

Chapter 2

Introduction to Functional MRI Hardware

Luis Hernandez-Garcia, Scott Peltier, and William Grissom

Abstract

The chapter gives an overview of peripheral devices commonly used in fMRI experiments, and it addresses the principles, performance aspects, and specifications of fMRI hardware. The general guidelines for MR-compatible hardware are also discussed. The target audience is quite broad and mathematical descriptions are kept to a minimum and qualitative descriptions are favored whenever possible.

Key words Functional MRI, Hardware, Peripheral devices, MRI, Multimodal acquisition, Neuroimaging

1 Introduction

This chapter is concerned with both the MRI hardware components and the multitude of peripherals that are necessary for functional MRI. Our primary aim is to describe the different components of each subsystem and to identify the important features and parameters. We hope this chapter will be of some use to those who want to get a deeper understanding of the electronics involved, but we mostly want to convey how each of the parts is responsible for the quality (or lack thereof) of the images and the experiment in general. Thus we will try to give minimum requirements for the performance of each component and describe what happens when those requisites are not met.

There is a myriad of subsystems to explore and we cannot possibly do justice to all of them in this chapter, so we will limit ourselves to the main ones and to those that most commonly affect the performance of the system.

While this chapter primarily addresses the principles, performance aspects, and specifications of the functional MRI hardware, it is important that we keep in mind that the objective is to carry out experiments on human subjects performing cognitive tasks. Thus we will also keep in mind the ergonomics and safety characteristics of the equipment.

Our target audience is fairly broad so we will try to keep mathematical descriptions to a minimum and give qualitative descriptions whenever possible. However, some of the descriptions and the requirements make a lot more sense in the context of the mathematical description of image acquisition and reconstruction. We also hope that this chapter can serve as a good introduction to each topic for those interested in the specific subjects. In a way, we approach this chapter as if we were trying to give advice to someone who is considering setting up a functional MRI facility and/or establishing a set of quality control protocols for such a facility. We will be careful to leave our descriptions as general as possible and to avoid endorsing specific vendors or commercial products.

In this second edition, we have done our best to update the contents to reflect the rapid progress in MR technology. In the last few years, we have seen considerable advances in the areas of parallel imaging, high-field magnets and gradient performance, and widespread adoption of these technologies. There are also exciting new developments in the construction of superconducting magnets that are reducing the need for liquid Helium. Complementary brain activity monitoring techniques are being used in conjunction with MRI, such as fNIRS, and new brain stimulation techniques are on the horizon, such as transcranial Direct Current Stimulation.

2 The MRI Scanner Environment

Let us begin by considering the surroundings of the MRI scanner. When deciding on the layout and location of an MRI scanner, there are several important questions one must ask. The first one is the scanner's purpose. Will it be used for clinical purposes or will it be dedicated to research on healthy subjects? In the case of research-dedicated scanners, one must think about a number of specific factors when designing the layout of the fMRI laboratory. This includes dressing rooms, and testing rooms where the subjects can be trained on the experimental paradigm prior to scanning. Whenever possible, it is important to make sure the control room is large enough to accommodate the needs of the researchers using it. It is not uncommon for fMRI experiments to require multiple pieces of custom stimulation/recording equipment in the control room and for several investigators to be present during the experiment, so that extra bench space and "elbow room" is very advantageous. When scanning clinical populations there are additional precautions and considerations, like the presence of MR compatible first aid equipment. We will not address that aspect in detail, as it can be an extensive discussion that will vary from case to case.

The first thing one notices about an MRI scanner is how big it is (the magnet alone can take up a space of roughly $4 \times 4 \times 6$ m) and



Fig. 1 These photos were taken during the installation of an MRI scanner at Resurgens Orthopaedics in Atlanta, GA on the 19th floor of their Crawford facility. Courtesy of Resurgens Orthopaedics, Atlanta, GA

one must find a site with sufficient space for the scanner. Access is also important, as the main magnet is typically delivered and installed in one piece. Furthermore, MRI magnets are filled with cryogenics, which are delivered in large dewars. Thus there must be a wide path to the loading dock that avoids stairs and is clear of obstacles. Typically, MRI scanners are housed in basements or ground floors near the loading docks of hospitals, although exceptions exist, as the one shown in Fig. 1.

Next one must consider how the magnetic field will affect its surroundings. Before the magnet is installed, one must consider how far the magnetic field will extend. Most people who work with MRI are familiar with the enormous forces that the main magnetic field can exert on objects in its proximity (i.e. the magnet room). Modern MRI scanners are actively shielded and contain the magnetic field fairly well within the magnet room. Even with shielding, sometimes a subtle but significant magnetic field can extend beyond the walls of the magnet room. Thus it is important to keep in mind two questions: how well the magnetic field is contained, and what sort of equipment is in the rooms adjacent to the magnet room. The first question is usually answered in terms of the location of the “5 Gauss line.”

The United States FDA regulates that the general public (anyone not working with an MRI scanner or being scanned) not be exposed to static magnetic fields over 5 G (5×10^{-4} T), and thus the 5 G boundary must be contained inside the magnet room. MRI scanner vendors will typically provide contour plots of the magnetic field superimposed on the blueprints of the room and provide consultation on the location of the scanner. One must realize, however, that smaller magnetic fields will extend beyond the walls of the

magnet room, so it is important to note how quickly the field decays and what is located on those adjacent rooms. Subtle magnetic fields can affect electronic equipment in many ways. For example, a moving charge in the presence of a magnetic field will experience a force perpendicular to the magnetic field. This effect was most obvious in CRT monitors (now obsolete), whose images would be skewed by the magnetic field, and in the performance of computer hard drives and magnetic media. In fact, magnetic media, including the magnetic strips on credit cards, floppy disks, ...etc. are typically erased when taken into the magnet room. Another example is that the life span of light bulbs near MRI scanners tends to be quite short because of the vibration of the filaments caused by switching the direction of the current in the presence of a large magnetic field. Hence, DC lights are often used in MRI scanner rooms to avoid this problem. Pace makers, neurostimulators, and implants must be kept outside the 5 G line, unless they have been tested and classified as MR compatible. A number of publications exist [1–3] and are updated regularly with classification of MR compatible devices.

Containment of the magnetic field can be achieved by two different kinds of shielding. Passive shields consist of building a symmetric box around the magnet out of thick iron walls (Fig. 2) that contain the magnetic field. Alternatively, active shields can be built as secondary electromagnets concentrically placed around the main magnet. The shield magnets are built such that the field

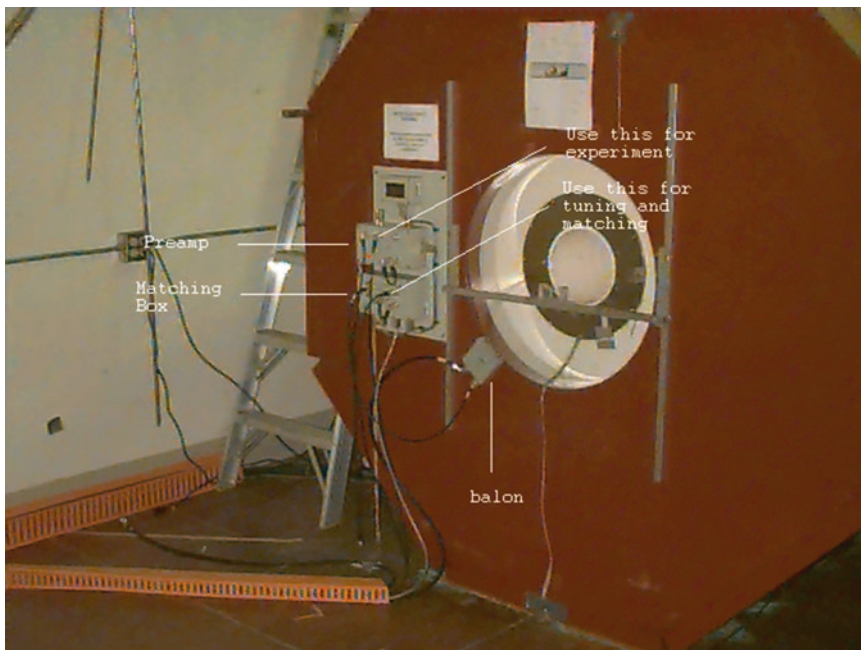


Fig. 2 A passively shielded 4.0 T magnet encased in a hexagonal iron cage to partially contain the main magnetic field

they produce points in the opposite direction of the main magnetic field. The strength of the shielding field is typically about half of the main field. For example, a 3 T actively shielded magnet can often be a 4.5 T magnet surrounded by a second, concentric and opposing 1.5 T magnet. Such a system would have a 3 T field inside of the bore, and because of the inverse square dependence of the magnetic field on the distance to the coil, the field outside of the magnets bore is dramatically reduced. Figure 3 shows a plot of the magnetic fields produced by the main magnet as a function of the distance to the center of the bore. The field produced by the shield and the net sum of both fields are superimposed on the same plot.

