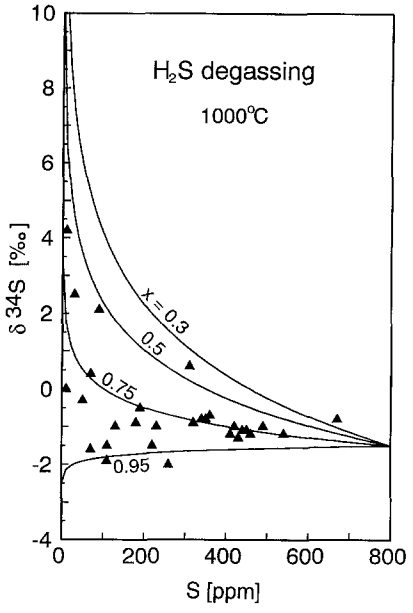

Fig. 1. Plot of $\delta^{34}S$ value of total sulfur versus sulfur content of volcanic rocks in Iceland (data from [9]). Theoretical curves are constructed for illustrating the influence of Rayleigh-type H_2S degassing on the isotopic composition of sulfur remaining in the melt at 1000 °C. The original magma is assumed to have the $\delta^{34}S$ value of -1.5‰ and the sulfur content of 800 ppm; x is the mole fraction of sulfur in the sulfide component of melt. For calculation principle, see [8]. The data from the Icelandic volcanic rocks are interpreted to indicate the H_2S outgassing during magma emplacement, with the sulfide-sulfur being dominant in the melt

utable to degassing under conditions of melt sulfide mole fraction close to the threshold value (0.90 – 0.93 for H_2S outgassing and 0.30 – 0.41 for SO_2 outgassing, depending on the degassing temperature). These theoretical expectations have been confirmed by natural observations [9, 10], as illustrated in Fig. 1 for the H_2S degassing in Icelandic volcanic rocks. Apparently, magma degassing can result in a sector (fan-shaped) distribution of data points in the plot of $\delta^{34}S$ versus sulfur content. The tip of the sector close to the highest sulfur content points to the primary $\delta^{34}S$ value of magma prior to degassing.

The incorporation of crustal sulfur into the mantle through subduction is a possible cause of the large variations in the $\delta^{34}S$ values of some mantle rocks. However, it is unlikely that the subducted sulfur could retain the isotopic heterogeneity in full scale under conditions of mantle melting. Because mantle magma degassing is a likely cause of the large $\delta^{34}S$ variations, there is no need to postulate that the mantle sulfur is isotopically inhomogeneous due to the recycling of crustal sediments, given that the sulfur in the mantle-derived materials is mainly residual one. In this context, sulfur isotopic homogeneity in the mantle is preferable, probably with the $\delta^{34}S$ variations within 0 ± 2‰. With respect to understanding of magmatic processes, simultaneous determination of sulfur content and isotopic composition in igneous rocks can aid us in distincting between degassing and assimilation during magma emplacement.

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In Vivo Nuclear Magnetic Resonance at 4.7 Tesla

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Magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) are powerful diagnostic tools in medicine. However, no standards exist for exposure of humans to higher magnetic fields. The biological effects of static magnetic field, magnetic field gradient, and the tissue-heating by radio frequency could be potential hazards during MR measurements. So far, no report has revealed any direct harmful effects of the magnetic field (reviewed in [1 – 3]). In recent years equipment with higher field (up to 4.7 T) has become available allowing a better separation of the signals and hence a reliable interpretation and a better signal-to-noise (S/N) ratio. Unfortunately, the impact of the high field strength is not known. It has been suggested by the Federal Health Agency in Berlin that humans should not be exposed to magnetic fields higher than 2 T [4].

In several studies the influence of magnetic fields of different strengths on physical parameters such as blood circulation in ear capillaries or EEG of the brain was analyzed. Grohmann et al. found impaired blood circulation in the

capillaries of frog tissues [5]. Dransfeld et al. [6] and Wunsch et al. [7] reported in 1984 that high magnetic fields induce temperature change in mice or man [8], later investigations, however, did not lend support to these results [3]. The cochlear tissue of the ear is sensitive to deficits in oxygen supply [9] due to alternations in blood circulation. Decreased amplitudes of brainstem auditory evoked potentials (BAEP) and increased latencies of P_V at 0.35 T in man were reported by von Klitzing [10] and at 0.4 T by Stojan [11]. In 1986 von Klitzing reported the influence of static magnetic fields on biological signals [12], and that changes in BAEPs could be observed even in a 0.2-T magnetic field [13 – 17].

