Chapter 2
Static Magnetic Fields (SMFs) on Human Bodies

Abstract This chapter summarizes the effects of static magnetic fields (SMFs) on human bodies. Some commonly seen SMFs, such as the weak earth magnetic field that we are all exposed to, moderate to ultra-high field magnetic resonance imaging (MRI) in the hospitals and research institutes, as well as SMF-based magnetic therapies, which have a long history but still lack of solid explanation or sufficient experimentation from a scientific point of view. Magnetobiology and biomagnetism are also briefly discussed.

Keywords Static magnetic fields • Earth magnetic field • Magnetic resonance imaging (MRI) • Magnetic therapy

2.1 Introduction

From a simplified view, the human body is mainly composed of weak diamagnetic materials, including water, proteins and lipids. The term diamagnetic means that it repels with the externally applied magnetic field. In a magnetic field, the motions of electrons in diamagnetic molecules make small changes, which generate weak magnetic fields in the opposite direction to the externally applied magnetic field. Although the diamagnetic properties of most living organisms are very weak, since the repulsive force is proportional to the product of the field intensity and the field gradient, the forces can be amplified by strong magnetic field. The most famous case is the "flying frogs" about 20 years ago, which we mentioned in Chap. 1. People put small diamagnetic objects such as water drops, flowers, grasshoppers as well as small frogs in the 16 T strong SMF produced by a vertical electromagnet and levitated those small objects. Theoretically the human body could also be levitated. However, due to the size and weight of our human bodies, the levitation would need a much stronger magnet and has not been accomplished yet.

In recent years, people have increased exposure to different kinds of electric magnetic fields, most of which are dynamic magnetic fields, such 50–60 Hz power line electromagnetic fields as well as radiofrequency electromagnetic fields. Therefore these magnetic fields have attracted paramount interests in the past, especially around 1970–2000. In the late 1970s and early 1980s, there were multiple

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epidemiologic studies suggested a link between occupational electromagnetic exposure with an increased incidence of leukemia, as well as some other diseases, such as breast cancers. However, although these associations raised many public concerns, further investigations failed to establish a link between the magnetic exposure with these diseases. There are many reviews and books about this topic and we will not discuss about the details here. The focus of our book is SMFs, which have non-changing magnetic fields over time (0 Hz). For SMFs, the most common ones that people are exposed to include the weak but widely spread earth magnetic field (~0.5 Gauss, ~50 μT), MRI scanners in the hospitals (0.5–3 T), as well as permanent magnets of various magnetic intensities that some people may use as alternative medicine for some chronic medical conditions such as chronic pain relief, as well as small magnets that are frequently used in household items such as refrigerators, toys and accessories.

For SMFs, the most updated fact sheet and guidelines by WHO (World Health Organization) and ICNIRP (International commission on non-ionizing radiation protection) were in 2006. For a general view of the current agreement of the magnetic field exposure standards, people can always check the website of ICNIRP for the most updated guidance for electromagnetic exposure (http://www.icnirp.org/). ICNIRP is an independent organization, which provides people with scientific advice and guidance on the health and environmental effects of non-ionizing radiation (NIR) (http://www.icnirp.org/en/frequencies/index.html). NIR is electromagnetic radiation that does not have enough energy to ionize atoms or molecules. Other than SMFs, ICNIRP also cover multiple topics about non-ionizing electromagnetic radiation, such as the electromagnetic radiation from the sun, household electrical appliances, mobile phones, Wi-Fi, and microwave ovens. Although some people may not agree with some specific points, ICNIRP guidelines are still the most well accepted standards for public exposure to non-ionizing radiation. It should be mentioned that due to the public attention, rapid development of technology and huge amount of accompanied studies, the most updated fact sheet and guidelines for radiofrequency magnetic fields published by WHO and ICNIRP were in 2014. Meanwhile, the safety issues of SMFs caused much less worries compared to mobile phones. The current updated fact sheet and guidelines by WHO and ICNIRP about SMFs are in 2006, which is already 10 years from now. There are also some fine and comprehensive reviews that people can look into (Schenck 2000; Valentinuzzi 2004; Feychting 2005).

In the meantime, with the development of high field MRI machines in the hospitals, people have increased exposure to high magnetic fields, which unsurprisingly raised new concerns. In 2011, Yamaguchi-sekino et al. wrote an updated review about the biological effects of electromagnetic fields and updated safety guidelines for strong SMFs (Yamaguchi-Sekino et al. 2011) that people can find many useful information. At the same time, there are various researches started to unravel the potential beneficial effects of SMFs on human, which may provide some action mechanisms of the magnetic therapy that have a long but debating history. Therefore, the effects of static magnetic fields and their effects on human bodies certainly require more research to get a better understanding.

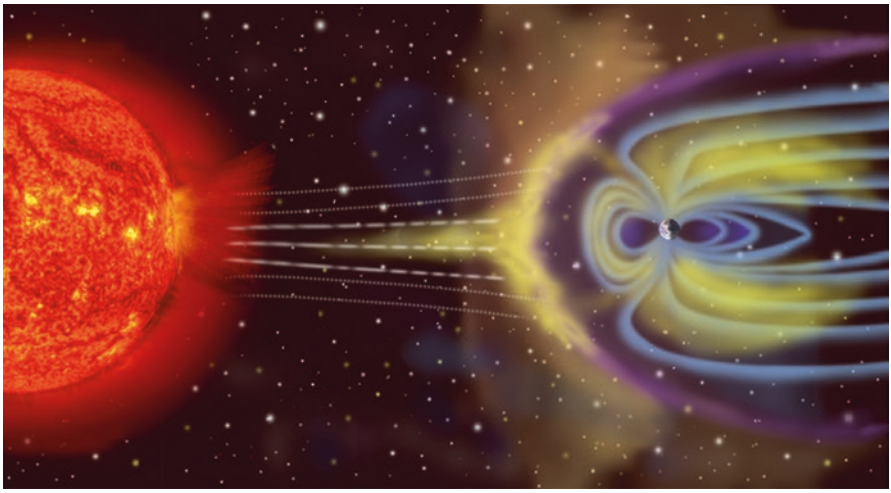

Fig. 2.1 Earth's magnetosphere (The picture was from the public domain created by NASA: https://commons.wikimedia.org/wiki/File:Magnetosphere_rendition.jpg)

