radii of 0.2 m (Fig. 1). The amplitude of the electric field, E, induced by the gradients along a path, l, depends on the time rate of change of the flux (7):

$$\oint (\bar{E} \cdot d\bar{l}) = \int \left(-\frac{d}{dt} \right) (\bar{B} \cdot d\bar{A}). \tag{1}$$

In Eq. [1], B is the magnetic field strength, A is the area, and t is the time. Reilly assumed that the z gradient magnetic field was uniform over and normal to a circular cross section of radius, r. The relation of dB/dt to the induced electric field could be expressed as:

$$2\pi r E = -\pi r^2 \frac{dB}{dt} \Rightarrow \frac{dB}{dt} = \frac{2E}{r}. \tag{2}$$

Reilly surveyed electrode-based stimulation literature and incorporated these data into his nerve and cardiac models. Reilly suggested that his spatially extended neural network (SENN) numerical stimulation model estimates are best approximated as an exponential curve. A better approximation (42,43) to Reilly's SENN model for nerves has been made using a hyperbolic (44,45) form that also appears to best fit actual experimental data (18,29,42,46,47):

$$\frac{dB}{dt} = b\left(1 + \left(\frac{c}{d} \right) \right), \tag{3}$$

where b is the mean dB/dt stimulation threshold for infinite pulse duration (ie, rheobase), c is chronaxie or the duration at which the stimulation threshold is twice the rheobase (rheobase being the threshold for infinitely long durations), and d is the pulse duration. Using the method described by Havel et al (43), the best hyperbolic model for mean nerve stimulation thresholds is b = 54 T/sec and c = 138 μsec. The results from Eq. [3] using the values of b and c obtained are compared with Reilly's estimates in Table 1. Note that thresholds rise for smaller values of d/c. Thresholds approach an asymptote for large values (rheobase) of d/c.
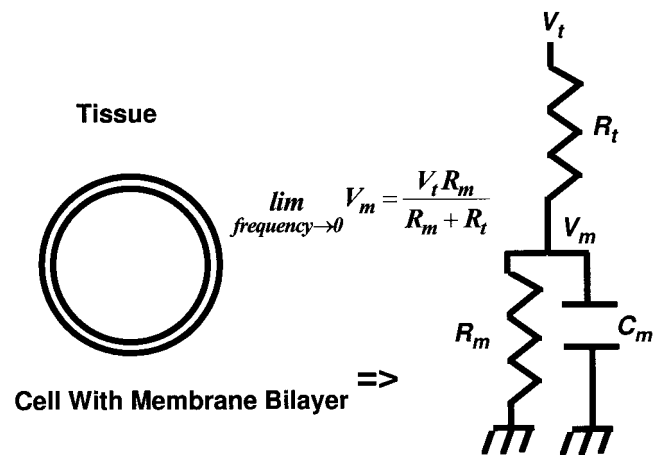
Cell membranes are lipid bilayers that may act as

Figure 2. Bilayer membrane and its linear electrical analog (nonlinearities are neglected in this model). R_t is the tissue resistance, R_m is the membrane resistance, and C_m is the membrane capacitance. The membrane time constant is $R_m \times C_m$. At low frequencies, the capacitive reactance appears infinite, and the transmembrane potential is independent of frequency (or ramp time). At high frequencies, the capacitive reactance approaches a short circuit, transmembrane potentials approach zero, and stimulation becomes impossible. Gradients with shorter ramp times require higher dB/dt to produce stimulation.
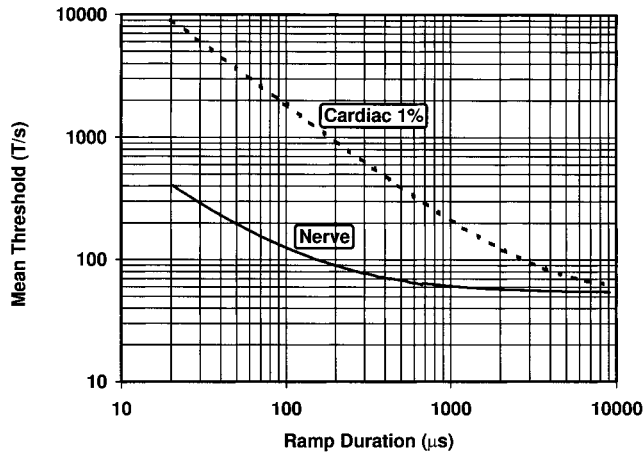
Figure 3. Reilly estimates for mean peripheral nerve stimulation thresholds and cardiac stimulation thresholds for the most sensitive population percentile. Note that the margin between nerve and cardiac thresholds is large for ramp durations less than 1 msec.

lossy capacitors (Fig. 2). Surrounding tissues will have finite electrical conductivity. Ignoring the non-inear properties of cell membranes, potentials applied between the tissue and the inside of the cell are low pass filtered. Transmembrane potentials at high frequency approach ground, while low-frequency potentials are only slightly attenuated. It is difficult to stimulate cells electrically above approximately 100 KHz (48). While the gradient of the electric field (7) may play a role in stimulation, practical effects may be small in contemporary MR scanners.

Reilly modeled gradient-induced cardiac stimulation in a manner similar to that done for mean nerve stimulation thresholds. Reilly predicted that the most sensitive population percentile should experience cardiac stimulation at a rheobase value of about 6 volts/m with a membrane time constant of 3 msec (Fig. 3). Reilly (7) estimated the mean cardiac stimulation threshold to be a factor of 2 above that of the most sensitive population percentile. He estimated the mean threshold for cardiac fibrillation to be another factor of 2.5 above the cardiac stimulation mean.

Unfortunately, mean nerve stimulation thresholds approach cardiac stimulation thresholds for the most sensitive population percentile when ramp durations exceed a few milliseconds (41). To provide adequate protection from cardiac stimulation at all gradient ramp durations, regulatory standards were set to a factor of 3 below peripheral nerve stimulation means (6,30–32). Note that for short ramp durations, mean nerve stimulation thresholds expressed in dB/dt can become large. However, the safety margin between nerve stimulation and cardiac stimulation increases as ramp duration is reduced.