Rather contradictory results have been reported by other groups. No changes of the action potentials of cochlea in guinea pigs due to flow restriction in blood capillary were found at higher field strength up to 8.5 T [18] or even at 10 T [19]. These investigations were very carefully designed to avoid device effects on the results. At lower field (1.5 T) alteration of human BAEP were not detected [20], and electrical functions of cat brain at 4.7 T did not change substantially [21]. Cardiac functions are also not affected [22], although periodic 50-Hz magnetic field change above 2 T seemed to influence the ECG of the heart [23].

These contradictions demanded further investigations on the whole-body influence of strong magnetic fields. In this communication we report the results of studies made on rabbits, mice, and guinea pigs exposed to a static magnetic field of 4.7 T. The results of these studies should broaden the scope of application of the 4.7-T instrument in MRI and MRS as a diagnostic tool particularly in the field of pediatrics.

All experiments were performed in a Bruker Biospec 47/40, with a 4.7-T superconducting magnet and a horizontal bore 40 cm in diameter. The spectrometer is equipped with a resonator imaging coil with an inner bore 34 cm in diameter, and double-tuned phosphorus-proton, carbon-proton, and fluor-proton surface coil 5 cm in diameter. Imaging experiments on rabbits were performed with a magnetic gradient of 0.15 mT/m and spectroscopy at 50, 80, and 200 MHz as 80-μs pulses (1024 pulses, 1-s cycle delay).

Guinea pigs have served as a suitable model for conductive hearing loss on maturation [24]. According to the working hypothesis, a diminished energy supply to the inner ears, leads to an increase in BAEP latencies and to a decrease in their amplitudes. In our experiment we observed the influence of a 4.7-T static magnetic field on the function of the inner ear of guinea pigs by monitoring BAEPs. Both ears were regarded as independent variables, because acoustically evoked potentials in one ear are most likely to be influenced solely by impairment of the microcirculation in the stria vascularis of the same ear. The unimpairment of both tympanic membranes was checked before each BAEP recording. Figure 1 shows a typical record of BAEP. The measured peaks are indicated as peaks I, III, and V.

The neural response thresholds for both ears were determined by decreasing the intensity in 5-dB steps. The 20-dB suprathreshold response was monitored five times and the 30-, 40-, and 50-dB suprathreshold responses once. The latencies of P_I, P_{III}, and P_V and the amplitudes of P_IN_I, $P_{III}N_{III}$, and $N_{IV}P_V$ were evaluated. The means of latencies and amplitudes of five 20-dB preexposure and postexposure suprathreshold recordings were caculated and depicted. Their standard deviations were used as reference to the peak variability within single recordings. The standard deviation of the latencies was between 0.03 (peak III) and 0.1 ms (peak V). The values of the 30-, 40-, and 50-dB suprathreshold responses were also registered. The postexposure values were subtracted from the preexposure values. The Wilcoxon rank sign