2.2 Earth Magnetic Field

The most common SMF that all people are exposed to is the earth magnetic field, geomagnetic field (GMF), which is around 0.5 Gauss/50 μT (0.3–0.6 Gauss, depending on locations). It is actually quasi-static, which means it can fluctuate slightly. Geomagnetic field is much weaker compared to other types of SMF exposure but it is present virtually everywhere and is exceptionally important to the living organism on earth. It is proposed that planets without an intact global magnetic field are subject to atmospheric stripping by the solar wind. For example, people think that Mars does not have a global magnetic field so that the solar wind has contributed to the loss of water and the erosion of Mars' atmosphere. In contrast, the earth has its magnetic field (magnetosphere), which is proposed to protect our whole planet from solar wind stripping (Fig. 2.1).

It is well known that birds, bees, turtles and some other animals are shown to sense earth magnetic fields for direction during migration (Lohmann and Johnsen 2000; Wiltschko and Wiltschko 2005; Johnsen and Lohmann 2008). There are many studies about the earth magnetic fields and magnetoception of animals. It is believed that many birds have a compass in their eyes because their retinas have magnetic field sensors, which make them "see" the earth magnetic field in addition to their normal vision. The magnetic sensor was assigned to cryptochromes for many years until recently another protein was also found to participate in magnetic sensing (details will be discussed in Chap. 5). Both CRY (cryptochrome) and MagR seem to be important for the magnetoception in birds but more *in vivo* studies are necessary to draw a definite conclusion. In addition, it is interesting that recently Vidal-Gadea et al. found that the nematode *Caenorhabditis elegans* orients to the earth's

magnetic field during vertical burrowing and the migrations and magnetic orientation required the TAX-4 cyclic nucleotide-gated ion channel in the AFD sensory neuron pair (Rankin and Lin 2015; Vidal-Gadea et al. 2015).

More information about the SMF effects on microorganisms, plants and animals will be discussed in Chap. 5. Although the progress in this particular field is big in the past few years, more efforts are definitely needed to unravel the exact and detailed mechanisms to explain the animal behaviours related to earth magnetic fields. For example, people found some interesting but enigmatic phenomena that dogs like to align their bodies along the earth magnetic field when they excrete (defecation and urination) (Hart et al. 2013).

For humans, although we also have the proteins that are believed to be the receptors for the magnetic fields, such as CRY and MagR, there is no solid evidence to support the presence of magnetoception. Although for now, we think humans cannot detect, or at least cannot feel the earth magnetic field, the magnetic sensing is still one of the most significant unsolved problems in the biology field. Actually, researchers have knockout the cryptochrome in flies to make them insensitive to the magnetic field and found that the magnetic reception can be restored by the human cryptochrome (Foley et al. 2011). This means that human cryptochrome is functional as a magnetosensor, at least in flies. However, why humans do not sense magnetic fields as birds do? Roswitha Wiltschko, who was one of the scientists who first discovered the magnetic sense of birds, said, "*To sense the magnetic field, one does not only need a molecule like cryptochrome, but also an apparatus that picks up the changes in that molecule and mediates it to the brain. Drosophila obviously has this apparatus, but humans? I have my doubts.*" It is possible that we have other sensations that dominate the magnetoception, or just because we miss some key components along the magnetoception pathway. It is interesting that Thoss et al. indicate that the GMF could actually affect human visual system (Thoss and Bartsch 2003; Thoss and Bartsch 2007) although the mechanism is not completely understood. Apparently, this field still remains blurred and we are still far away from understanding the nature of it in both animals and potentially, in humans. More research is certainly needed to answer these fundamental questions.

It is interesting that there are some researches on humans show that GMF could produce some neurological and cardiovascular effects. Burch et al. indicate that the GMF can affect melatonin secretion (Burch et al. 2008), which is a possible mechanism for the neurological and cardiovascular effects of altered GMF. In addition, Lipnicki et al. show that there may even be some association between GMF activity with dream bizarreness (Lipnicki 2009). However, there are also some reports that reported negative results. For example, in 2002, Sastre et al. examined the effects of controlled changes in the GMF on fifty human volunteers for electroencephalogram (EEG) and did not find any obvious correlation (Sastre et al. 2002). Since different aspects were measured in these individual studies, they are not exactly comparable. It is obvious that more researches are needed to address this question.

On the other hand, there are also some evidences showing that in the absence of GMF, frequently referred to Hypomagnetic field (HMF, which is not high magnetic field in other cases), the gene expression, cell proliferation, migration and adhesion