One must also consider how the environment will affect the MRI scanner. In this regard, the most important issue is the presence of electromagnetic noise sources. MRI scanners construct images from radio frequency (RF) electromagnetic signals. Thus, radio stations, cell phones, and other wireless communications will interfere with the MRI experiment and severely degrade image quality unless they are properly isolated. MRI rooms are usually encased in a copper shield box that blocks external RF radiation, and contains the MRI's RF radiation as well. The quality of the shield is critically important to the performance of the scanner and it must be tested carefully before the magnet is ramped up to field. Typically attenuations for RF shielding are 100 dB at the operating frequency range. A slightly defective soldered seam between copper sheets, or a nail going through the copper sheeting are

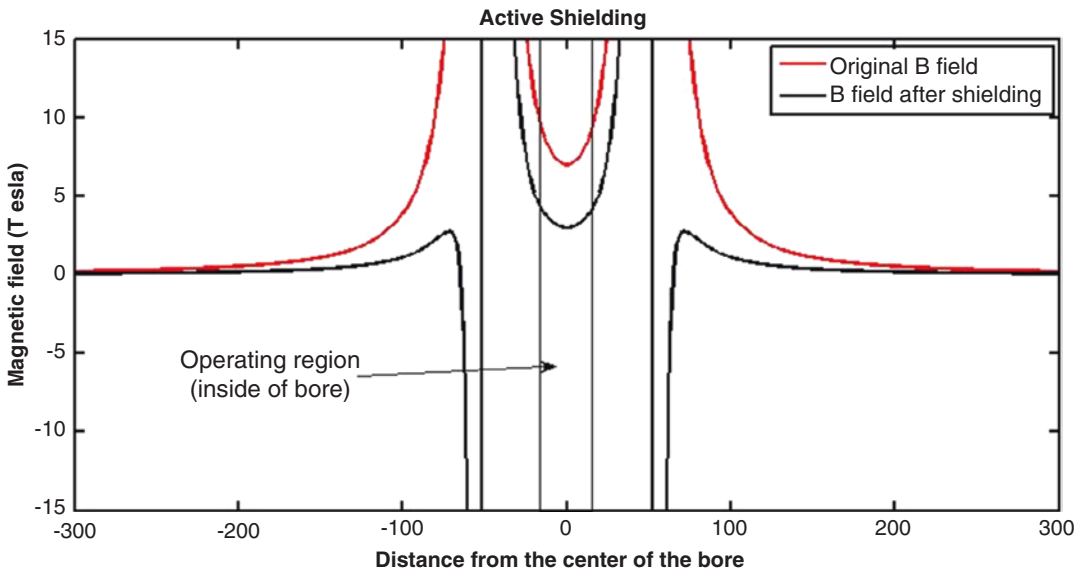


Fig. 3 A plot of the magnetic field strength along the radial direction. The thick vertical lines denote the location of the coil's windings. The thinner line denotes the operating region where the sample is placed. Ideally, this region should have a flat magnetic field, and additional fields (shims) are necessary

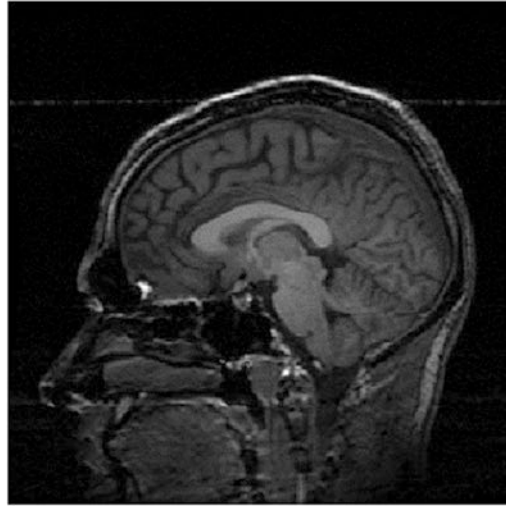


Fig. 4 The streaks in the image are caused by the presence of electromagnetic frequency noise at a single frequency. This is typically introduced by the presence of badly shielded electronic equipment in the room. The AC power supply running at 60 Hz to the device is in this case the culprit of the artifact

sufficient to let RF noise into the room that ruins images, so testing of the room shielding must be stressed. Figure 4 shows an example of the effects of an RF noise source on an MR image

Good shielding of the room is not enough. MR-related electronic equipment produces RF noise and can act as an antenna that passively carries RF noise from the outside into the room. There are also a number of peripherals that are needed for functional MRI in order to provide stimulation and record data from the subject (see Sect. 4). It is preferable to keep all electronics out of the magnet room, but if the electronic equipment must be inside, it must be tested thoroughly for RF noise. If it is indeed noisy, care must be taken to shield the equipment to prevent image artifacts (Copper mesh is very useful for building RF shields).

Consider the case of a button response box. Typically, one keeps the bulk of the electronic components out of the magnet room, but the buttons themselves must be in the scanner and they need to communicate with the response recording electronics. Even if fiber-optic technology is used to carry signals into the room, RF noise can enter through the same opening as the fiber optic cabling. The solution is to build a “penetration panel” into the shield. This is a panel on the wall that is outfitted with waveguides and filtered connectors. The role of a waveguide is to block any electromagnetic radiation that is not parallel with the direction of the waveguide, and at the same time, to guide the EM waves



Fig. 5 On the left is the penetration panel that connects the MRI scanner electronics to the magnet hardware. The image on the right is a second penetration panel used for all the additional stimulus/response equipment needed for fMRI

produced inside it. The filtered connectors typically remove high frequency radiation that may be carried by the cabling of the peripherals. Examples of penetration panels used for scanner cabling and for general, user-specific peripherals are shown in Fig. 5. Additional precautions against RF contamination is the use of twisted-pair and coaxial cabling to contain the fields produced inside the transmission lines.

MR scanner equipment must be kept in stable temperature and humidity conditions, as these can change the performance of the electronics and the field strength. All the amplifiers and computer equipment required for MR imaging can generate a significant amount of heat, so it is important that the environmental temperature-regulating equipment be powerful enough to handle it. Changes in the scanner performance can mask changes in brain activity so the scanner's performance be maintained as constant as possible.

To put things in perspective, the MRI electronics equipment produces approximately 50,000 BTU per hour. Typical requisites for the temperature and humidity in the room are variability of less than 3 °C per hour and 5% per hour, respectively. Normal operating ranges are in the 15–32 °C temperature range and 30–70% humidity range. Of particular interest are the gradient coils, since they can heat up significantly as a result of the large currents that run through them. As gradient coils heat up, their performance is

degraded and thus they require its own cooling system to keep them stable. This system is usually a cooling loop involving a water chiller that can remove about 14,000 BTU per hour.¹

It is also noteworthy that the scanner's performance can be affected by other unexpected environmental factors. Outside magnetic fields and vibrations can be an issue. For example, nearby construction can produce vibrations that will affect the MR signal's stability if the floor is not adequately mechanically damped. It is thus important to carry out vibration tests of the site before installation proceeds. Large moving objects, such as nearby trains can also generate magnetic fields that affect the scanner's stability [4]

One other issue that can cause a great deal of grief to investigators is the production of small electromagnetic spikes inside the magnet room. These occur when metal objects in the room vibrate (typically because of the gradients) and bang against each other or when arcing occurs across badly-soldered connections in home-made equipment. The RF receiver hardware is sensitive enough to pick up these spikes. Spikes in the k -space data translate into stripe patterns in the images (Fig. 6). It is thus very important to make sure that all metal equipment is well secured.