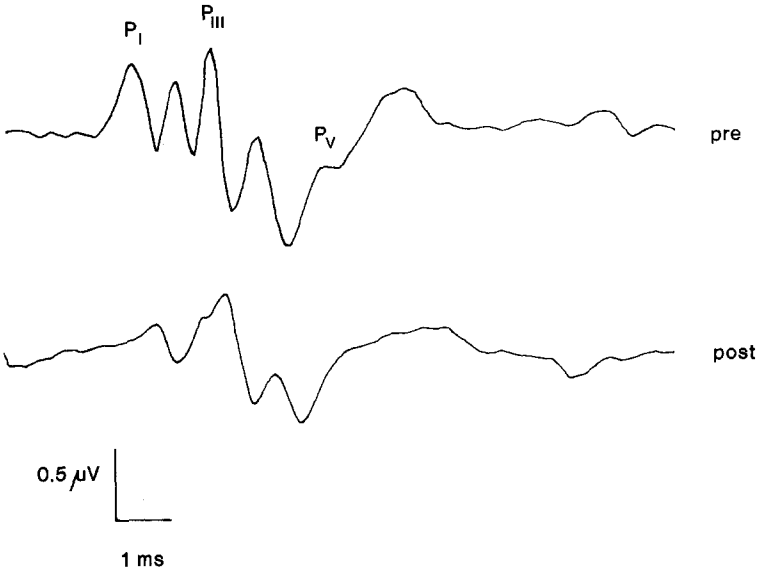

Fig. 1. Typical BAEP result of guinea pig. Latencies and amplitudes of peaks I, III, and V are indicated. In animal gp 71, only the sensation threshold of the left ear (below) was elevated to a degree that exceeded the standard deviation fixed by the stimulus generator (± 5 dB) after magnetic field exposure. The BAEPs were registered under Nembutal anesthesia (3 mg per 100 g body weight) on day 1. This recording served as standard for each animal under investigation. On day 2 animals were anesthesized and exposed under isothermal conditions (heating jackets) to the 4.7-T magnetc field for 1 h. The orientation of the animal was nearly parallel to the field, in a fixed position. The control animals were held at a distance of about 5 m to the magnet (field strength about 0.5 mT). After the exposure the BAEPs of the animals were monitored. The electrodes used were sterile needles, which were cautiously pinned under the skin at the mastoids of both ears (negative electrodes) and at the vertex (positive electrode). A clip was fixed to a hind leg as the ground electrode. Stimulation and BAEP recording were performed with a Nicolet Med 80. Acoustical pulses of alternating polarity of 0.14 ms duration at a repetition rate of 21.1 s^{-1} were used as "clicks". The click was guided directly into the auditory passage through a tube. The tube introduced a well-defined 0.85-ms delay of the stimulus. While clicks were presented at the ipsilateral ear, a masking noise of 50 dBSL was given to the contralateral one. The signals were amplified by a factor of 10000 at a bandpass of 150 – 1500 s^{-1}. BAEPs were obtained after averaging 1500 responses to the click stimulus.

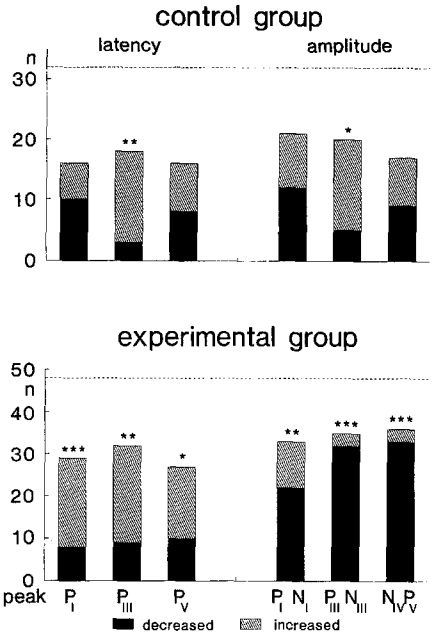

Fig. 2. Comparison of the exposed guinea pigs (n = 12 ears, 48 individual measurements) with control animals (n = 8 ears, 32 individual measurements). Decrease (*black bars*) and increase (*striped bars*) of latencies and amplitudes of the BAEPs are shown after "exposure" compared to the values of day 1. *Dotted lines*, total measurements made; distances from the bars to the dotted lines indicate results within the standard deviation of the measurements; *asterisks*, statistical differences between the number (n) of the decrease and the increase responses according to the Wilcoxon rank sign test method (*, $p<0.05$, **, $p<0.01$, ***, $p<0.001$)

test [25] gives the deviation of latencies and amplitudes after the exposure ($p<0.05$). The individual responses of each animal are summarized in Table 1. Figure 2 compares exposed (n = 12 ears, 48 individual measurements) and control guinea pigs (n = 8 ears, 32 individual measurements). Latencies and amplitudes of peaks I, III, and V were classified into three types: increasing (striped bars, "+" in Table 1) if they were higher after than before the exposure for all four sound intensities; decreasing (black bars, "−" in Table 1) in the opposite case; and inconsistent ("o" in Table 1) if the values oscillated. The classification was made only if the before/after difference exceeded the standard deviation made from five measurements at 20-dB threshold.

In control animals only the latency and amplitude of peak III differed from chance level. Both were lower on day 1 than at the second measurement. We cannot determine whether the effect reflects the variability of the recordings on succeeding days (deviation by altered positions of the electrodes) or different depth of anesthesia. The results of the BAEPs in the control group are statistically stable.