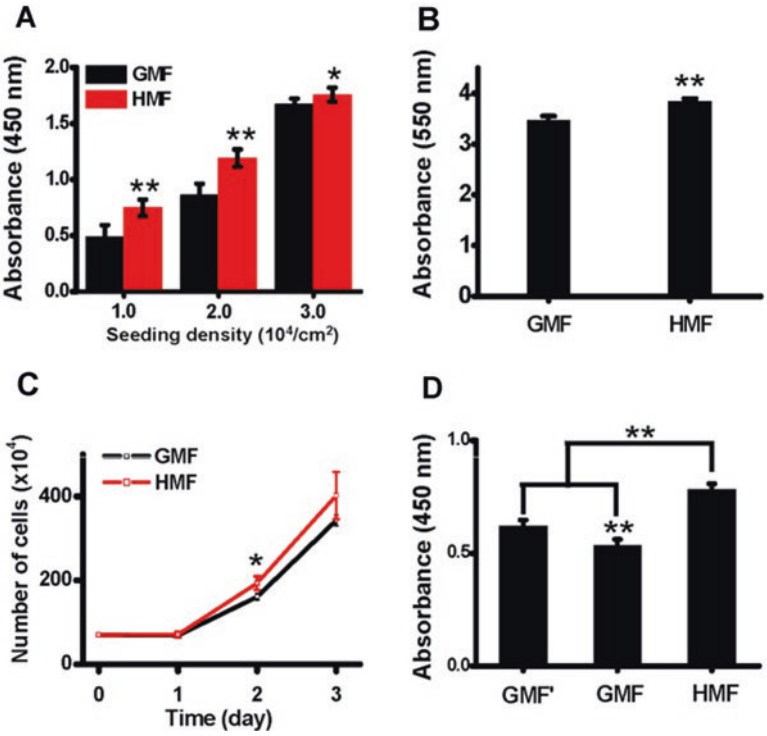

Fig. 2.2 The proliferation of SH-SY5Y neuroblastoma cells was accelerated in the Hypomagnetic field (HMF). (a) Cell proliferation assay by CCK-8 kit (n =6). **(b)** Cells were seeded at $2.0 \times 10^4/cm^2$ in 6-well plates and cell proliferation was measured by crystal violet staining after 48 h incubation in the GMF and HMF (n =6). **(c)** Cells were seeded at $2.0 \times 10^4/cm^2$ in 60 mm petri dishes and incubated for 48 h in the GMF and HMF. The numbers of SH-SY5Y cells were measured at day 1, day 2, and day 3 by hematocytometery (n =3). **(d)** Cells were seeded at 1.5×10^4 cells/cm^2 in 96-well plates. Cell proliferation was measured after 48 h incubation in the reference field (GMF′), in the GMF control shelf (GMF), and in the HMF (n =6). Error bar =s.d.; n =3; *p < 0.05; **p < 0.01 (Image was from Mo et al. 2013, an open access article)

of some human cancer cells could be affected (Martino and Castello 2011; Mo et al. 2013, 2014, 2016). For example, Mo et al. did multiple studies about the effects of HMF on human SH-SY5Y neuroblastoma cells. In 2013, they showed that continuous HMF exposure significantly increases the proliferation of human SH-SY5Y neuroblastoma cells (Fig. 2.2) by promoting cell cycle progression (Mo et al. 2013); In 2014, they compared the transcriptome profiles of SH-SY5Y cells exposed to either the HMF or the GMF and found multiple genes are differentially expressed, including MAPK1 and CRY2 (Mo et al. 2014). In 2016, they found that in HMF, SH-SY5Y cells have reduced F-actin cytoskeleton as well as reduced adhesion and migration (Mo et al. 2016). In addition, HMF was also found to reduce the ROS level in human pancreatic AsPC-1 cancer cell line and bovine pulmonary artery endothelial cells (PAEC) (Martino and Castello 2011), which is consistent with some studies reporting that SMFs could increase ROS in some cancer cells (will be

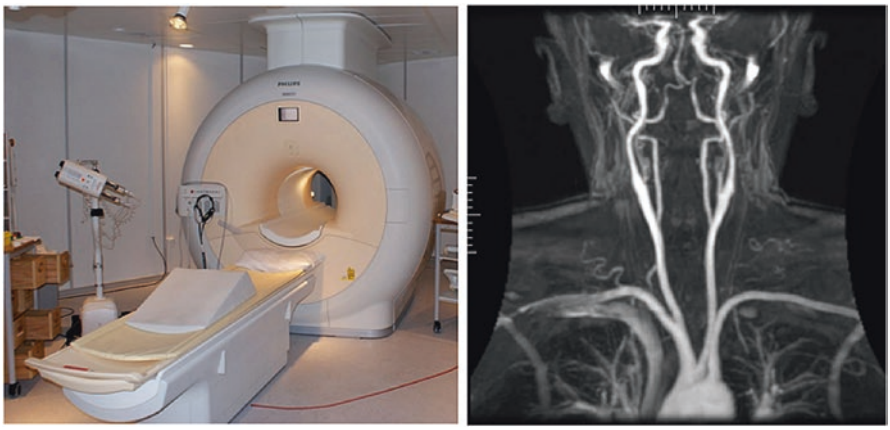

Fig. 2.3 Magnetic resonance imaging (MRI). *Left*: A MRI machine in the hospital (https://commons.wikimedia.org/wiki/File:MRI-Philips.JPG). *Right*: Magnetic resonance angiography (MRA), pictures of the arteries (https://commons.wikimedia.org/wiki/File:Mra1.jpg)

discussed in Chap. 4). In addition, they also did some studies in *Xenopus laevis* (African clawed frog) and found that HMF could cause a decrease in horizontal third cleavage furrows and abnormal morphogenesis in Xenopus embryos (Mo et al. 2012). Their results indicate that a brief (2 h) exposure to HMF is sufficient to interfere with the development of Xenopus embryos at cleavage stages. Although their study was done in frogs, the impact of HMF on mitotic spindle and cell division could also be potentially comparable in other organisms, including humans. This is especially critical for developing embryos.

In conclusion, based on the current available evidences, no matter whether or not humans can sense the earth magnetic fields for direction like some animals do, it is likely that our bodies are indeed affected, or more accurately, protected by the earth magnetic fields. However, more investigations are strongly needed to draw an unambiguous conclusion.

2.3 Magnetic Resonance Imaging

Besides the weak earth magnetic field (50 μT), nowadays people have more chances to get exposed to much stronger SMF, such as MRI scanners in the hospitals. MRI has a superior soft-tissue contrast compared to other radiological imaging methods, which makes it a powerful tool in many physiological and functional applications. The SMF of the MRI system is exceptionally strong compared to the earth magnetic field. Currently, most MRI scanners in hospitals for regular patients are 0.5–3 Tesla, which is around 10,000–60,000 times greater than the earth magnetic field. Figure 2.3 shows a MRI machine and a magnetic resonance angiography (MRA) picture achieved from MRI.