A useful option to consider for a functional MRI lab is a mock MRI scanner. This is advantageous since it allows subjects to get

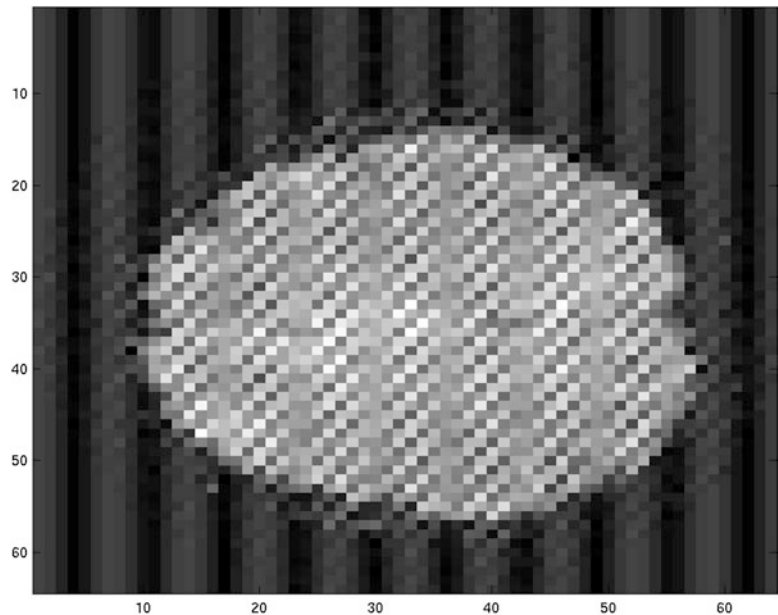


Fig. 6 A T2*-weighted image showing white pixel artifact. Spikes in k -space results in sinusoidal patterns in image spike

¹These numbers are based on the specification of a 3 T scanner by General Electric (MR750).

used to the fMRI experience prior to their actual scans, in a safe environment. This can help alleviate subjects' apprehension and claustrophobia, and lead to reduced head motion and improved task performance.

For completeness, replication of the entire MR suite would be preferable, but usually this is limited by available space and resources. The most important factors to reproduce are the spatial dimensions, audio environment, and visual stimulus presentation of the MRI scanner.

It is important to have the subject familiarize themselves with the restrictive space in the MR scanner. This includes the inner diameters of both the bore of the main magnet and the head coil being used. These restrictions, combined with the distance the subject travels into the magnet from the home position of the patient bed, combine to give the overall physical experience. MR or CT patient beds and scanner housing may be recycled for this use, or the mock MR scanner can be built from scratch as the one shown in Figs. 7 and 8.

The audio environment of the scanner is also an important consideration. Having an audio recording of the actual scanner to play in the mock MR scanner will let the patient adjust to the jarring transition when the scanner starts playing sequences, and the to the volume of this noise throughout the scan. Inclusion of audio feedback can also demonstrate to the subjects that the scanner operator will be able to communicate with them between scans.

A duplication of the fMRI visual stimulus presentation can also serve to acclimatize the subjects. The standard forward- or rear-projection systems used to present visual stimuli are relatively easy to replicate in a non-MR environment, and allow the subject to get used to task presentation during the scan.

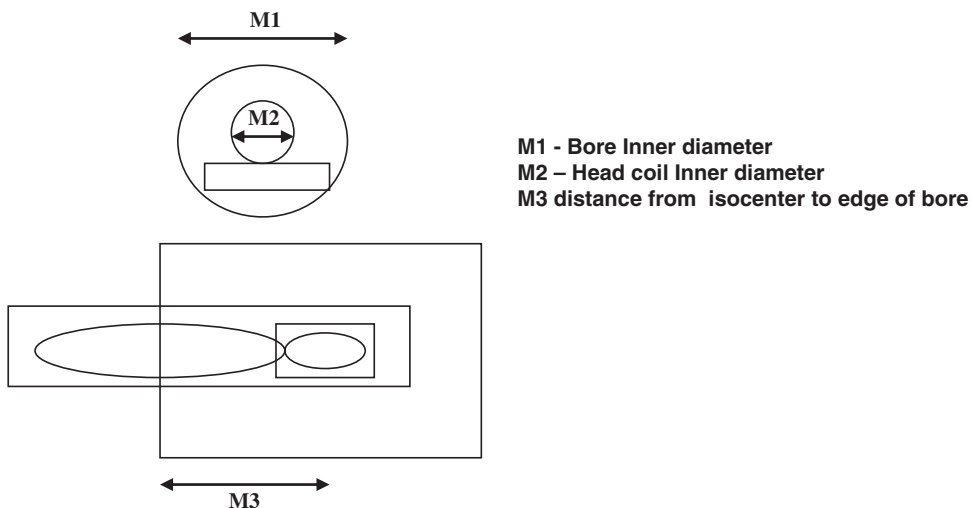


Fig. 7 Diagram of mock scanner showing critical dimensions



Fig. 8 Example of a mock MRI scanner (University of Michigan)

An MR mock scanner can help to increase patient comfort and task performance, especially in some target populations (e.g., individuals with autism, children), and can be used for screening (e.g., individuals with claustrophobia, large physical dimensions). It can also be useful for the training of fMRI lab personnel or the designing, troubleshooting, or rehearsing of complicated fMRI experiments.

3 The MRI Scanner

We can divide the components of an MRI scanner into four categories. The magnet, the magnetic field gradients, the RF Transmit/Receive hardware, and the data acquisition electronics.

3.1 *The Magnet*

We will begin by considering the magnet. Typical MRI magnets, like the one shown in Fig. 9, are large solenoid coils made of superconducting metal (niobium alloys, typically). They are kept cooled at approximately 4 K by liquid Helium in order to achieve and maintain superconductivity.² The magnet is “ramped up” to field by introducing a current through a pair of leads that produces the desired magnetic field. Once the specified current has been built up, the circuit is closed such that the current “re-circulates” through the coil constantly and there is no need to supply more power to it. It is crucial to maintain the low temperature to prevent the coil from resisting the current flow.

A new, exciting development is the “dry magnet.” The term refers to superconducting magnets that are cooled without liquid

² For more information on superconductivity, see [5]



Fig. 9 A 3T magnet during installation at the University of Michigan's FMRI Laboratory

helium. This new generation of magnets uses cryo-coolers [6] that run constantly in order to maintain the temperature of the magnet in the super-conducting range. Cryo-coolers still use helium, although in its gaseous state and in much smaller quantities. A major advantage of this cooling technology is that it allows ramping the magnet up and down much more safely, quickly, and inexpensively, since no liquid helium fills are required in the process. At the time of this writing and to our knowledge, these are only currently available from one vendor of MRI systems (MR solutions) and only for preclinical systems. It is expected that this technology will be adopted for clinical MRI systems in the near future, but most MRI scanners in the world are still cooled by liquid Helium.

If the windings ever warm up and become resistive (i.e., they lose their super-conducting state), they dissipate the electric power as heat. This very undesirable event is termed “quenching.” As the magnet’s windings become more resistive, the very high current circulating through the coil produces heat, such that the liquid helium that is responsible for maintaining the superconducting temperature boils off. This rapid boiling of the helium quickly exacerbates the problem and the superconducting state is quickly lost. The very large currents can potentially produce enough heat to melt or severely damage the windings. The greatest danger however, is that the rapid rate of helium boiling can build up a great deal of pressure in the magnet and also flood the room with helium gas and suffocate whoever is there. While helium is not toxic, it displaces the oxygen in the room. Thus, it is crucial that the magnet be outfitted with emergency vents (manufacturers of MRI scanners typically include emergency quench ventilation systems). Additionally, magnet rooms are outfitted with oxygen

sensors that sound an alarm when the oxygen level falls below safe levels. It must be stressed that all personnel be trained in emergency quench procedures in case the emergency systems fail.

Having considered what can happen when the magnet fails, let us now return to the more cheerful subject of what the magnet can do.

The key parameter in the magnet is its field strength (B_0), as it determines many properties of the images. Primarily, field strength determines the amount of spins that align with and against the field. The higher the field strength, the larger the population of aligned spins that can contribute to the MR signal. More specifically, the population of spins aligned with the magnetic field (n_+) and against it (n_-) is described by the Boltzmann equation

$$\left(\frac{n_+}{n_-}\right) = \exp\left(\frac{\gamma h B_0}{kT}\right) \quad (1)$$

where γ is the gyromagnetic constant for the material, h is Plank's constant, k is Boltzmann's constant, T is the temperature of the sample, and B_0 is the strength of the magnetic field. Hence, the higher the field, the more spins will contribute to the signal and thus yield a higher the signal to noise ratio (SNR) .