Table 1. Individual responses (latency/amplitude) of guinea pigs on exposure to 4.7-T magnetic field

Animal	Ear	Peak I	Peak III	Peak V
Control animals (n = 8)				
gp 90	Right	−/+	−/o	−/o
	Left	−/−	o/+	−/o
gp 104	Right	−/o	−/o	−/o
	Left	o/o	+/+	o/o
gp 147	Right	−/o	o/−	−/−
	Left	−/o	o/+	o/o
gp 153	Right	+/o	+/o	+/o
	Left	−/+	+/o	+/o
Exposed animals (n = 12)				
gp 70	Right	−/−	o/−	o/−
	Left	+/−	+/−	o/−
gp 71	Right	+/+	+/−	+/o
	Left	+/o	+/−	+/o
gp 93	Right	o/+	−/o	o/o
	Left	+/+	o/−	o/+
gp 98	Right	+/−	+/−	+/−
	Left	+/−	+/−	+/−
gp 109	Right	−/o	o/−	o/−
	Left	o/o	+/o	o/o
gp 110	Right	−/+	−/+	−/+
	Left	−/−	−/−	−/−

In the experimental group, we found the BAEP latencies and amplitudes of peak I, III, and V recorded after the exposure both statistically different from those recorded before the exposure. The alterations would indicate an impairment of the energy metabolism of the inner ear; in the majority the latencies are increased and the amplitudes decreased after exposure. However, a uniform change in one or the other direction was not observed.

Table 1 shows clearly the paradox situation that only the experimental guinea pig gp 98 really shows the expected pattern according to the statistical evaluation: increased latencies and decreased amplitudes in all evaluated peaks of both ears after the exposure. This pattern of alteration was not observed in other experimental animals, as seen in Table 1.

In contrast, a pattern indicating an impairment of the metabolism of the inner ear was also found in the control group: increased latencies appear in all three peaks of the right ear of gp 153, and in peaks III and V of the left ear. Representative results of BAEP measurement are shown in Fig. 3a: latencies and amplitudes of one control animal (gp 153) – and Fig 3b: two individual experimental animals with different reactions, gp 98: "expected" case according to the "mean" statistical evaluation; and gp 110: the atypical reaction, in which the latency of one ear changed in one direction, and that of the other ear showed changes in both directions.

The different methods of evaluation demand a cautious consideration of the statistical results. The response type expected as a consequence of metabolic alteration of the stria vascularis was rare in the group exposed to the 4.7-T field, although more often than in the control group. Therefore, the possibility cannot be ruled out, that in some cases exposure in a 4.7-T static magnetic field for 1 h might lead to a transient impairment of the local metabolism in the inner ear. This problem requires more and systematic investigations.

The research described thus far was based on rather short-term exposures and physical parameters.

We chose an additional approach to investigate effects of a static magnetic field on organisms with the aim of detecting cell damage, for example, caused by alterations of structures either of the plasma membrane or membranes of subcellular organelles, inevitably leading to permeability changes and an increase in enzyme activities in blood plasma. Possible chromosomal damages of fast-dividing cells in animal embryos under the influence of the static magnetic field were also studied in a long-term experiment.

The static magnetic field force on structures with asymmetric susceptibility such as biological membranes may cause plasma membrane leakage and damage of subcellular compartments. Levels of liver enzymes appearing in the serum are clinically relevant parameters for many diseases that affect cell structures. The appearance and elevated concentration of the cytosolic and mitochondrial enzymes determined in this study are most sensitive indicators of cell damages in the liver, kidney, or