MRI is considered to be a safe technique as long as the operation follows the guidelines. So far, after several years of monitoring, there are no harmful effects reported on frequent MRI operators, patients or NMR (nuclear magnetic resonance) users. There are also some lab studies at cellular levels about the safety of MRI. For example, in 2003, Schiffer et al. used conditions that are relevant for patients during MRI for their effects on HL60 and EA2 cells. They examined different types of magnetic fields, including SMFs of 1.5 and 7.05 T, extremely low frequency magnetic gradient fields (ELFMGFs) with +/− 10 mT/m and 100 Hz, as well as +/− 100 mT/m and 100 Hz, pulsed high frequency MF in the radiofrequency (RF) range (63.6 MHz, 5.8 microT), and a combination of these different magnetic fields. They exposed the cells for up to 24 h and did not find cell cycle changes (Schiffer et al. 2003). Recently, Sammet wrote a review about the magnetic resonance safety (Sammet 2016). For example, people with pacemakers should not use MRI because the pacemakers may be reprogrammed or turned off by the magnetic field. People with some other implants, such as ferrous intra-cranial vascular clips, should also avoid MRI because the strong magnetic field of MRI may cause possible movement of the implants. Cell phones and credit cards may be damaged by the magnetic fields so that they should also be kept out of the MRI room. In addition, the patients should be moved slowly into the magnet bore to reduce the possibility of vertigo and nausea. It has been shown that no short term cardiac or cognitive effects are observed following significant exposure to 8 T (Kangarlu et al. 1999) and the 2009 ICNIRP guidance (ICNIRP 2009) concluded that there is no indication of serious health effects from acute exposure of stationary humans to SMFs of up to 8 T, except that people may have unpleasant feelings such as vertigo. Based on the available scientific data, the limit of exposure for general public was set to 400 mT. This is calculated by applying a reduction factor of 5 on 2 T, which has been proved to have no demonstrated robust effect on animals (Gaffey and Tenforde 1983; Tenforde 2005) or humans. The exposure of SMFs above 8 T requires approval of the research protocol by an Institutional Review Board as well as the informed consent of the subjects. It is well recognized that for the regular exposure to the MRI, there are some commonly experienced symptoms including nausea and headaches, which are all reversible.

Although the magnetic field intensities of the range of MRI machines in hospitals (0.5–3 T) are currently considered to be safe to human bodies, more investigations are still needed to achieve a more complete understanding. Large amount of data show that there is no increased risk for leukemia or other types of cancers by SMFs. In fact, increasing experimental evidences from biological labs indicate that the SMFs could inhibit cancer cell growth and have a potential in cancer treatment in the future, which will be discussed in later chapters in this book. In addition, the whole body exposure of mice to the 3 T homogeneous SMF of a clinical MR resulted in a statistically significant antinociceptive activity (Laszlo and Gyires 2009). However, besides the potential beneficial effects of MRI within the 0.5–3 T range, it should be mentioned that there are also some studies indicate that they may have some other effects on human. For example, 3 T SMF was shown to suppress human chondrocyte growth *in vitro* and affect recovery of damaged knee cartilage *in vivo* in the pig model (Hsieh et al. 2008).

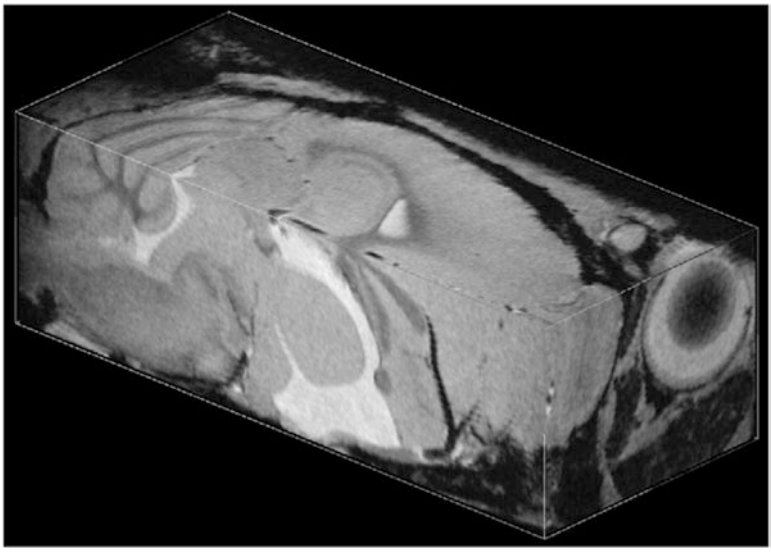

Fig. 2.4 A 21.1 T MRI used on mouse brain. MRI Gradient recalled (FLASH) proton *in vivo* MR image of a mouse head, in plane resolution for image is $50 \times 50\ \mu m^2$ and an apparent resolution in third direction of 50 μm (Image was adapted with permission from Schepkin et al. 2010. Copyright © 2010 Elsevier Inc.)

MRI machines with higher magnetic field strength are already developed. For now, there are 7–9.4 T MRI machines have been used on animal studies in research as well as on human bodies at preclinical stage (Kangarlu et al. 1999; Adair 2000; Miyakoshi 2005; Zhang et al. 2015). For the short-term exposures experienced by volunteers and patients, no readily demonstrated health risks were identified. In addition, since the publication of the 2009 ICNIRP guidance (ICNIRP 2009), there have been a large number of studies evaluating the physiological and neurobehavioral influence in human bodies exposed to SMFs of up to 9.4 T. Current findings show that for the SMFs used in MRI up to 9.4 T, there are no known detrimental biological effects on human bodies. In the meanwhile, people are currently investigating on building MRI machines with ultra-high magnetic fields. Increased magnetic fields can help providing enhanced sensitivity, higher resolution as well as decreased acquisition time. For example, high magnetic fields increased our capability to observe and investigate *in vivo* biological processes that are unavailable or obscure in low magnetic fields. In 2010, Schepkin et al. tested mouse and rat brains using a 21.1 T MRI, the highest field MRI to date, at the National High Magnetic Field Laboratory (NHMFL) in the United States. They were able to achieve imaging resolution of 50 μm (Fig. 2.4), which is much higher than the lower field MRIs. In addition, they also compared 21.1 T MRI to 9.4 MRI and found that the 21.1 T MRI can provide much more detailed features about the tissues and blood vessels in the rodent brain (Schepkin et al. 2010). This showed the promising future of developing similar MRI for human. However, it is still not very clear about the biological effects

of higher magnetic fields, especially the ultra-high magnetic field of 20 T and above. Since our knowledge of the biological effects of SMFs will guide us for future increase in magnetic field intensity for MRI to benefit medical diagnosis and treatment, more studies are definitely needed to investigate the biological effects of ultra-high magnetic fields, which are necessary for the future application of ultra-high field MRI machines on humans.