The field strength also determines the resonance frequency of the spins, ω_0 , in a linear fashion according to the Larmor equation.

$$\omega_0 = \gamma B_0 \quad (2)$$

Where γ is again the gyromagnetic constant, which is specific for the nucleus in question. The resonant frequency will in turn determine the characteristics of the RF transmit and receiver subsystems (see Sect. 3.3). Field strength also affects both the longitudinal and transverse relaxation rates of the materials via the resonant frequency as predicted by the equations

$$\frac{1}{T_1} \propto \left\{ \frac{\tau_c}{1 + \omega_0^2 \tau_c^2} + \frac{4\tau_c}{1 + 4\omega_0^2 \tau_c^2} \right\} \quad (3)$$

and

$$\frac{1}{T_2} \propto \left\{ 3\tau_c + \frac{5\tau_c}{1 + \omega_0^2 \tau_c^2} + \frac{2\tau_c}{1 + 4\omega_0^2 \tau_c^2} \right\} \quad (4)$$

where τ_c is the correlation time (a measure of the tumbling rate and frequency of collisions between molecules) of the species. Note that T_1 is more heavily dependent on B_0 than T_2 .

While T_1 and T_2 typically get longer, T_2^* gets shorter at higher fields. Recall that T_2^* is the rate of transverse signal loss accounting for both T_2 and macroscopic field inhomogeneity, that is

$$\frac{1}{T_2^*} = \frac{1}{T_2} + \frac{1}{T_2'} = \frac{1}{T_2} + \gamma \Delta B_0 \quad (5)$$

where T_2' is the relaxation due purely to the field inhomogeneity. This inhomogeneity in the magnetic field is usually produced by inhomogeneity in the magnetic susceptibility across the sample, e.g., the air in the ear canals has very different susceptibility than the water in brain tissue. The distortion of the magnetic field caused by magnetic susceptibility is described by

$$B_0' = B_0(1 - \chi) \quad (6)$$

where χ is the magnetic susceptibility of the sample, B_0 is the original magnetic field and B_0' is the resulting magnetic field after considering the magnetic susceptibility. Thus the change in the field gets worse as the magnetic field increases.

The implications for functional imaging are that most imaging and spectroscopy applications benefit in terms of SNR, and that the bold oxygen level-dependent (BOLD) effect is more pronounced at higher fields. But, as is common in MR, there is a tradeoff. As the field increases, and T_2^* effects get shorter, susceptibility artifacts get much more pronounced. This is particularly significant, as the BOLD effect is observed by T_2^* weighted imaging, which is very sensitive to susceptibility artifacts.

Arterial Spin Labeling techniques [7] also benefit from higher field strength, as the longer T_1 means longer duration of the label. Another major practical implication of working at a higher field is that the resonant frequency of protons is proportionally higher, and thus RF pulses deposit more power into the subject. The US FDA regulates the amount of RF power that can be used on a human subject cannot exceed 1.5 W/Kg.

The higher frequency of the pulses also means a shorter wavelength and the formation of standing waves in the sample during transmission. Hence, it is more challenging to achieve uniform excitation patterns across the imaging slice and parts of the imaging slice appear artificially brighter than others. Figure 10 (left) shows an example of this phenomenon (usually referred to as “dielectric effects”) in brain images at 3 T [8–10]. The right panel of the figure shows the corrected image.

To put things in context, at the time of this writing, T_2^* weighted imaging techniques required for BOLD fMRI are fairly challenging at 7 T and not many groups are doing human work at these high fields, although there is an increasing trend toward 7 T. Presently there are only two research groups that have 9 T human imaging systems. At this time, 7 T magnets are predominantly used for small animal research systems. The “de facto” standard field strength for human fMRI systems in the last few years has become 3 T, although many sites still use 1.5 T scanners for fMRI.

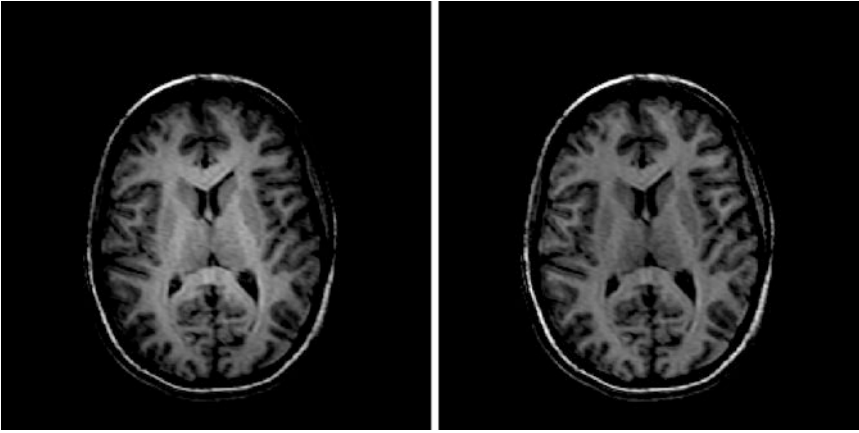


Fig. 10 Illustration of the dielectric effect on a high-resolution, T1 weighted, SPGR image. The center of the image appears brighter, because of the formation of standing waves in the RF pattern. As a result, the center of the field of view receives a higher flip angle than the periphery of the image. The image on the right has been corrected by removing the low frequency spatial oscillation with a 2D FIR filter

Besides the strength, one must consider the spatial homogeneity and temporal stability of the magnetic field. The magnetic field's homogeneity is crucial since the lack of it translates into severe image distortions. One challenge is that the shape of the magnetic field changes when an object (i.e., the subject) is introduced into the field. Consequently, MRI systems are usually outfitted with a set of small pieces of iron installed around the bore of the magnet, referred to as “passive shims.” The location of the passive shims is carefully chosen to make the field more homogeneous. In order to adjust the field homogeneity for individual subjects, additional electromagnets whose field can be dynamically changed when the patient are used. These are referred to as active shims and the process of shaping the field is referred to as “shimming.” There are many types of shim coils that are used to superimpose magnetic fields for shimming purposes. The shim coils are designed to produce spatial magnetic field gradients. These fields are typically shaped as linear, quadratic, and higher order functions of spatial position. While typical clinical scanning procedures require adjustments to the linear shims from patient to patient, it is our experience that T2* weighted (BOLD) fMRI benefits greatly from higher order shimming. Modern scanners are equipped with automatic shimming procedures [11] that can typically achieve homogeneities over a 1500 cm³ region of less than 20 Hz RMS, approximately.

In addition to being homogeneous, it is quite important that the magnetic field be as constant as possible over time. The field tends to drift over time due to a number of factors, among them temperature of the room and the equipment, as mentioned previously. These drifts are typically subtle and slow enough that they do not affect clinical / structural imaging. FMRI, however, is

based on subtle signal changes over time and therefore, drifts act as significant confounds, especially in slow paradigms. Statistical and signal processing tools do exist to reduce these drifts effects, but it is much more desirable that they be reduced during acquisition. Unfortunately, there are many sources of drift in the MRI hardware, so it is important that the magnet undergo extensive stability testing before it becomes operational and that quality control tests including stability measurements be performed regularly. The scanner's stability can be measured on a phantom over a small region of interest. Figure 11 illustrates a typical stability test.