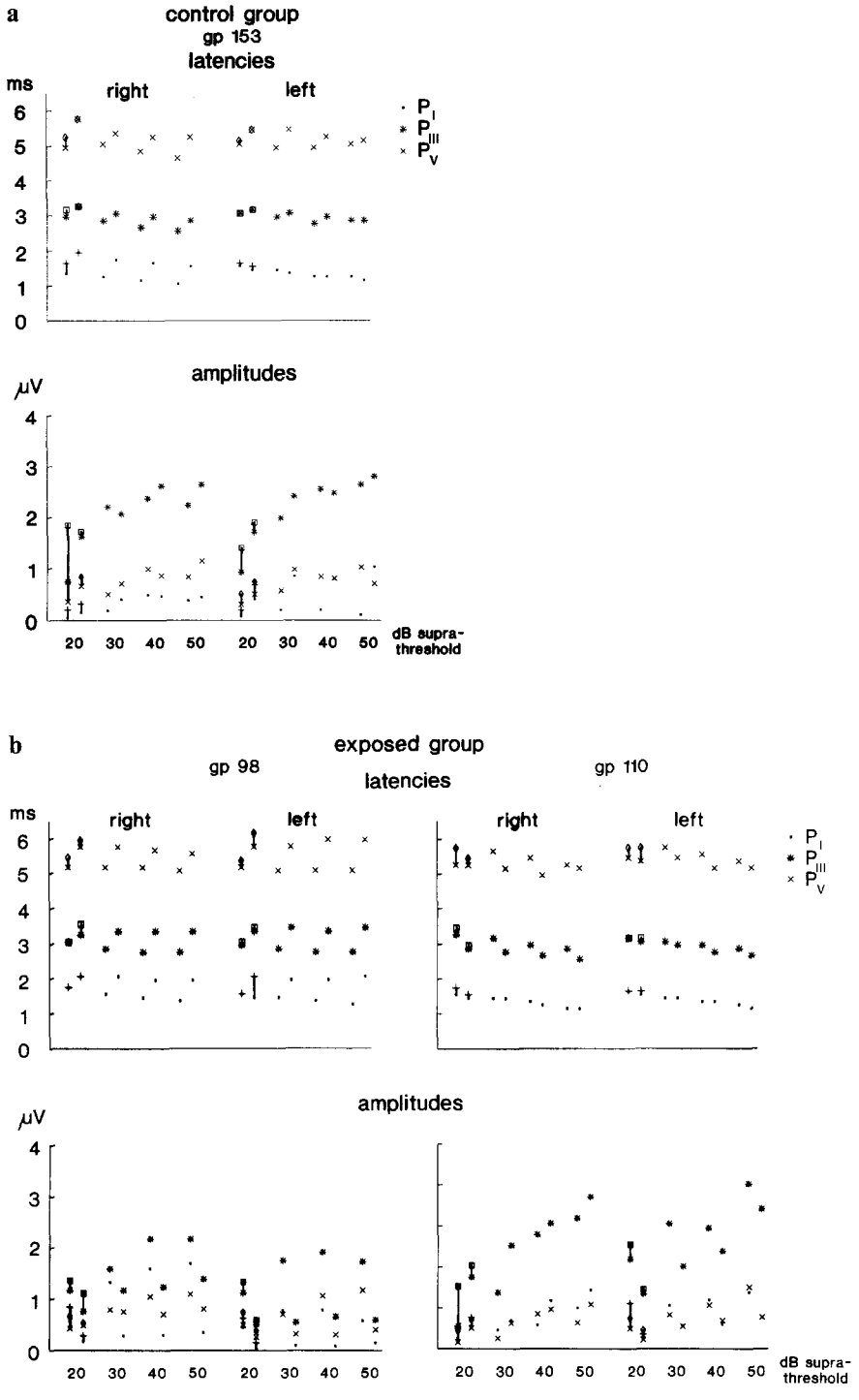

Fig. 3. a) Representative evaluation of the results of BAEP measurements of the control group. The values before and after are grouped tightly together. *Bars* at 20-dB suprathreshold indicate the standard deviation of the measurements. The latencies of all three peaks increased slightly in the second measurement at the same loudness of the click, while at the same time decreasing latencies were observed with increasing loudness. The amplitudes were less uniform; both increasing and decreasing amplitudes were observed among the "after" values. The amplitudes itself are increasing with increasing sound intensity. b) Treated animals. Animal gp 98 shows the typical increase in latencies and simultaneously decreasing amplitudes, which were expected in the case of disturbed inner ear circulation. In contrast, gp 110 shows partly inconsistent reaction to the exposure. Peaks I, III, and V show decreasing latencies, and the right ear shows increasing amplitudes of all three peaks, while its left ear reveals decreasing amplitudes

muscle. The following serum enzymes were determined by routine laboratory methods: GOT, GPT, γ-GT, AP, LDH, HBDH, CK, CK-MB, and amylase. The time intervals between the field exposure and the collection of serum samples are a compromise since the pathological enzyme appearance in the blood plasma is a function of time. The triglyceride and cholesterol content of the blood plasma were also determined.

Zero-time blood samples (ca. 3 – 4 ml) were collected from the ear vein of the animals 1 day before they were exposed to the magnetic field. The second and third blood samples were collected 6 and 24 h after exposure to the magnetic field. In general sampling occurred after sedation by Nembutal (0.5 ml, i.m.). Anesthesia by Nembutal does not influence the levels of the enzymes studied here.