Regulatory standards (6,30–32) presently adjust for stimulation threshold differences between sinusoidal and trapezoidal pulse trains (16,18,43,46,48,49) by defining d (see Eq. [3]) as the half-period of a sinusoid or the ramp time (from minimum to maximum gradient amplitude) of a trapezoid. Mansfield and Harvey (16)

analyzed sinusoids and trapezoids from an imaging perspective. For equal phase (area under the gradient waveforms), sinusoids are more likely to result in stimulation. Harvey and Katznelson (49) suggest that sinusoids are more accurately modeled by considering them as trapezoids with the same dB/dt, but with the ramp duration defined as the $1/\pi$ times the period of the sinusoid.

Reilly noted that monophasic pulses have lower peripheral nerve stimulation thresholds than biphasic pulses (4,41). Probably some of the charge stored across nerve and muscle cell wall bilayers is removed when biphasic pulses change polarity (Fig. 2). Similarly, Reilly noted that stimulation thresholds from repetitive pulse trains drop (as much as approximately a factor of 2) with longer train length. An asymptote is reached within approximately 8 pulses. The charging capacitor model shown (Fig. 2) predicts lower thresholds for monophasic pulse trains if the leaky capacitor is not completely discharged between pulses. Note that the hyperbolic fit (Eq. [3]) appears to work well for pulse durations and separations typically used in MR imaging.

Another observation is that Eq. [3] could be written in terms of the peak gradient magnetic field, B, at the nerve stimulation mean:

$$B = b(d + c) = bd + B_{min}. \qquad (4)$$

In Eq. [4], B_{min} (= b c = 74.5 gauss) is the minimum gradient magnetic field required to achieve the stimulation mean (4,16,29,41,47). Note that patients in gradient magnetic fields less than B_{min} should have a finite probability (<50%) of stimulation. In addition, note that limiting to B_{min} is too conservative, ie, if d = c, the mean stimulation threshold is 2 B_{min}. Note that by multiplying both sides of Eq. [4] by half the patient radius (radius = 0.2 m), a minimum magnetic vector potential for nerve stimulation may be found. This magnetic vector potential is about 0.0006 volts/m.

Similar arguments (13,29,41) show that the most sensitive population percentile should experience cardiac stimulation (extra induced beats) when the peak gradient field reaches about 1875 gauss. Limiting peak gradient fields to approximately 600 gauss should provide a wide safety margin against cardiac stimulation. Equivalently, limiting the gradient magnetic vector potential to 0.006 volt s/m should protect patients from cardiac stimulation.

Irnich (18,47) emphasizes that stimulation depends on mean (rather than peak) dB/dt changes, independent of waveform. He prefers the hyperbolic form of the strength-duration curve such as that shown in Eq. [3] over the exponential form (4), which is sometimes used. Irnich also shows that cardiac stimulation limits may be avoided by limiting mean changes in the gradient magnetic field.

Most gradient systems operate in the audio frequency range with peak magnetic fields less than 200 gauss. If a surface exceeds a local temperature of at least 41°C (perhaps from ohmic losses), then burns may be possible. The rate of power deposition in tissue depends on the product of conductivity and the square of the prod-
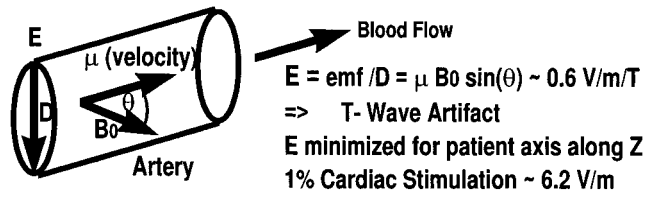
Figure 4. Electric field induced across an artery by flowing blood in a static magnetic field. This magnetohydrodynamic effect can lead to a distortion of the *T* wave on an electrocardiogram. At very high field strengths for patients normal to the static magnetic field, the effective dB/dt threshold for cardiac excitation might be lowered. However, the induced electric field would appear during the portion of the cardiac cycle when the heart is least susceptible to stimulation.

uct of frequency and (gradient or radiofrequency) field strength. For most present-day systems, radiofrequency-induced heating should be several orders of magnitude higher than gradient-induced heating.

Another potential concern is electric fields induced by flowing blood in very high field MR scanners. This magnetohydrodynamic effect (50) derived from the Lorentz force, f, per unit charge, q. if θ is the angle made between the static magnetic field of the MR scanner and the blood velocity vector, v (= approximately 1 m/sec in the aorta), then the transverse electric field, E_m, induced (Fig. 4) may be written as:

$$E_m = \frac{F}{q} = vB \sin(\theta). \tag{5}$$

This transverse electric field is responsible for the well-known T-wave elevation observed on electrocardiograms of patients monitored in high static fields (51). In most MR scanners, the aorta is nearly parallel to the static magnetic field and E_m is small. Reilly estimates that cardiac stimulation in the most sensitive population percentile requires about 6 volt/m. So, it is conceivable that patients in hypothetical very high field open magnets could experience magnetohydrodynamic electric fields sufficient to be of concern. The concern may be ameliorated somewhat because it would occur during the refractory portion of the cardiac cycle—when it is difficult to stimulate.

Very little research appears to have been conducted on implant (52) concerns at high dB/dt levels. Presumably, gradient-induced heating issues are not likely provided radio frequency heating is not of concern. However, implants near the heart or another muscle or a nerve may be of concern. Any current limiting devices used to prevent radiofrequency heating may also pro-

tect against stimulation by limiting current density. The lack of reports on implant concerns with high dB/dt is encouraging.