The physical configuration and shape of the magnet also plays an important role in many of these parameters. While “open” MRI systems exist and are used for large or claustrophobic subjects, their field strength is typically not sufficient for functional MRI applications and their use is limited to clinical applications that do not demand high-quality imaging. Among the closed bore systems, one can choose between short and long bore systems. Short bore systems are intended for head-only applications and can sometimes offer improved performance over smaller regions. Long

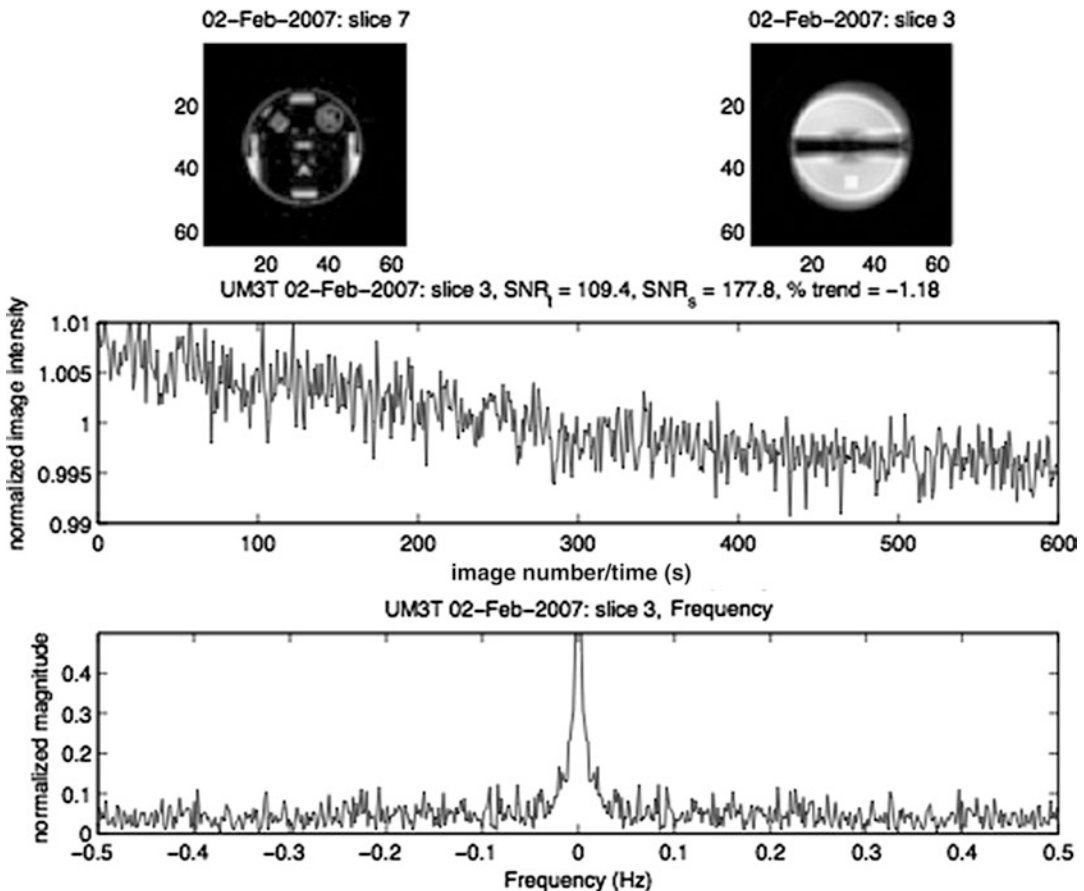


Fig. 11 A typical stability test showing the time course and its frequency content in a phantom (*above*)

bore systems, although more cumbersome, achieve greater field homogeneity over a larger area, which is beneficial for some applications, such as arterial spin labeling.

When considering magnets, it is crucial that we also consider safety issues. The most obvious issue is the very powerful force that magnetic fields of the magnitude required for MRI exert on ferromagnetic objects. These forces are inversely proportional to the square of the distance between the object and the dipole, and are directly proportional to the mass of the metal in question. recall that the magnetic field produced by a current is described by the Biot-Savart law:

$$B(r) = \frac{\mu_0}{4\pi} \int \frac{IdL \times r}{|r|^3} \quad (7)$$

where I is the current, L is a unit vector in the direction of the current, r is another unit vector pointing from the location of the wire to the location of interest, and $|r|$ is the distance from the location of interest to the current source.

One must obviously be very careful to keep ferromagnetic objects out of the magnet room. Typical accidents occur when someone forgets about small metallic objects in their pocket and they fly out of their pocket and strike someone. Accidents sometimes happen because there may be a very subtle force on the object at a specific location in the room leading an unsuspecting investigator to believe that the object is not ferromagnetic. However, moving the object a very small amount toward the magnet can translate into a very rapid increase of the magnetic field, since the magnetic field increases with the inverse of the square of the distance, as mentioned. A small step in the wrong direction while carrying a ferromagnetic object can be the difference between a gentle tug on the object and the object being launched into the bore of the magnet, to the horror of the investigator and the subject. It is thus paramount that strict screening procedures be followed before allowing people into the magnet room. Sometimes small bar magnets and airport security style metal detectors are used to verify the absence of ferromagnetic objects on the subject's body or to test allegedly MR compatible equipment.

These forces can also affect metal implants in the subject's bodies. Pacemakers, neurostimulators, and other implanted electronic devices are likely to malfunction putting the subject at great risk. It is thus crucial that subjects be thoroughly screened for the presence of implants, shrapnel, or other metal sources in their bodies. Having said that, many modern implants are built of titanium and nonreactive materials that are not ferromagnetic and are therefore "MR compatible." A number of publications exist cataloging medical devices and their MR compatibility according to model and manufacturer [1, 2] (and on the web: <http://www.mrisafety.com/>).

3.2 Magnetic Field Gradients

In order to produce images, an MRI scanner needs a spatially varying magnetic field (see image reconstruction chapter) under tight control by the user. This is accomplished by using an additional set of coils that add extra magnetic fields to the main field. A set of such coils is shown in Fig. 12. By supplying customized current waveforms to these coils, the user can change the distribution of the magnetic field's shape at will. In broad terms, by varying gradient's strength can be varied over time during the pulse sequence, one can obtain MR signals whose phase distribution is a function of the spatial distribution of the sample.

The ideal gradient set is capable of quickly changing the magnetic field as a linear function of spatial location along each of the Cartesian axes. Typical gradients in clinical and functional MRI are between 10 to 40 mT/m, but specialized gradient inserts exist that can produce larger gradients (in the range of 100 mT/m). Small bore animal systems can be outfitted with more powerful gradients (up to approximately 400 mT/m). The main challenges in MRI gradient design and construction usually consist of producing linear gradients in space and time, and the production of eddy currents. Motivated by the need to achieve finer spatial resolution and better axon fiber tracking through diffusion tensor images (DTI), Massachusetts General Hospital has developed a high-performance gradient insert that can achieve up to 300 mT/m in a human system, whereas standard clinical gradients rarely exceed 50 mT/m. This system is utilized at present primarily for experiments concerning the "Human Connectome Project" [12] (www.human-connectomeproject.org).

The spatial linearity of the gradients must be maintained over the volume of the sample to be imaged, or the images will appear warped (although these distortions can be corrected during reconstruction if the true shape of the gradient is known). The spatial

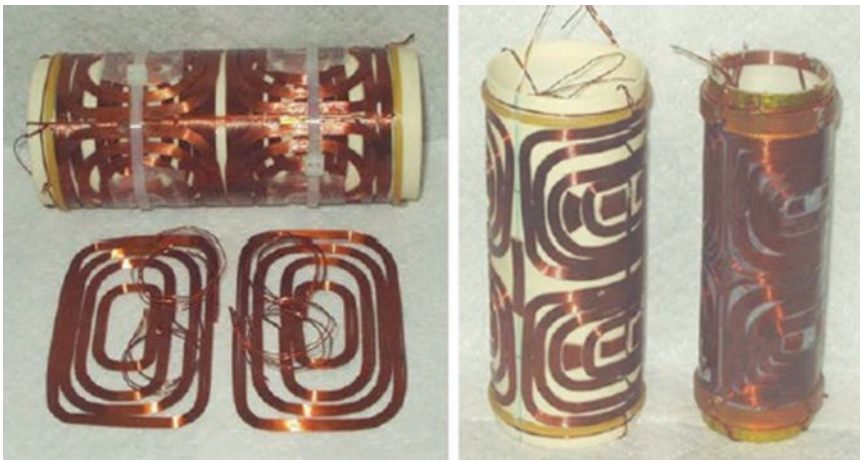


Fig. 12 Gradient coils from Doty Scientific (reproduced with permission of Doty Scientific)

linearity of the gradient fields is primarily a function of the shape of the gradient coils, and a great deal of effort goes into their design and construction (we will not go into those details here). Typical MRI scanner head gradients can maintain 95 % linearity over 30 cm.