Therefore, although current MRI machines in the hospitals are considered to be safe, the long term consequences and their potential beneficial effects on human bodies are still incomplete identified. In addition, obvious advantages of ultra-high field MRI machines encourage people to create ultra-high field MRIs for technical benefits. This also calls for attention for necessary studies for the accompanied safety issues. More efforts are needed to help establish guidelines for occupational staff and patient exposures to high SMFs.

2.4 Magnetic Therapy Using SMFs

Looking back into history, magnetic therapy has been debated for thousands of years and there were multiple rounds of up and downs (Basford 2001). It is interesting that the lack of solid scientific explanation for the working mechanism of magnetic field on human bodies does not really prevent people from using magnets at their own wish. Although it is never a mainline medicine, there are still many people currently using magnetic therapy as an alternative and complementary treatment for some chronic diseases, such as arthritis, wound healing and analgesic therapy (pain relief). Every year, the magnetic therapy products have billions of dollars in sales worldwide. In fact this is mostly because many people using magnetic therapy do find themselves benefiting from them, such as some products designed for pain relief. For example, there are some magnetic therapy products on amazon.com. A few of these products have hundreds of positive comments claiming that they could alleviate the pain and discomfort, especially the magnet bracelet that has some relative stronger magnets embedded. By browsing the magnetic therapy products on the market, it is not surprising that the magnetic bracelets that received good reviews usually have their magnetic flux densities clearly labelled and most of them are within the range of hundreds to thousands of gausses (0.01–1 T).

Despite the fact that magnetic therapy has a long history, it is still not well accepted by the mainstream medicine. In some cases, it is even considered to be pseudoscience. The doubts people have are mainly due to the lack of consistency and scientific explanations (as discussed in Chap. 1). There are many efforts that have been devoted to trying to resolve this issue and some of them did provide positive results. For example, In 1997 Vallbona et al. conducted a well-controlled study on fifty post-polio patients and found that the 300–500 Gauss (0.03–0.05 T) SMFs (active magnetic device) significantly reduced the patient pain level from 9.6 to 4.4 ($p < 0.0001$) on a 10-point scale (Vallbona et al. 1997) (Table 2.1**, top**). It is interesting that the sham exposure system that maximally mimics the magnetic device

Table 2.1 Moderate intensity SMF reduced pain level in post-polio patients

Pretreatment and posttreatment pain scores			
	Active magnetic device (n = 29)	Inactive device (n = 21)	Significance
Pretreatment pain score (mean ± SD)	9.6 ± 0.7	9.5 ± 0.8	NS
Posttreatment pain score (mean ± SD)	4.4 ± 3.1	8.4 ± 1.8	P < 0.0001
Change in score (mean ± SD)	5.2 ± 3.2	1.1 ± 1.6	P < 0.0001
Proportion of subjects reporting pain improvement by magnetic activity of the treatment device			
	Active magnetic device (n = 29)	Inactive device (n = 21)	
Pain improved	N = 22 (76%)	N = 4 (19%)	
Pain not improved	N = 7 (24%)	N = 17 (81%)	

The *top* table shows that the pain score is efficiently reduced by active magnetic device. The *bottom* table shows that the % of patients that have effective pain relief is much higher in the active magnetic device group. Both tables were based on results from (Vallbona et al. 1997)

(inactive device) also had some placebo effects and reduce the patient pain level from 9.5 to 8.4. However, it is obvious that the pain level change in the SMF-treated group is fivefold more efficient than the placebo-device group (5.2 vs. 1.1, $p < 0.0001$). In addition, 76% of the patients in the active magnetic device group reported much reduced pain while the placebo-device group only have 19% patient (Vallbona et al. 1997) (Table 2.1**, bottom**). This study is well known and much better than most other magnetic therapy studies in a scientific point of view. It was done with proper controls, which provided people with convinced evidences that SMFs could indeed have beneficial effects on pain relief. More studies are needed to carry out in scientific way like this to test the claims made in the field of magnetic therapy.

Another two scientifically done studies in the field of magnetic therapy were by Alfano et al. and Juhasz et al. In 2001, Alfano et al. did a randomized, placebo-controlled, 6-month trial conducted from 1997 through 1998 on people with fibromyalgia (Alfano et al. 2001). In addition to sham controls, they compared a group of people that was exposed to sleep pads with magnets that provided low uniform static magnetic field of negative polarity (Functional Pad A) with a group exposed to sleep pads with magnets that varied both spatially and in polarity (Functional Pad B). In fact, they did find that the Functional Pad A had the most significant effects and both Functional Pad A and B groups showed improvements in functional status, pain intensity level, tender point count, and tender point intensity after 6 months of treatment, but they did not differ significantly from changes in the control groups (Alfano et al. 2001). Therefore although this study show that the magnetic sleep pads have the potential to work, the effects were not statistically significant. I think the major reason for the lack of efficiency in their study might be the magnetic field strength, which is too low (below 1 mT). Increasing the magnetic field strength to

hundred to thousand gauss might work. However, scientific studies are needed to be done to prove this. Moreover, in 2014, Juhász et al. did a randomized, self- and placebo-controlled, double-blind, pilot study included 16 patients diagnosed with erosive gastritis. They used inhomogeneous SMF-exposure intervention at the lower sternal region over the stomach with peak-to-peak magnetic induction of 3 mT and 30 mT m(−1) gradient at the target site. They did found clinically and statistically significant beneficial effect of the SMF- over sham-exposure on the erosive gastritis symptoms. The average effect of inhibition was 56% ($p = 0.001$). This indicates that inhomogeneous SMF could be a potential alternative or complementary method for erosive gastritis (Juhasz et al. 2014). It is interesting that their magnetic field intensity seems much lower than most other studies that have positive results.