ENERGY CONSIDERATIONS

In a manner similar to that used by Mouchawar et al (53), it is possible to find how the energy required for stimulation varies with ramp duration. Recall that the energy per unit volume, W_v, stored in the magnetic field is related to the square of the magnetic field. Using the mean stimulating magnetic field, B (Eq. [4]) and the magnetic permeability, μ, it is possible to express energy requirements as:

$$W_v = \frac{B^2}{2\mu} = \frac{b^2(d^2 + 2cd + c^2)}{2\mu}. \tag{6}$$

From Eq. [6], minimum stimulation energy is clearly required as ramp duration approaches zero. For ramp durations much greater than chronaxie, energy required for stimulation rises with the square of ramp duration. Peripheral nerve stimulation is designed to be a safe indicator of high gradient dB/dt levels. However, at ramp durations approaching a few milliseconds, cardiac stimulation in the most sensitive percentile of the population should approach mean nerve stimulation levels. Fortunately, Eq. [6] shows that energy required for peripheral nerve stimulation at d = 2000 μsec would be 79 times that required for mean nerve stimulation at d = c = 138 μsec! Using the experimental value (29) of c = 365.1 μsec and d = 138 μsec reduces the estimated energy factor to a still impressive 22.

STIMULATION PARAMETERS

Investigators often report mean stimulation threshold with different parameters. For example, stimulation has been reported in terms of estimated electric field strength, slew rate, peak gradient magnetic field, peak dB_z/dy along the long axis of the patient, and the peak d|B|/dt in the space available to the patient. The National Electrical Manufacturer's Association (NEMA) (54) has developed a standardized procedure for reporting stimulation parameters in terms of dB/dt. In the NEMA standard, peak d|B|/dt produced by simultaneous, combined gradients from all three gradient axes is found along a patient-simulating cylinder with a radius of 0.2 m. Table 2 shows calculations for hypothetical Maxwell coil pairs of varying radii, simulating Z gradient coils. Coil current is adjusted so an electric field of 6 V/m is generated at 20 cm off axis in the plane

Table 2
Comparison of Stimulation Parameters for a Hypothetical Maxwell Pair Assuming an Electric Field Threshold of 6 V/m for 1-msec Ramp Duration (assuming *Z* coincides with one of the coils)

Coil radius (m)	Coil length (m)	dB/dt @ r = 0 m	dB/dt @ r = 0.2 m	dB/dt ratio (0.2:0 m)	Electric field (V/m)
0.3	0.52	48.5	76.7	1.58	6
0.35	0.61	51.9	70.4	1.36	6
0.4	0.69	54	67.2	1.24	6
0.45	0.78	55	65.4	1.19	6

of one of the coils. Comparisons of dB/dt calculated in the plane of one of the coils on axis and 20 cm off axis (in the coil plane) are shown. Note that dB/dt measured on axis increases with radius as current required to produce 6 V/m at 20 cm off axis increases more rapidly than radius. In contrast, dB/dt measured 20 cm off axis drops as coil radius increases. Thus the ratio of dB/dt 20 cm off axis and dB/dt on axis depends on coil geometry. The ratio approaches unity as coil radii grow much larger than 20 cm. Note that while dB/dt changes at the two locations as coil radius changes, stimulation probability is unchanged (the electric field at 20 cm is maintained constant). Recent numerical simulations of nerve stimulation by z gradient coils by Carbunaru and Durand (55) show that electric fields are better predictors for stimulation thresholds than dB/dt. The finite element modeling of Mouchawar et al (33) also showed induced electric fields to be good predictors of stimulation.

Figure 5. Cardiac stimulation data. The Nyenhuis data point was for dogs in small gradient coils. Here the results have been scaled to human size. The Nyenhuis data are from nonrepetitive capacitor discharges. Reilly's model estimate for the mean cardiac threshold (= twice the most sensitive 1% value) is shown as the solid line.

EXPERIMENTAL DATA

Gradient-Induced Stimulation Studies in Animals

Bourland et al (10,20,29) and Nyenhuis et al (12) found strength duration curves for gradient-induced nerve stimulation in the dog . Single capacitor discharges were delivered to dog-sized gradient coils. Stimulation studies included both z and transverse gradient coils with and without a 1.5-T static magnetic field present. The lowest stimulation thresholds observed were for peripheral nerve. The thresholds were not significantly different at 0 T compared with 1.5 T (with the static field along the long axis of the dog). At nerve stimulation thresholds, muscle twitching was observed. Mean nerve stimulation thresholds, when corrected for pulse shape and when adjusted for pulse train length, appeared to agree roughly with Reilly (4) for the induced electric field required.

At approximately three times the mean peripheral nerve stimulation thresholds, Bourland et al (25,29) observed the mean threshold for magnetically stimulated respiration in the dog (8). At about nine times the mean peripheral nerve threshold, the gradient-induced mean cardiac stimulation threshold (25–29) was reported for dogs at a ramp duration of 530 μsec (Fig. 5). Hardware constraints made cardiac stimulation possible at only one "ramp duration time" (530 μsec). Bourland et al (29) reported that the energy stored in the gradient magnetic field required for the mean cardiac stimulation threshold in the dog at 530 μsec is 80 times that required for the mean peripheral stimulation threshold. Recall Reilly's (7) estimate that the cardiac stimulation threshold for the most sensitive population percentile is half the mean. Also recall that stored energy is proportional to the square of the magnetic field strength. Then cardiac stimulation in the most sensitive population percentile should require 20 (and the mean fibrillation threshold should demand 500) times the energy needed for the peripheral nerve stimulation mean. No significant differences were observed with or without a static magnetic field of 1.5 T present along the lon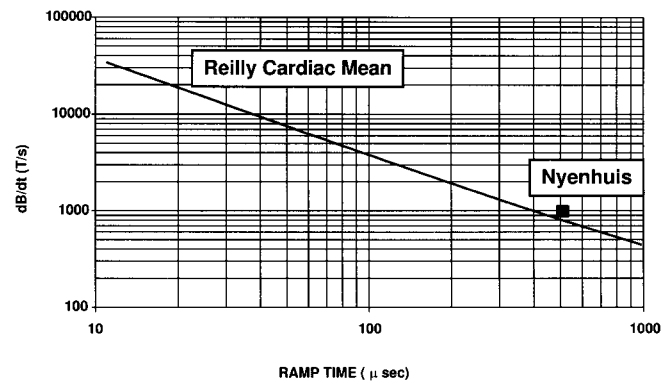g axis of the dog. No significant differences were observed whether cardiac stimulation experiments were done with arrested hearts or beating hearts. From dog experiments, Bourland et al (29) estimated the mean gradient magnetic field required for human cardiac stimulation as 0.43 T. Reilly found that the most sensitive percentile is half the mean, which would make Bourland's most sensitive percentile 0.215 T. Extrapolation from Reilly's work predicts a similar value of 0.1875 T.