The gradient coils must also be able to produce magnetic field gradients very quickly and accurately. The inductive nature of the coils causes their response to the input currents to be severely dampened. In order to correct this problem, typical gradient currents are “pre-compensated” in order to produce the desired waveform [13, 14]. An example of precompensation is illustrated in Fig. 13. Most maintenance or quality assurance protocols include gradient linearity and pre-compensation.

The rate at which a gradient is achieved is referred to as the slew rate. Slew rates of about 200 T/m/s can be generally achieved. However, there are FDA limitations (these are determined by the imaging sequence type and the duration of the stimulation. Typically the maximum allowed rate of change in magnetic field is approximately 20 T/s), since the sudden changes in the magnetic field can induce currents in the peripheral nervous system, causing muscle contractions and unpleasant or even painful sensations in the patient. This phenomenon is referred to as peripheral nerve stimulation (PNS) .

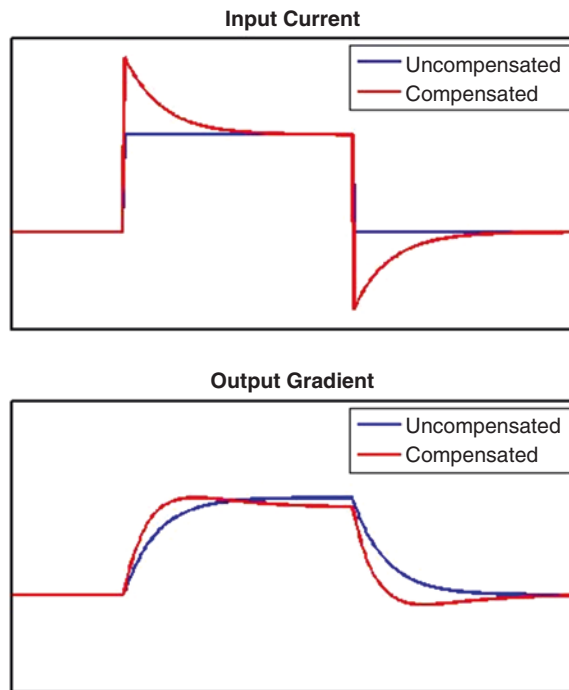


Fig. 13 Simplified illustration of gradient current compensation. The inductive effects of the gradient coils are partially corrected by modifying the input currents to the coil

Active shielding of gradients is necessary to contain the gradient fields and reduce the interactions between gradient coils and other conductors in the scanner. The principles are the same as the active shielding of the main magnetic field (see Sect. 3.1). In other words, a coil producing an opposite gradient field is built around the main gradients in order to cancel the fields outside the area of interest [15, 16].

Gradient vibration and noise are another issue to consider in gradient design. As the gradients are rapidly turned on and off, especially in echo planar sequences, they experience torques due to the presence of the main magnetic field. Thus the coils vibrate violently thus causing the familiar banging MRI sounds. The sound levels are quite loud and require that the subject's wear ear plugs. Active shielding can help reduce the vibrations and acoustic noise produced by the gradients [16].

3.3 RF Hardware

MRI scanners employ RF hardware to generate oscillating magnetic fields that cause the magnetization vector to tip into the transverse plane, and for signal reception. To create signal, an MRI scanner uses a powerful amplifier (generally 1–25 kW) to drive an excitation coil with a large pulse of electric current. In the reception stage, the receive coil is used to pick up the MR signal, which is then processed to create an image. The components of the RF chain that an fMRI user should pay attention to are the transmit and receive coils. Historically, the transmit and receive coils used for fMRI were the same. Today, given the widespread use of parallel imaging to improve image quality via reduced acquisition time, fMRI experiments typically use the scanner's body RF coil for transmit, and a set of multiple coils contained in a single housing that sit close to the head for receive. This approach is referred to as "parallel imaging" [17, 18] and, in FMRI, it's used to improve image quality via reduced acquisition time. Head coils can take many shapes and functional forms, however, for the purposes of SNR and image homogeneity comparisons, there are two main classes of coils: single-channel and multichannel or phased-array coils.

An RF coil is a resonant circuit, and can be modeled as a simple loop containing an inductor, a capacitor, and a resistor (Fig. 14). The inductor and capacitor represent actual circuit components lumped together with the inductance and capacitance of the sample. When a source of electrical current that oscillates at the circuit's resonant frequency is placed across its terminals, the impedances of the inductor and capacitor cancel, and the coil delivers the maximal amount of energy to the sample. In a reciprocal manner, current measured at the coil terminals due to energy radiated by the sample will be of maximum amplitude when that energy oscillates at the coil's resonant frequency. Because the frequency at which biological spins oscillate is determined by the main magnetic field strength via the Larmor relationship, an RF coil must be "tuned" to resonate at this frequency.

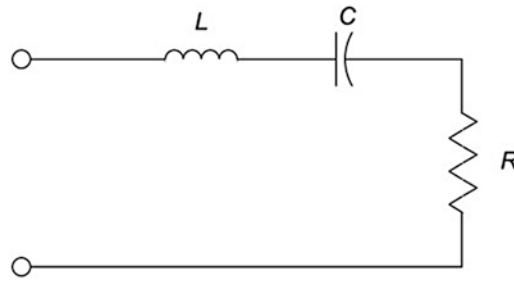


Fig. 14 Series Resistor-Inductor-Capacitor (RLC) circuit representing an RF coil and a biological sample

Single-channel surface coils are the simplest RF coil design. These are typically used to image small areas close to the surface of the skin, as their penetration depth drops sharply with distance from the coil. They consist of a simple loop that induces an oscillating magnetic field when a current is passed through it.

Although the phase information is routinely discarded in image reconstruction, MR signals are inherently vector quantities. RF coils are used to generate an oscillating magnetic field, and the signal emitted back by the sample is a rotating electromagnetic field. However, a simple surface coil can only produce and detect only one component of that vector: the component that is perpendicular to the plane of the coil. Quadrature coils typically consist of two perpendicular coils that transmit at 90° phase from each other. The resulting magnetic field is the vector sum of the two perpendicular fields. Quadrature reception can also be achieved with the same coils by adding phase to one of the channels in the receive chain.

The most popular quadrature-channel head coils generally take on a “birdcage” design (Fig. 15a). This classic design provides good SNR and image homogeneity characteristics, owing to the unique nature of the magnetic field that it creates [19]. Another type of single-channel coil commonly used in studies of the occipital cortex is a quadrature occipital coil (Fig. 15b), which provides high SNR in this localized region of the brain, and has a compact design compared to full head coils, allowing the experimenter greater freedom in stimulus hardware setup.

In contrast, multichannel or phased-array coils (Fig. 15c) are composed of a set of discrete and independent “surface” coils, arranged around the head. Generally, these coils can be brought into a tighter conformation around the head, which improves SNR. Taken alone, images obtained with individual surface coils will possess lower SNR and poor image homogeneity compared to a birdcage coil, however, when images from the coils are combined in a sum-of-squares reconstruction, excellent SNR can be achieved [20], though image homogeneity will still be worse than for a birdcage coil. Furthermore, most phased-array coils can be used only