Current evidences show that magnetic field strength is a key issue for potential magnetic therapy applications. Overall, it is believed that magnetic fields with too weak strength are not enough to produce enough energy. As mentioned above, the permanent magnets most people used for magnetic therapy have been proved to be effective ranging from hundreds to thousands of gauss. For example, in 2002, Brown et al. showed that 0.05 T SMF for 4 weeks could reduce chronic pelvic pain in patient (Brown et al. 2002). In 2011, Kovacs-Balint et al. did a research on 15 young healthy human volunteers and found that a inhomogeneous 0.33 T (Bmax) SMF exposure for 30 min could increase the thermal pain threshold (TPT) (Kovacs-Balint et al. 2011). However, it is possible, and very likely, that different symptoms have different requirement for the magnetic field intensity, as well as other magnetic field parameters.

Besides human studies, there are also some animal and cellular studies about the potential application of SMFs in multiple diseases. For example, in 2008 Gyires et al. showed that the inhomogeneous 2–754 mT SMF could significantly reduce the visceral pain (57%, $P < 0.005$) elicited by intraperitoneal injection of 0.6% acetic acid in mice (Gyires et al. 2008). In 2009 Laszlo et al. showed that 3 T MRI had significant beneficial effects on pain relief in mice (Laszlo and Gyires 2009). In 2012, Okano et al. found that gradient moderate intensity SMF of 0.7 T (Bmax) exposure for 4–6 hours could reduce the nerve conduction velocity of C fibers, which are responsible for pain transmission (Okano et al. 2012). In 2013 Kiss et al. did a study in mice show that moderate intensity of both inhomogeneous (3–477 mT) and homogeneous (145 mT) SMFs that are provided by permanent magnets can have a significant beneficial effects on pain relief (Kiss et al. 2013). In 2013, Vergallo et al. examined the effect of inhomogeneous SMF (0.476 T max) exposure on the production of different cytokines from human lymphocytes and macrophages (Vergallo et al. 2013). They found that the moderate intensity inhomogeneous SMF treatment for 6–24 h has a significant inhibitory effect on the release of pro-inflammatory cytokines IL-6, IL-8, and TNF-a from macrophages as compared to control. In addition, the SMF increased the production of anti-inflammatory cytokine IL-10 from lymphocytes. As brought up multiple times before, most of these magnetic field intensities that show positive results for pain relief and inflammation reduction are a few hundred to a few thousand Gauss. However, we do not exclude the possibility that lower magnetic field intensities will also have some effects on

some biological samples, or have some other different effects. There were also some mechanistic studies about the SMF-induced pain relief. Gyires et al. showed that the analgesic action induced by inhomogeneous 2–754 mT SMF could be inhibited by subcutaneous administration of naloxone, irreversible micro-opioid receptor antagonist beta-funaltrexamine and delta-opioid receptor antagonist naltrindole, but not the kappa-opioid receptor antagonist norbinaltorphimine, which suggests that the antinociceptive effect is likely to be mediated by micro and delta-opioid receptors (Gyires et al. 2008). More details and information are discussed in Chaps. 6 and 7 for the potential application of SMFs in cancer and other diseases.

In the meantime, not surprisingly, there are some experimental evidences showing that certain magnetic therapy products fail to produce positive effects, even for the magnets that have enough magnetic field intensities. For example, Richmond et al. compared a magnetic wrist strap with (1502–2365 gauss), a demagnetised (<20 gauss) wrist strap, an attenuated (250–350 gauss) magnetic wrist strap, and a copper bracelet. Their results show that wearing a magnetic wrist strap or a copper bracelet did not appear to have any meaningful therapeutic effect, beyond that of a placebo, for alleviating symptoms and combating disease activity in rheumatoid arthritis (Richmond et al. 2013). For now we are not sure about the reason for this lack of efficacy, however, as mentioned in Chap. 1, magnetic field parameters will greatly influence the effects of SMF on biological samples. In addition, there are multiple other factors that have led to the large variations in the clinical or research work about the SMFs, which we will discuss more in Chap. 4 in this book. For example, although lacking scientific mechanistic foundations so far, it is interesting that there are multiple claims about the differential effects of the two different magnetic poles on human bodies (Table 2.2). In fact, there are two recent papers observed differential effects of different magnetic field directions (De Luka et al. 2016; Milovanovich et al. 2016). Although more research is strongly needed to confirm their results, I think people should pay attention to the magnetic poles or directions when they investigate the biological effects of magnet fields in the laboratory, or simply want to try some magnetic therapy products.

The differential effects of the magnetic field direction and north/south poles need to be further confirmed by more scientific researches, and ultimately to provide clear scientific explanations. For now, I myself are not clear why two different poles can make any differences because there is no physical difference between the North and South pole of the magnet, at least from our current scientific knowledge. However, it is possible that some unknown mechanism indeed exists to explain these observations. Moreover, since it has already been shown that magnet could levitate single cells when the magnetic field is upward to balance the gravity (Durmus et al. 2015), it makes more sense to me if it is the magnetic field direction that made the differences that people claimed. More interestingly, Durmus et al. demonstrate that each cell type (i.e., cancer, blood, bacteria, and yeast) has a characteristic levitation profile, and they have identified unique differences in levitation and density blueprints between breast, esophageal, colorectal, and non-small cell

Table 2.2 The North and South magnetic poles are claimed to have different "healing effects" by some magnetic therapy manufactures