Gradient-Induced Stimulation Studies in Humans

Several investigators including Budinger et al (11), Cohen et al (9), Bourland et al (10,20,29,56), Schaefer et al (17,19), Rohan and Rzedzian (14), Schmitt et al (46), Ehrhardt et al (21), Ham et al (23), Abart et al (22), and Havel et al (43) have conducted gradient-induced stimulation studies in humans. Comparison of various studies is difficult. Investigators often report stimulation in different terms (dB/dt at various locations, on axis, at 20 cm radius, peak dB/dt in patient space, dB_z/dt, root mean square dB/dt, or gradient slew rate). Ramp duration may imply the time from minimum to maximum gradient amplitude or it might mean the time from zero to maximum. Sinusoidal "ramp duration" may be taken as the half-period of the sinusoid, the entire period of the sinusoid, or as $1/\pi$ of the period of a sinusoid. Gradient coils may not be of the same dimensions and some may have active shields, while others do not. Global thresholds are sometimes found by searching numerous patient locations along z, while some investigators report "thresholds" for only one z location. Finally, definitions for x and y gradients are sometimes permuted.

In Figs. 6–8, experimental data are plotted for the x (left/right), y (anterior/posterior), and z (superior/inferior) gradients approximately translated into maximum d|B|/dt at 20 cm radius using the convention that the half-period of a sinusoid is the ramp duration. In addition, Reilly's estimates are plotted. In general, Reilly's estimates approach experimental data in the 100–1000 μsec range presently typical of clinical MR. Using sinu-
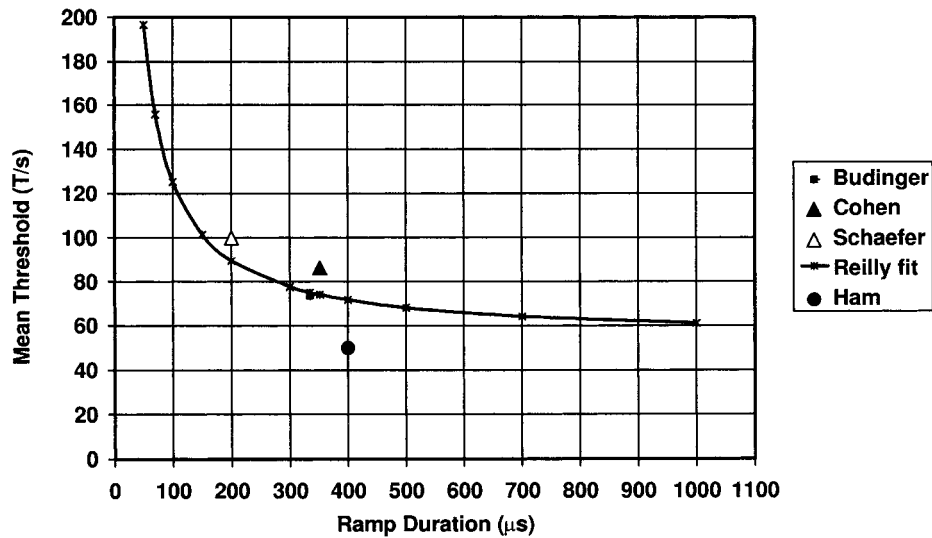
Figure 6. Mean human nerve stimulation thresholds by *X* (left/right) gradients. Bourland data also include thresholds for "uncomfortable" and "intolerable" levels. Cohen and Budinger values are from sinusoidally oscillating gradients plotted assuming gradient ramp duration corresponds to a half-period. Schaefer and Ham data are from trapezoids. Ramp durations for trapezoids are taken from minimum to maximum gradient amplitude. Reilly's model estimates are also shown.

soidal gradients on the x axis at 45 T/sec, Rohan et al (14) reported no stimulations in 60,000 images on 227 volunteers.

In a human study using trapezoidal gradient trains on single axes, Schaefer et al (17) found that anatomical sites of stimulation varied with gradient. However, magnitudes of the lowest thresholds were in a narrow range. Peripheral nerve stimulation sites for x-gradients included the bridge of the nose, left side of thorax, iliac crest, left thigh, buttocks, and lower back. Peripheral nerve stimulation sites for y gradients included the scapula, upper arms, shoulder, right side of thorax, iliac crest, hip, hands, and upper back. Peripheral nerve stimulation sites for z gradients included the

scapula, thorax, xyphoid, abdomen, iliac crest, and upper and lower back. Typically, stimulation sites were at bony prominences. Bone is less conductive than the surrounding tissue. Bone may increase current densities (and therefore electric fields) in narrow regions of tissue between the bone and the skin, resulting in lower dB/dt stimulation thresholds than expected for the homogeneous case (32).

Maximum gradient magnetic field components correspond to the gradient axis. Assuming equal d|B|/dt for the various gradient axes, gradient-induced electric fields are highest for the largest normal body cross section. Y gradients have the lowest dB/dt stimulation thresholds (Fig. 7), presumably because x-z cross sec-
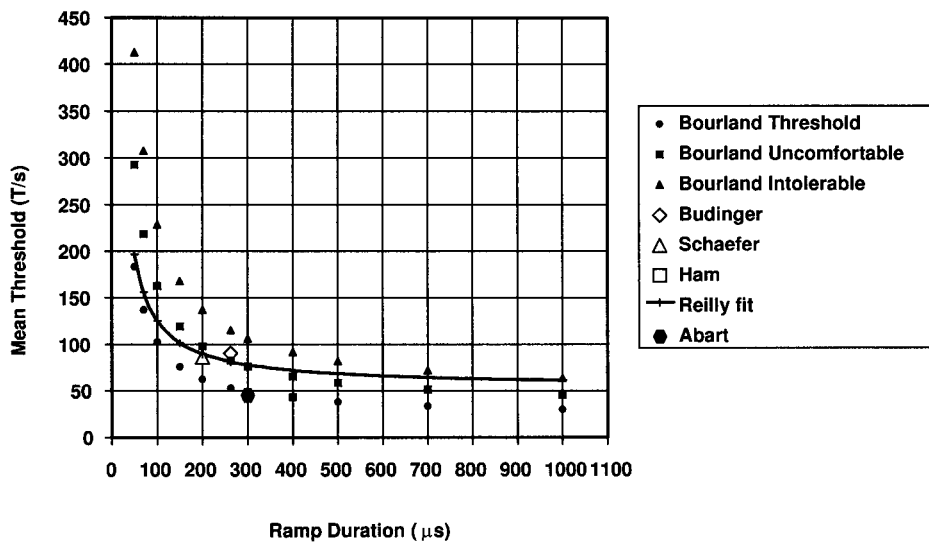