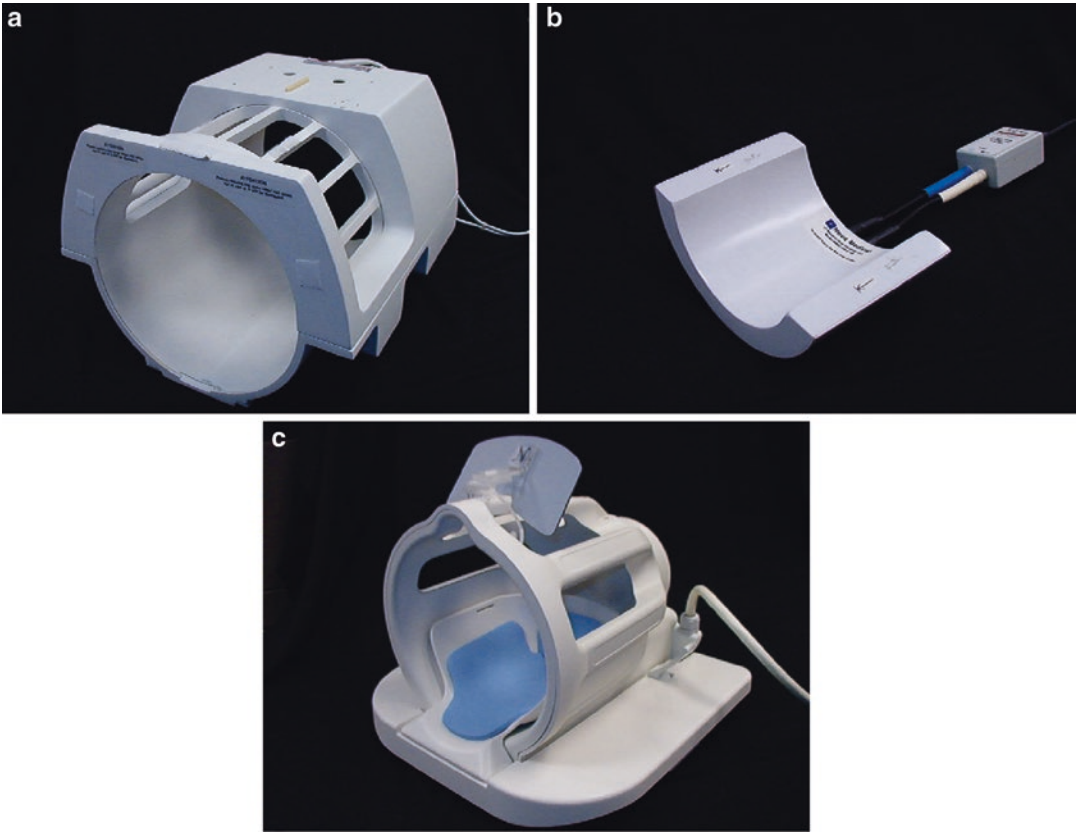


Fig. 15 (a) Transmit/receive birdcage head coil. (b) Receive-only quadrature occipital coil (c) 8-channel phased-array coil

for reception, so a separate coil (usually the scanner's body coil) must be employed for excitation, which can result in degraded image homogeneity, as well as increased SAR in areas outside the head. The central advantage to phased-array coils is that they allow the use of parallel imaging techniques, such as SENSE [17] and GRAPPA [21], when paired with RF signal chains capable of receiving multiple channels simultaneously, which are now commonly available from most MR vendors. Parallel imaging exploits the inhomogeneity of images obtained with surface coils to accelerate image acquisition, which results in a reduction of artifacts in fMRI images, as in Fig. 16. This comes at the cost of reduced SNR. Phased-array head coils used for fMRI commonly have 32 individual coil elements, and can be effectively used to reduce image acquisition time by a factor of 2–4. Scanners with up to 128 receive channels are available from MR vendors.

A birdcage coil generally provides a lot of flexibility in stimulus presentation setup, due to the large amount of room within the coil. One can use goggles, projector/mirror systems, and a range of other solutions in conjunction with a birdcage coil (as we discuss

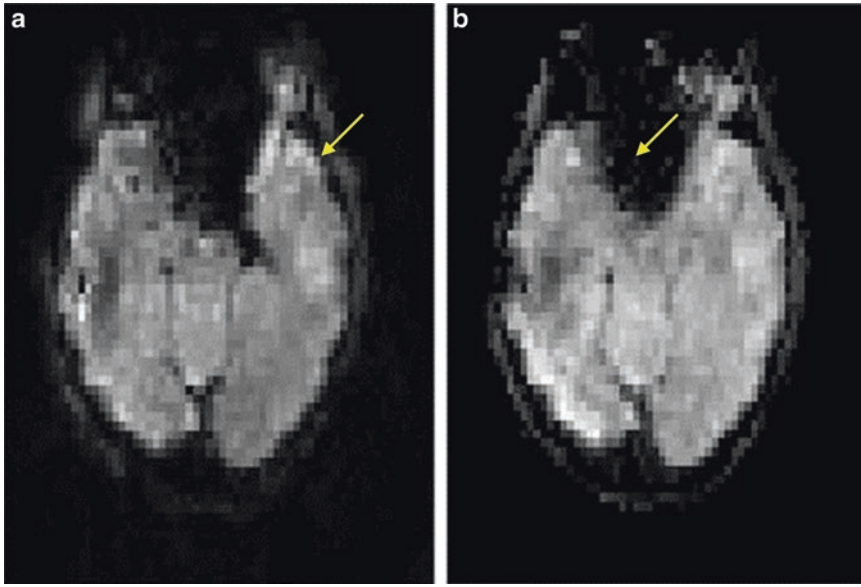


Fig. 16 Comparison of fMRI images obtained using conventional (a) and parallel imaging (b) in the inferior brain. In this example, parallel imaging with an 8-channel phased-array coil was used to reduce data readout time by a factor of 2. This reduced signal loss and image distortions due to susceptibility, particularly in the region indicated by the arrows. (Courtesy of Yoon Chung Kim, University of Michigan Functional MRI Laboratory)

later). In comparison, current phased-array coil designs limit presentation options, since the coils forming it are placed closer to the head, which may prevent the use of visors. However, phased-array coils are generally compatible with the most commonly used projector-based visual stimulus setups. When using visor-based stimulus systems, one must ensure that the electronics of the visor are properly shielded to prevent image artifacts of the type shown in Fig. 4. The “streaking” artifact shown in this image was caused by a visor with an electromagnetic “leak,” that coupled to the receive coil and manifested as a false MR signal. The form of the artifact will depend on the pulse sequence used; in this example the streak is localized, while in another pulse sequence the artifact may be spread over the entire image.

In the near future, the design of multichannel receive coils is likely to be in part driven by simultaneous multislice imaging, a recent parallel imaging-based scan acceleration technique in which multiple slices in a volume are excited and read out simultaneously, leading to a scan acceleration factor equal to the number of simultaneously-excited slices [22, 23]. Whereas conventional parallel imaging is applied to accelerate the acquisition of each slice’s data individually and thus requires a circumferential density of receive coils around the head in the plane of the slice, a simultaneous multislice acquisition requires a density of coils in the slice dimension (typically head-foot in fMRI) to successfully separate

the simultaneously-excited slices' signals. Using appropriate coils and sequences, acceleration factors of 2–5 are common in simultaneous multislice exams [24].

Finally, it is now a common option for 3 T MRI scanners to be equipped with two transmit channels, which are used to independently adjust the signals transmitted into the two ports of the scanners' integrated quadrature body coil in order to produce more uniform RF fields, on a subject-to-subject basis. While this capability is primarily driven by the need for more uniform RF fields in body MRI, it may also provide some benefit in improving field uniformity in brain MRI [25]. Furthermore, multichannel transmit methods are currently being developed by several researchers to alleviate through-plane signal loss artifacts in the lower brain [26, 27].

3.4 Computing Resources

Functional MRI experiments generate large datasets. The raw data alone for a single subject, scanned for one hour, weighs in between 100 and 200 MB. Combine this with the space needed for image reconstructions and analysis, and one should budget a storage and scratch space of around 2 GB for every hour of scanning. In this section, we will provide some guidelines and suggestions on how to set up a computing environment to handle all this data. The two major factors influencing the design of your environment will be (1) money, and (2) the expertise available, in terms of computer systems and MRI data processing.

The data stream in a typical laboratory consists of four main stages. The first stage is the MRI scanner, which produces either raw, unreconstructed data, or reconstructed images that are ready for post-processing and analysis. If a lab has an MR physicist at its disposal, then the former case is often true, since an MR physicist may develop image reconstruction codes that provide improved image quality over vendor-provided software, and that can add in improved reconstruction techniques as they are developed. Assuming images have been reconstructed, the second stage consists of slice timing correction, realignment, coregistration, warping, and smoothing, which are all operations that prepare the dataset for statistical modeling and analysis. The third stage is statistical modeling and analysis. The fourth stage is data backup, though it is advisable to make backups of data at more than one point in the stream.

The majority of fMRI labs maintain one powerful workstation or computer cluster to do the bulk of their processing. Users can log into this computer from their own machines to initiate processing or view and download the preprocessed data for local analysis. The central advantage to this model is that the large and complicated software packages used to process fMRI need only be maintained on one machine, which greatly simplifies maintenance. A secondary advantage is that this model allows users greater flexibility in choosing the operating system of the computers they use; the

workstation can be running a Unix derivative, which has benefits in terms of networking, stability, and the availability of fMRI software packages, while the users can be using Windows PC's or Macintoshes, which are generally more user-friendly systems. All computers that will be involved in processing or storing data should be connected with the fastest network possible, such as a gigabit network.