Claimed "healing effects" of different magnetic poles by many magnetic therapist	
North pole-"Negative"	South pole-"Positive"
Inhibits Relieves pain	Excites Increases pain
Reduces inflammation	Increases inflammation
Produces an alkaline effect	Produces an acid effect
Reduces symptoms	Intensifies symptoms
Fights infections	Promotes microorganisms
Supports healing	Inhibits healing
Reduces fluid retention	Increases fluid retention
Increases cellular oxygen	Decreases tissue oxygen
Encourages deep restorative sleep	Stimulates wakefulness
Produces a bright mental effect	Has an over productive effect
Reduces fatty deposits	Encourages fatty deposits
Establishes healing polarity	Polarity of an injury site
Stimulates meletonin production	Stimulates body function
Normalizes natural alkaline PH	

For now, it is not clear whether this is real. Different magnetic field direction could generate some differences. However, although from the scientific point of view there is no explanation for this, I do not exclude the possibility that their claim might be true. More scientific studies are encouraged to explore this question

lung cancer cell lines, as well as heterogeneity within these seemingly homogenous cell populations (Durmus et al. 2015). This indicates that various cell types in the human body might respond totally differently to the magnetic fields. More researches are needed to confirm this.

It is worth to mention that currently many researches related to magnetic therapy as well as the biological effect studies about magnetic fields are not well described or properly controlled. In 2008 and 2009, Colbert et al. wrote two important and comprehensive reviews (Colbert et al. 2008, 2009), which stated that *"Complete descriptions of the SMF dose that was applied to human participants are notably lacking in the majority of SMF therapy studies published to date. Without knowing the SMF dose that was delivered to the target tissue, we cannot draw meaningful inferences from clinical trial results. As research on SMF therapy progresses, engineers, physicists and clinicians need to continue to work together to optimize SMF dosage and treatment parameters for each clinical condition. Future publication of SMF studies should include an explicit assessment of the SMF dosage and treatment parameters outlined in this review, so as to be able to replicate previous studies, validly assess outcomes and make objective, scientific comparisons between studies."* The parameters they outlined include the magnet materials, magnet dimensions, pole configuration, measure field strength, frequency of application, duration of application, site of application, magnet support device, target tissue, distance from magnet surface,

Table 2.3 10 essential static magnetic field dosing parameters

	Static magnetic field dosing parameters
1	Target tissue(s)
2	Site of magnet application
3	Distance of Magnet surface from target tissue(s)
4	Magnetic field strength
5	Material composition of permanent magnet
6	Magnet dimensions: size, shape, and volume
7	Magnet polar configuration
8	Magnet support device
9	Frequency of magnet application
10	Duration of magnet application

Adapted from (Colbert et al. 2008). We recommend that people should all follow these standards when reporting their results

which all have great potential to directly affect the outcomes (Colbert et al. 2008, 2009) (Table 2.3). Many related researches need replication and we hope we can make great advancement after we have the proper knowledge of the magnetic field and biological systems, which will not only be helpful for WHO to assess any possible health consequences, but also improve the current status of magnetic therapy, which definitely needs much more rigorous experimentation. In fact, FDA has already approved the use of TTF (tumor treating fields), which delivers low-intensity, intermediate-frequency (100–300 kHz), alternating electric fields to treat newly diagnosed and recurrent glioblastoma, which works by disrupting cancer cell division, with no significant damage to normal non-dividing cells (Kirson et al. 2004; Pless and Weinberg 2011; Davies et al. 2013). Although TTF is a type of electromagnetic field therapy using low-intensity electrical fields, not SMFs, it may shed light on the SMF investigations for their potential clinical usage.

2.5 Magnetobiology and Biomagnetism

Generally speaking, magnetobiology is about the effects of magnetic fields on living organisms, which is the focus of this book. In contrast, biomagnetism refers to the magnetic fields that are generated by living organisms, which is not our main focus in this book, but will be briefly discussed here.

As mentioned in the beginning of this chapter, the human body is mainly composed of weak diamagnetic materials, such as water, proteins and lipids. However, our human bodies also generate currents that produce small magnetic fields (Cohen et al. 1980).

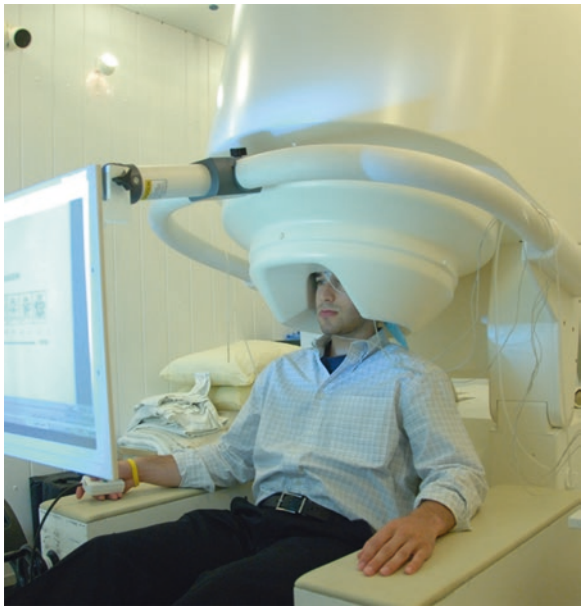

Fig. 2.5 MEG scanner with patient from National Institute of Mental Health (This image is on the public domain. Credit should be given to "National Institute of Mental Health, National Institutes of Health, Department of Health and Human Services". https://en.wikipedia.org/wiki/File:NIMH_MEG.jpg)

Neurons in our brain, nerve cells, and muscle fibers are all excitable cells that can generate currents when they are activated. Magnetic fields produced by the human body have been measured, which are actually very weak (10^{-10}–10^{-5} gauss). Most of the body's fluctuating magnetic fields, such as those from the heart or the brain have been extensively studied and developed. Electrocardiogram (ECG) measures the electrical activity of the heart and electroencephalogram (EEG) measures the electrical activity of the brain, both of which have been widely used in clinic.