Figure 7. Mean human nerve stimulation thresholds by *Y* (anterior/posterior) gradients. Bourland data also include thresholds for "uncomfortable" and "intolerable" levels. Budinger values are from sinusoidally oscillating gradients plotted assuming gradient ramp duration corresponds to a half-period. Bourland, Schaefer, Ham, and Abart data are from trapezoids. Ramp durations for trapezoids are taken from minimum to maximum gradient amplitude. Reilly's model estimates are also shown.

Figure 8. Mean human nerve stimulation thresholds by Z (superior/inferior) gradients. Bourland data also include thresholds for "uncomfortable" and "intolerable" levels. Budinger values are from sinusoidally oscillating gradients plotted assuming gradient ramp duration corresponds to a half-period. Bourland, Schaefer, and Ham data are from trapezoids. Ramp durations for trapezoids are taken from minimum to maximum gradient amplitude. Reilly's model estimates are also shown.
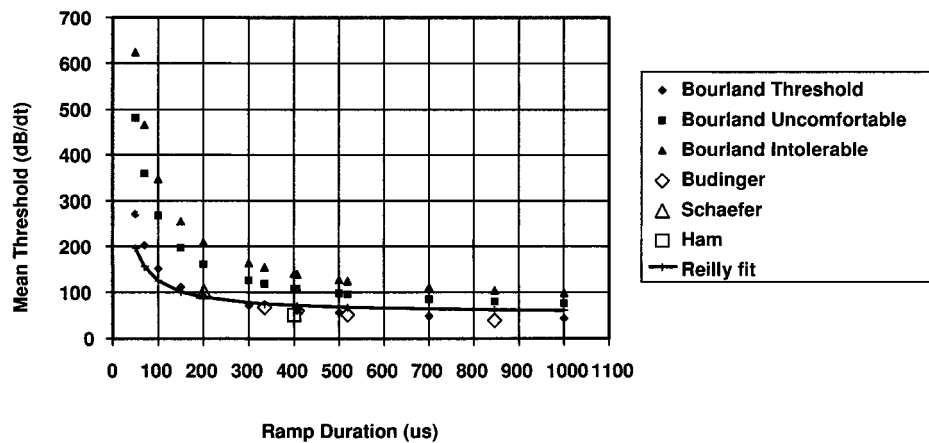
tions of the body are usually larger than other cross sections. For example, using the conventions stated above, Bourland et al (29,56) found strength duration curve parameters (Eq. [3]) of b = 22.07 T/sec and c = 365.1 μsec (= > B_{min} = 80.6 gauss compared with the model value derived above of 74.5 gauss) for the y gradient, compared with b = 31.67 T/sec and c = 378.2 μsec (= > B_{min} = 119.8 gauss) for the z gradient. Bourland's observations imply that simultaneous gradients at equal ramp durations probably add approximately as vector sums. Approximate experimental confirmation has been reported by Schaefer et al (19) and by Ham et al (23). It is noteworthy that data reported by Ham et al for stimulation from three simultaneous gradient axes are nearly identical to the y axis human data of Bourland et al (29,56) when transformed into the same terms.

Ehrhardt et al (21) reported stimulation in patients hands when were clasped. Schaefer et al (17) found that volunteers whose hands were clasped had mean y gradient thresholds 68% of mean thresholds for patients whose hands were not clasped. Schaefer et al found that clasping hands had no effect on x or z gradient thresholds. Presumably, a larger eddy current loop, normal to the y axis, is formed by clasping hands. Avoidance of y frequency-encoding gradients during echoplanar scans reduced the possibility of nerve stimulation.

Pain Stimulation

At dB/dt levels higher than the mean peripheral nerve threshold for the population, a few patients may be above their threshold for discomfort or intolerable pain. Both Budinger et al (11) and Bourland et al (29,56) studied gradient-induced pain thresholds. Bourland et al, in a study of 84 human subjects, found for y gradients that the typical subject was uncomfortable when dB/dt was increased to about 50% above his/her nerve stimulation threshold. For y gradients the typical subject found stimulation intolerable at a level about double the nerve stimulation threshold. Bourland et al

found for z gradients that the typical subject was uncomfortable when dB/dt was increased to about 70% above his/her nerve stimulation threshold. Again, for z gradients the typical subject found stimulation intolerable at a level about double the nerve stimulation threshold. Population parameters for mean threshold, discomfort, and intolerable pain are summarized in Table 3. The pain to perception thresholds found by Bourland et al appear similar to those reported by Budinger et al. Figure 9 shows the population stimulation data of Bourland et al for the y gradient axis at a ramp duration of 300 μsec. In Fig. 9, it is clear that perhaps 2%–5% of patients may feel uncomfortable at the mean (50%) nerve stimulation level.