Table 2 shows the enzyme concentration in the serum of the magnet group and of the control group, respectively. In general, no clinically significant changes in the serum enzyme profile was induced by the exposure to the static magnetic field at 4.7 T. However, a significant increase in muscle creatine kinase (CK) acitivity was found in some of the blood samples of experimental or control rabbits. Older animals revealed a higher CK level than younger ones. No correlation between CK acitivity and the field exposure was observed. Enhanced CK level on days 2 and 3 was presumably due to the reactions of the rabbits upon blood collection.

Our results are in agreement with those of other reports: no anomalies in numerous hematological and serum parameters were found in rats exposed to 60-Hz electric fields [26]. Battocletti et al. [27] studied the exposure of rhesus monkeys to 2-T magnetic fields and found no effect on blood parameters. The influence of the magnetic field on isolated cells has also been reported [28, 29].

The third approach in our study is based on the presumption that in addition to biomembranes macromolecules such as DNA may also be affected by the magnetic field. Fast-dividing cells of embryonic tissue may be very sensitive to the magnetic field.

The teratogenic effect of the 4.7-T field on embryonic development was analyzed in the following way: two

Table 2. Analysis of the blood plasma enzyme level of rabbits: aspartate aminotransferase (GOT, EC 2.6.1.1), alanine aminotransferase (GPT, EC 2.6.1.2), γ-glutamyl-transpeptidase (γ-GT), alkaline phosphatase (AP, EC 3.1.3.1), lactate dehydrogenase (LDH, EC 1.1.1.27), creatine kinase (CK, EC 2.7.3.2) and amylase (EC 3.2.1.1). Two-year-old New Zealand White and Chinchilla rabbits fed ad libitum (weight 2 – 5 kg) were used for the experiments ("magnet group", $N = 18$). Control animals ($N = 2$) were kept in the animal house. One rabbit was tested at a time. It was placed in a plastic cage (40 cm long, 20 cm wide) inserted in the center of the bore hole of the magnet where the field was relatively uniform. Each animal was exposed to the magnetic field four times for a period of 2 h. At least a 1-week interval separated the exposure experiments with the same animal

	Magnet group			Control group		
	– 24 h	6 h	24 h	– 24 h	6 h	24 h
GOT	8	13	10	20	26	21
GPT	23	23	26	43	52	57
γ-GT	3	3	4	2	2	2
AP	55	54	55	25	26	13
LDH	362	466	357	665	667	819
CK	544	1657	1748	803	6161	3200
Amylase	628	632	671	679	694	562

groups of six *Balb/c* mice from a 2-month-old litter was chosen. The experimental group was exposed 16 h per day to the static magnetic field of 4.7 T. The mice, five females and one male, were allowed to breed freely. A group of six mice of each subsequent generation (4 weeks old) were chosen for further observation. The remaining animals were removed from the experiment. After a 1-year observation period the mice were in their 5th generation. No alteration of the phenotype of the inbred mice or any teratogenic effects were observed. All animals reached a normal body weight of 28 – 34 g.

Studies related to that described above have been reported. No statistically significant differences between human peripheral lymphocytes exposed to electromagnetic fields were found by Cohen et al. [30]. Short-term exposure of bone marrow cells were carried out by Prasad, who found no chromatid or chromosomal aberrations [31]. During our experiments, Heinrichs et al. [32] and McRobbie et al. [33] reported studies on magnetic field exposure of pregnant mice at 0.35 T and gradient magnetic field of 3.5 – 12 kT/s. Kay et al. [34] investigated the effect of MRI on *Xenopus laevis* embryogenesis. No effects of the magnetic field were observed in these studies.

The results of these studies allow the following conclusions. In guinea pig small changes of BAEPs were observed in both directions, although more animals showed an increase in the latencies and a decrease in the amplitudes of the measured peaks. The serum enzyme analysis of rabbits exposed for prolonged times to 4.7 T gives no indication for significant cell membrane perturbances leading to plasma or mitochondrial membrane permeability. No teratogenic effects on the embryogenesis of inbred mice was observed, even after a 1-year exposure over four generations.

Although studies with volunteers are indicated to further support our conclusions obtained in the animal models, we conclude that MR techniques at 4.7 T for diagnostic and research purposes on humans can be performed safely.

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