It is well accepted that the human brain can be divided into multiple areas, and each of them are responsible for different aspects of behaviour. The accurate and efficient connectivity between these areas are critical for normal function of a healthy brain. Although a single neuron could only produce very weak current, it can be amplified when the neurons are clustered and aligned together and excited simultaneously. In this case, the neurons can produce magnetic fields that are strong enough to be detected using superconducting quantum interference devices (SQUIDs) (Zimmerman et al. 1970; Hamalainen et al. 1993). Weak alternating magnetic fields outside the human scalp, produced by alpha-rhythm currents, were demonstrated. The fields near the scalp are about 1×10^{-9} gauss (peak to peak) (Cohen 1968). Magnetoencephalography (MEG) (Fig. 2.5) is a non-invasive sophisticated technique that captures the magnetic fields generated by synchronized intraneuronal electrical activity, which yields rich information on the spatial, spectral and temporal signatures of human brain function. It is capable of imaging electrophysiological brain activity with good (~5 mm) spatial resolution and excellent (~1 ms) temporal

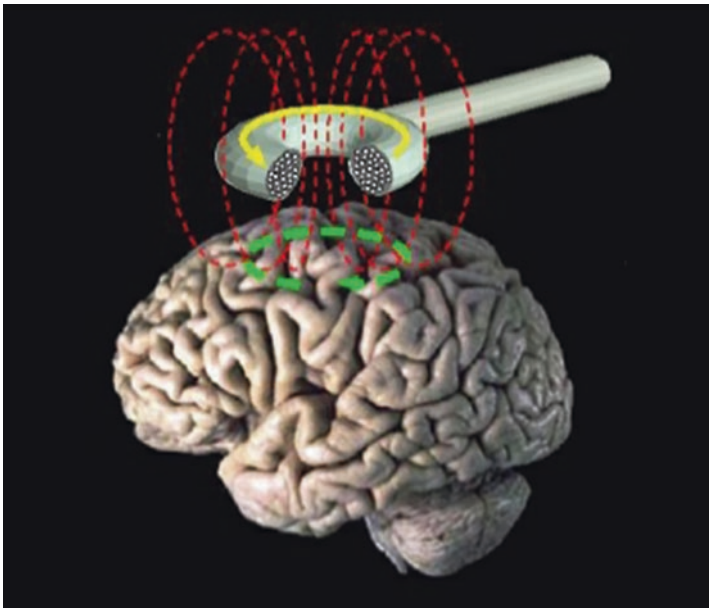

Fig. 2.6 A schematic diagram of transcranial magnetic stimulation (TMS) (This image is on the public domain and it contains materials that originally came from the National Institutes of Health. Picture website: https://en.wikipedia.org/wiki/Transcranial_magnetic_stimulation#/media/File:Transcranial_magnetic_stimulation.jpg)

resolution and provides significant value in elucidating the neural dynamics of the human connectome in health and disease (O'Neill et al. 2015). There are many very useful reviews and research articles for MEGs showing that neuroimaging methods like MEG represents an outstanding approach to better understand the mechanisms of both normal and abnormal brain functions (Brookes et al. 2011; He et al. 2011; Pizzella et al. 2014; Kida et al. 2015; O'Neill et al. 2015; Pang and Snead 2016; Stefan and Trinka 2016). Similarly, magnetocardiogram (MCG) measures the magnetic fields of the heart, which is a complementary or alternative tool for noninvasive detection of coronary artery disease (Kandori et al. 2010; Wu et al. 2013).

In addition, MEG appears to be more sensitive than EEG and can provide additional and different information compared to EEG (Cohen 1972). MEG is not only useful for functional neurosurgery but also for connectivity analyses. Since MEG could offer additional insights not possible by MRI when used to study complex network function, people are combining MEG (which has high temporal resolution) with functional MRI (fMRI), which has high spatial resolution, to provide more information on human brain function (Hall et al. 2014). In particular, MEG is most widely applied to the study of epilepsy, a brain disorder that causes people to have seizures (Kim et al. 2016; Pang and Snead 2016). In addition, simultaneous MEG/EEG recording and analysis could provide complimentary information and better detection sensitivity for tracing primary epileptic activity (Hunold et al. 2016;

Stefan and Trinka 2016). Moreover, for chronic neurological disorders such as epilepsy, functional connectivity detected through hemodynamic (fMRI) and electromagnetic techniques (EEG/MEG) help to identify the interactions between epileptic activity and physiological networks at different scales. fMRI and EEG/MEG functional connectivity help in localizing important drivers of epileptic activity and can also help in predicting postsurgical outcome (Pittau and Vulliemoz 2015). Beyond the diagnosis benefit of MEG, transcranial magnetic stimulation (TMS) (Fig. 2.6) is another electromagnetic method that uses a "coil" placed near the head to stimulate small regions of the brain and is used to diagnose or treat multiple diseases such as stroke and depression. In fact, TMS is currently covered by some health insurance in the United States to treat diseases like depression.

2.6 Conclusion

Since human body itself is an electromagnetic object, it is not surprising that the magnetic fields can produce some effects on us. However, the electrochemical processes within the human bodies are very complicated and still remain incompletely understood. Therefore the actual physical effects of magnetic fields on human bodies will still need continuous efforts to achieve a complete understanding. In the meantime, magnetic therapy may be an alternative or complementary method in the clinical use, especially in cases when conventional therapy options are unavailable. In addition, whether the magnetic therapy works does not depend on our understanding for its underlying biological mechanisms. As Dr. Basford said in his review (Basford 2001)*"An electric or magnetic therapy is first discovered by the populace, resisted by the medical establishment, and then discarded—only to arise again in the future in a slightly different form. Although sophistication has increased, this pattern is likely to continue into the future until clear treatment benefits and, one hopes, a convincing mechanism of action are established."* Currently, what we should do is to try our best to unravel the mysteries so that we can maximize the benefit we can get from these nature powers. In the meantime, we should alert people that there are numerous unreliable websites or products about magnetic therapy. We believe that with the increasing efforts to use legitimate and scientifically backed methods in the field of magnetic field research, we will gain more mechanistic insights to facilitate the clinical application of SMFs and make magnetic therapy scientifically respectable.

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