Cardiac Stimulation Probabilities

The paramount concern for time-varying magnetic fields is to protect patients from life-threatening ventricular fibrillation. What is the probability of gradient-induced cardiac stimulation at the mean nerve stimulation threshold? Recall that Reilly (7) showed that cardiac stimulation follows a log-normal distribution with the most sensitive percentile half the mean. According to this analysis, stimulation probabilities may be estimated (Fig. 10). For gradient ramp durations of 1000 μsec, the probability of cardiac stimulation in

Table 3

Comparison of y and z Gradient Coil Stimulation Parameters (see Eq. [3]) in Bourland's 84-Subject Study*

	y gradient mean	z gradient mean
Threshold b (T/sec)	22.1 ± 5.7	31.7 ± 8.3
Threshold c (μsec)	365.1 ± 116.5	378.2 ± 170.3
Uncomfortable b (T/sec)	32.8 ± 7.4	54.9 ± 16.1
Uncomfortable c (μsec)	397.1 ± 129.8	388.3 ± 258.2
Intolerable b (T/sec)	45.3 ± 22.5	71.2 ± 32.1
Intolerable c (μsec)	405.6 ± 215.9	388.1 ± 196.1

*Note values for b have been scaled by a factor of 1.48 for y and 1.21 for z to convert to maximum dB/dt values at 0.2 m off axis. Values are mean ± SD.
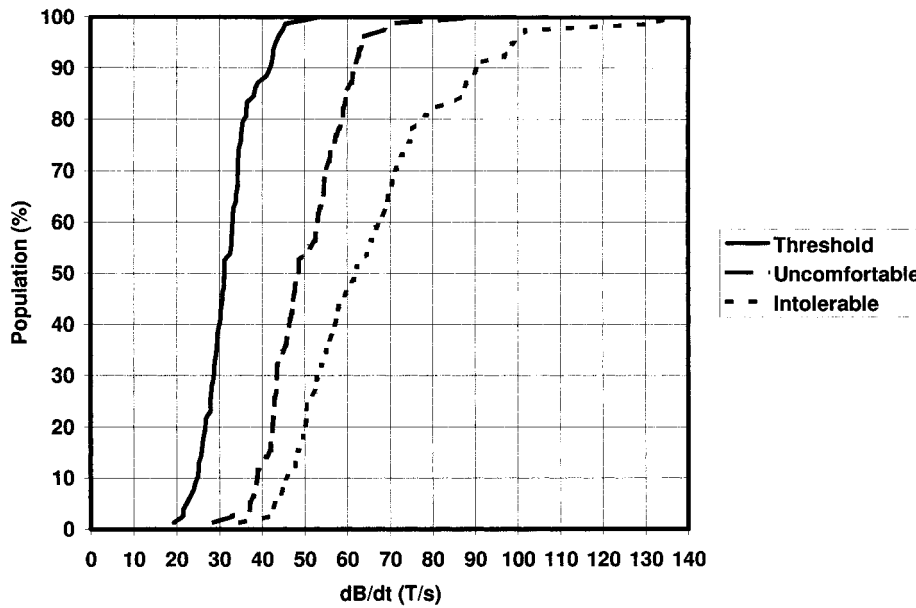
Figure 9. Percentage of *Y* gradient axis subjects in the Bourland et al study experiencing threshold stimulation, discomfort, and intolerable stimulation at a ramp time of 300 μsec. Maximum dB/dt values on axis (0.3 m from isocenter) are reported. Note that for the dB/dt value that produced the mean threshold (50%), a small percentage of subjects would experience uncomfortable stimulation.

patients scanned at the peripheral nerve stimulation threshold should be about 10^{-10}. For 100-μsec ramp durations, the probability should drop to about 2×10^{-29}. Note that the stimulation probability increases with gradient ramp duration. As the number of patients receiving MR scans annually approaches 10^7, it is important to maintain stimulation probabilities well below $1/10^7$. Note that the peak gradient magnetic field for peripheral nerve stimulation at 1000 μsec approaches the 600-gauss limit suggested above for cardiac safety.

SAFETY STANDARDS

Current MR safety standards (2,6,30–32) have proved effective in keeping time-varying fields below the level of
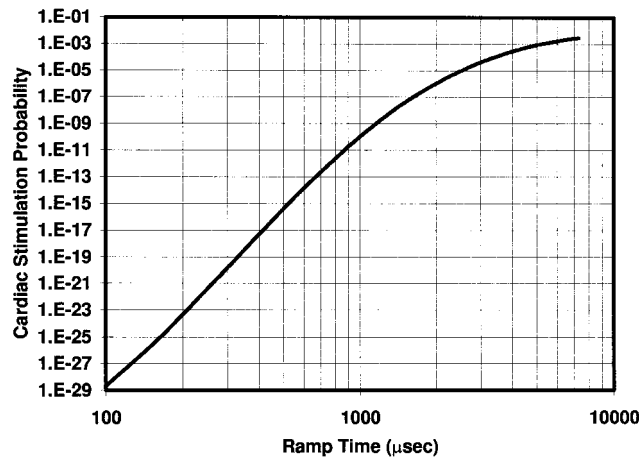

Figure 10. Estimated probability of cardiac stimulation assuming dB/dt levels are at the mean peripheral nerve stimulation threshold. Note that for short ramp times, the probability of cardiac stimulation is nearly zero.

concern. Safety standards have evolved to protect patient safety without unduly hampering development of important diagnostic imaging techniques. Early standards called for dB/dt limits of about 20 T/sec. Current guidance in the United States (31) classifies time-varying gradient fields as significant risk when the "time rate of change of gradient fields (dB/dt) is sufficient to produce severe discomfort or painful nerve stimulation." When gradient ramp times are less than 1 or 2 msec, gradient-induced cardiac stimulation (and fibrillation) probabilities are near zero (13,41) provided dB/dt levels (including resultant dB/dt from simultaneous gradients) (19,23) are so low that painful nerve stimulations (11,29,56) are rare. Ramp times exceeding 2 msec are not common. Human scans with high dB/dt levels at gradient ramp times longer than 1 or 2 msec should not be attempted if gradient magnetic fields approach or exceed 600 gauss. Probably due to the problems of how and where to measure dB/dt, there are no numerical dB/dt limits in the United States at this time.

A widely used safety standard for magnetic resonance was developed by the International Electrotechnical Commission (IEC) (32). In the IEC MR safety standard, there are three operating modes. In the "normal operating mode" no special vigilance is required on the part of the operator to ensure patient safety. The "first controlled mode" may be entered only when the operator takes deliberate action. During exams using the first controlled mode, operators must continually maintain contact with patients for safety concerns. The "second controlled mode" is entered only for research purposes and only with prior approval from a human studies committee (or Investigational Review Board [IRB]). Presently, the upper dB/dt limit of the normal mode is 20 T/sec for gradient ramp times, t, exceeding 120 μsec

and is less than 2400/(ramp time in μsec) T/sec for ramp times between 12 and 120 μsec. For the first controlled mode, the upper dB/dt limit (in T/sec) is 60000/(ramp time in μsec) to prevent cardiac stimulation. The IEC first controlled mode upper limit is unlikely to be reached by commercial scanners. Note that an updated IEC standard is presently under development.

DISCUSSION

It appears that current safety standards adequately protect patients. It also appears that using electric field as the primary stimulation parameter removes limitations imposed by gradient coil geometry. For example, a head-sized gradient coil should require much higher dB/dt values than would be needed from a whole-body gradient coil to induce stimulation. However, induced electric fields required for stimulation would be independent of coil size. Estimating induced electric fields in homogeneous materials is not difficult and may be adequate for safety standards. Finite-element (32) models or other numerical techniques may be required for accurately determining induced electric fields in electrically inhomogeneous humans. Cardiac stimulation is very unlikely in present-day systems. Fortunately energy considerations alone made cardiac stimulation unlikely. While peripheral nerve stimulation is not of concern, gradient-induced patient discomfort should be avoided. Future work may be needed to understand stimulation characteristics of biplanar gradients (38) and "top-hat" gradients (39). Interventional MR systems typically operate below nerve stimulation levels. For any interventional systems capable of stimulation, the stimulation of workers as well as patients should be considered. Investigations of implant safety at high dB/dt would be useful.

REFERENCES

1. Mansfield P, Morris PG. NMR Imaging in biomedicine. In: Waugh JS, editor. Advances in magnetic resonance, suppl 2. New York: Academic Press; 1982. p 32–83.
2. Saunders RD, Smith H. Safety aspects of NMR clinical imaging. Br Med Bull 1984;40:148–154.
3. Budinger TF, Cullander C. Health effects of in-vivo nuclear magnetic resonance. In: Margulis AR, Higgins CB, Kaufman L, Crooks LE, editors. Clinical magnetic resonance imaging. San Francisco: Radiology Research and Education Foundation; 1983. p 303–320.
4. Reilly JP. Peripheral nerve stimulation by induced electric currents: exposure to time-varying magnetic fields. Med Biol Eng Comput 1989;27:101–110.
5. Budinger TF. Nuclear magnetic resonance technologies: health and safety. Ann NY Acad Sci 1992;649:1–19.
6. Athey TW. Current FDA guidance for MR patient exposure and considerations for the future. Ann NY Acad Sci 1992;649:242–257.
7. Reilly JP. Principles of nerve and heart excitation by time-varying magnetic fields. Ann NY Acad Sci 1992;649:96–117.
8. Dalziel CF. Electric shock. Adv Biomed Eng 1973;3:223–248.
9. Cohen MS, Weisskoff R, Kantor H. Sensory stimulation by time varying magnetic fields. Magn Reson 1990;14:409–414.
10. Bourland JD, Nyenhuis JA, Mouchawar GA, et al. Human peripheral nerve stimulation from z-gradients. In: Proceedings of the Society for Magnetic Resonance in Medicine Annual Meeting, 1990. p 1157.
11. Budinger TF, Fischer H, Hentshel D, Reinflder HE, Schmitt. F. Physiological effects of fast oscillating magnetic field gradients. J Comput Assist Tomogr 1991;15:609–614.

12. Nyenhuis JA, Bourland JD, Mouchawar GA, et al. Comparison of stimulation effects of longitudinal and transverse MRI gradient coils. In: Proceedings of the Society for Magnetic Resonance in Medicine Annual Meeting, 1991. p 1275.
13. Schaefer DJ. Dosimetry and effects of MR exposure to RF and switched magnetic fields. Ann NY Acad Sci 1992;649:225–236
14. Rohan ML, Rzedzian RR. Stimulation by time-varying magnetic fields. Ann NY Acad Sci 1992;649:118–128.
15. Schaefer DJ. Bioeffects of MRI and patient safety. In: American Association of Physicists in Medicine (AAPM) monograph no. 21: the physics of MR imaging. New York: American Institute of Physics; 1993. p 607–646.
16. Mansfield P, Harvey PR. Limits to neural stimulation in echo-planar imaging. Magn Reson Med 1993;29:746–758.
17. Schaefer DJ, Bourland JD, Nyenhuis JA, et al. Determination of gradient-induced, human peripheral nerve stimulation thresholds for trapezoidal pulse trains (abstract). In: Proceedings of the Society of Magnetic Resonance 2nd Annual Meeting, San Francisco, 1994. p 101.
18. Irnich W, Schmitt F. Magnetostimulation in MRI. Magn Reson Med 1995;33:619–623.
19. Schaefer DJ, Bourland JD, Nyenhuis JA, et al. Effects of simultaneous gradient combinations on human peripheral nerve stimulation thresholds. In: Proceedings of the Society of Magnetic Resonance 3rd Annual Meeting, Nice, France, 1995. p 1220.
20. Bourland JD, Nyenhuis JA, Noe WA, et al. Motor and sensory strength-duration curves for MRI gradient fields. In: Proceedings of the Society of Magnetic Resonance 4th Annual Meeting, New York, 1996. p 1724.
21. Ehrhardt JC, Lin CS, Magnotta VA, Fisher DJ, Yuh WTC. Peripheral nerve stimulation in a whole-body echo-planar imaging system. J Magn Reson Imaging 1997;7:405–409.
22. Abart J, Eberhardt K, Fischer H, et al. Peripheral nerve stimulation by time-varying magnetic fields. J Comput Assis Tomogr 1997;21:532–538.
23. Ham CLG, Engels JML, van de Weil GT, Machielsen A. Peripheral nerve stimulation during MRI: effects of high gradient amplitudes and switching rates. J Magn Reson Imaging 1997;7:933–937.
24. Reilly JP. Cardiac sensitivity to electrical stimulation. US Food and Drug Administration Report MT 89–101, 1989.
25. Bourland JD, Nyenhuis JA, Mouchawar GA, et al. Physiologic indicators of high MRI gradient-induced fields. In: Proceedings of the Society of Magnetic Resonance in Medicine 10th Annual Meeting, San Francisco, 1991. p 1276.
26. Bourland JD, Nyenhuis JA, Mouchawar GA, et al. Z-gradient coil eddy-current stimulation of skeletal and cardiac muscle in the dog. In: Proceedings of the Society of Magnetic Resonance in Medicine 10th Annual Meeting, San Francisco, 1991. p 969.
27. Nyenhuis, JA, Bourland JD, Schaefer DJ, et al. Measurement of cardiac stimulation thresholds for pulsed z-gradient fields in a 1.5 T magnet. In: Proceedings of the Society of Magnetic Resonance in Medicine 11th Annual Meeting, Berlin, 1992. p 586.
28. Bourland JD, Nyenhuis JA, Schaefer DJ, et al. Gated, gradient-induced cardiac stimulation in the dog: absence of ventricular fibrillation. In: Proceedings of the Society of Magnetic Resonance in Medicine 11th Annual Meeting, Berlin, 1992. p 4808.
29. Bourland JD, Nyenhuis JA, Schaefer DJ. Physiologic effects of intense MRI gradient fields. Neuroimaging Clin North Am 1999;9:363–377.
30. United States Food and Drug Administration. Guidance for content and review of a magnetic resonance diagnostic device 510(k) application: safety parameter action levels. Center for Devices and Radiological Health Report. Rockville, MD: US FDA, 1988.
31. United States Food and Drug Administration. Magnetic resonance diagnostic devices criteria for significant risk investigations, 1997, at URL http://www.fda.gov/cdrh/ode/magdev.html
32. IEC. Particular requirements for the safety of magnetic resonance equipment for medical diagnosis. In: Diagnostic imaging equipment, publication IEC 60601-2-33, medical electrical equipment, Part 2. International Electrotechnology Commission, International Electrotechnical Commission (IEC), 3, rue de Varembé, P.O. Box 131, CH-1211 Geneva 20, Switzerland, 1995.
33. Mouchawar GA, Nyenhuis JA, Bourland JD, et al. Magnetic stimulation of excitable tissue: calculation of induced eddy-currents with a three-dimensional finite element model. IEEE Trans Magn 1993;29:3355–3357.

34. Nyenhuis JA, Bourland JD, Schaefer DJ. Analysis from a stimulation perspective of magnetic field patterns of MR gradient coils. J Appl Phys 1997;81:4314–4316.

35. Schenck JF. Axial magnetic field gradient coil suitable for use with NMR apparatus, 1986, US patent number 4617516.

36. Schenck JF, Hussain MA, Edelstein WA. Transverse gradient coils for nuclear magnetic resonance imaging, 1987, US patent number 4646024.

37. Roemer PB, Hickey JS. Self-shielded gradient coils for nuclear magnetic resonance imaging, 1986, US patent number 4737716.

38. Petropoulos LS, Morich MA. Thrust balanced biplanar gradient set for MRI scanners, 1999, US patent 5942898.

39. Barber WD, Roemer PB, Rohling KW. Open gradient coils for magnetic resonance imaging, 1995, US patent 5378989.

40. Bergeon J. General Electric Memo, 1985.

41. Reilly JP. Applied bioelectricity: from electrical stimulation to electropathology. New York: Springer; 1998. p 194–411.

42. Schaefer DJ. Safety aspects of switched gradient fields. Magn Reson Imaging Clin North Am 1998;6:731–747.

43. Havel W, Nyenhuis J, Bourland J, et al. Comparison of rectangular and damped sinusoidal dB/dt waveforms in magnetic stimulation. IEEE Trans Magn 1997;33:4269.

44. Lapicque L. Tome premier. Soc Biol 1907;1:615–618.

45. Lapicque L. Definition experimental de l'excitation. CR Acad Sci 1909;67:280–285.

46. Schmitt F, Wielopolski P, Fisher H, Edelman RR. Peripheral stimulations and their relation to gradient pulse shapes. In: Proceedings of the Society for Magnetic Resonance in Medicine 2nd Annual Meeting, San Francisco, 1994. p 102.

47. Irnich W. Electrostimulation by time-varying magnetic fields. MAGMA 1994;2:43–49.

48. Kennelly AE, Alexanderson EFW. The physiological tolerance of alternating-current strengths up to 100,000 cycles per second. Electrical World 1910;56L:154–156.

49. Harvey PR, Katznelson E. Modular gradient coil: a new concept in high-performance whole-body gradient coil design. Magn Reson Med 1999;42:561–570.

50. Kolin A. Improved apparatus and technique for electromagnetic determination of blood flow. Rev Sci Instrum 1952;23:235–240.

51. Beischer DE, Knepton JC Jr. Influence of strong magnetic fields on the electrocardiogram of squirrel monkeys (*Saimiri sciureus*). Aerospace Med 1964;35:939.

52. Shellock FG. Pocket guide to MR procedures and metallic objects: update 1994. New York: Raven Press, 1994. p 5–73.

53. Mouchawar GA, Bourland JD, Nyenhuis JA, et al. Closed-chest cardiac stimulation with a pulsed magnetic field. Med Biol Eng Comput 1992;30:162–168.

54. NEMA. Measurement procedure for time-varying gradient fields (dB/dt) for magnetic resonance imaging systems. NEMA standards publication no. MS 7-1993. Washington, DC: National Electrical Manufacturers Association, 1994.

55. Carbunaru R, Durand DM. Axonal stimulation under MRI magnetic field z gradients: a modeling study. Magn Reson Med 1997; 38:750–758.

56. Bourland JD, Nyenhuis JA, Foster KS, et al. Threshold and pain strength-duration curves for MRI gradient fields. In: Proceedings of the International Society of Magnetic Resonance in Medicine Annual Meeting, Vancouver, 1997. p 1974.