The central processing workstation should have as much RAM as possible. By today's computing standards, each CPU should have at least 2 GB RAM available to it, so that it may store the entire dataset and related files. The reason for this is to minimize the frequency with which the computer accesses its hard disk processing, which costs large amounts of time. The second main consideration is the number of CPU's the computer should have. This will largely depend on the number of simultaneous processing streams one expects to have running on the computer. The third consideration is storage. The main computer should be connected to a large data storage device, so that all current experiments can be instantly accessed, without requiring reloading of backed-up data. This device should be a set of hard disks configured in a redundant manner, such as a RAID array.

One of the central computing dilemmas that an fMRI lab will continually deal with is making data backups. There are two main questions to answer here: (1) at what points in the processing stream should backups be made, and (2) what form should backups take? Backups of the initial MR data are absolutely necessary, since an experimenter may be asked to reproduce their results at a later date, or bugs may be found in the post-processing stream (stage two), which will require re-processing the original data. After this stage in the stream, the choice of where to do backups will depend on the amount of backup space available and the speed with which the second and third stages may be executed, should the analyzed data be lost. The more points at which backups are made, the more quickly an experimenter could recover after a data loss or processing interruption. A laboratory also has many options in choosing backup forms, and it may be best to use a combination of them. Perhaps the simplest backup form is mirroring the data, i.e., storing the data in another set of hard disks whose sole purpose is to store backed-up and archived data. This solution is particularly simple in that backups can be fully automated, and instantly accessed. The other two main options are tape storage and optical media (DVD). While automated machines may be purchased to manage tape backups, hard disk capacity is rapidly outstripping tape capacity, and the mechanical nature of these machines makes them prone to frequent failure. On the other hand, DVD backups are more reliable and cheap, but they require human interaction to load DVD's and execute burning software. A backup schedule will also have to be worked out by the laboratory.

Because computer components (i.e., disks, CPU's, and video cards) frequently fail or need replacement, it is advisable to set aside part of the lab's initial capital for yearly computer maintenance. It is also advisable to purchase extended warranties for the computers, as they will be heavily used and if they fail, this can save the lab a significant amount of money in the long run. Furthermore, as technology advances, the lab should build into their operational budget the cost for new machines every few years.

4 Stimulus Presentation and Behavioral Data Collection Devices

There is a small but increasing number of manufacturers of stimulus presentation hardware and software. We will not review specific products or vendors but limit ourselves to describe the important characteristics of these devices.

Some components of the stimulation and response recording equipment must go inside and/or near the magnet. These must not be susceptible to magnetic forces for obvious safety reasons. Additionally, the presence of metals in headphones and head mounted displays can generate field distortions that cannot be compensated by shimming, even if they are not ferromagnetic. This results in severe image degradation and it is thus important that the devices be thoroughly tested on phantoms for image degradation.

As we alluded to before, electronic equipment in the scanner room must be adequately shielded to avoid introducing RF noise into the system. For example, LCD displays for visual stimulation inside the magnet are typically encased in a fine wire mesh that acts as a Faraday cage to contain RF leakage. Other audiovisual electronic equipment used in the MR environment, such as projectors and button response units are typically encased in brass or aluminum for the same reasons. Regardless of the manufacturers' best intentions, sometimes the shielding is not adequate or becomes damaged over time in subtle ways. Just as in the case of the room's RF shielding, an exposed wire or bad shielding connections can produce severe RF contamination of the images. Thus, it is paramount that the stimulation devices be checked upon purchase and periodically for RF leaks that may develop during delivery, installation, or daily use.

There are different technologies commercially available for MR compatible visual stimulation. The simplest approach is perhaps an LCD projector outfitted with narrow focus lenses that project the images into a back projection screen placed inside the bore of the magnet. The subject then can see the display through a set of mirrors that are mounted on the head coil assembly. The main advantages of this approach are simplicity and lower cost. The disadvantages are related to positioning issues and a reduced visual field for the subject.

Another approach to MR compatible visual stimulation is fiber optic display visors. This sort of display system is based on an optical signal converter that carries an SVGA quality image through an array of micro optic fibers to a head mounted display inside the scanner's head coil. This approach is very attractive in that there are no electronic components that need to be installed inside the scanner room and the display can be placed very accurately in front of the subject's eyes, maximizing the available visual field. The drawbacks are that in addition to being expensive, the fiber optics used in the array are very fine and brittle, so that regardless of the high quality of fabrication, there will always be a small number of broken fibers that result in dead pixels or small streaks in the image.

One of the more popular approaches is to display the images on a shielded LCD screen mounted in front of the subject's head. This screen can be either a large one that is mounted outside the scanner's RF coil, or a small one in a visor that the subject wears inside the coil. The advantages of this are the large visual field and ease of use of the system. The drawbacks are the high cost and the interactions between the display electronics and the magnet. Some of these devices become dimmer when placed inside the magnetic field. Additionally, if any RF leaks develop, they severely degrade the images, especially in the visor type systems since they sit inside of the RF coil.

Auditory stimulation is typically performed in the MR environment through two different kinds of headphones: pressure waveguide types, and shielded piezoelectrics. Both of these are highly effective devices. The pressure waveguide headphones keep the speakers outside of the magnet's bore and the sound is carried through rigid tubing into the headphones. The piezoelectric headphones are akin to standard speaker technology but use piezoelectrics to produce the vibrations. They require RF shielding of the cables and the electronics to prevent artifacts. Perhaps the biggest challenge for auditory stimulation is reduction of the MRI scanner's noise. There is very limited space inside the scanner's head coil for building an effective muffler into the headphones but fairly effective noise reduction (typically around 30 dB) can be achieved. The headphones' acoustic insulation is sometimes achieved by gel padding that attenuates the sound very effectively by forming a tight seal around the ear. Caution must be used as the gel in the padding produces an MR signal and is visible in the images so it must be taken into consideration during registration and normalization of structural images. The gel's resonant frequency is typically not the same as water and produces some off-resonance artifacts, but these tend to be mild.

MR compatible microphones for patient communication and verbal response recording are typically based on piezoelectric technology and require both electronic and acoustic shielding to reduce the scanner sound. To our knowledge of the present state of the art,

the acoustic shielding of the microphone from the scanner sound is somewhat effective, but communication with the subject during the scan is still challenging. Some systems are equipped with active noise cancellation with limited success. Consequently, investigators often use pulse sequences with “quiet” (i.e., no gradient pulses) periods during the subject response time instead [28, 29].

Other response recording devices are primarily “button response units (BRU)” that are built into hand rests and strapped to the subject’s hands. They typically carry only DC currents through twisted pair cables and RF noise is not an issue as the electronics to drive the system are kept outside the scanner room. There are a number of other response units, such as MR compatible joysticks and keyboards that are manufactured by small companies. While these are typically safe and effective, one should test all such equipment immediately upon purchase not only for functionality but for RF leakage, and ferromagnetic forces. Periodic RF testing of peripherals should be an integral of the fMRI facility’s QA procedures.

5 Subject Monitoring

When running an fMRI experiment, it can be desirable to monitor and record subjects’ status and peripheral signals during an fMRI experiment, to use as correlates of subject behavior or as nuisance signals in data correction. Some possibilities include monitoring cardiorespiratory rhythms, galvanic skin response, head motion, or eye-tracking. As stressed in the previous sections, all these considerations should fit with the comfort and safety of the subject.

In general, when considering recording peripheral signals on fMRI subjects, one should pay attention to: synchronization with the MR scanner, adequate sampling of the signal in question, and avoiding introducing signal noise in both the MR data and the recorded peripheral signals.

5.1 Scanner Synchronization

In order to match the recorded external signals with the fMRI data being recorded, synchronization with the start of the scan must be achieved. This can be done using a TTL pulse to/from the scanner from/to the external device or recording media. For instance, a logic pulse from the MR scanner to the computer recording physiological noise can be set to trigger the recording sequence. Commercial MR scanners from the main vendors (GE, Siemens, Philips) all have the capability to send or receive TTL sync pulses.

5.2 Physiological Monitoring

A limit to the effectiveness of functional MRI in detecting activation is the presence of physiological noise, which can equal or exceed the desired signal changes in an fMRI experiment [30]. These physiological fluctuations that are present during an fMRI scan can obscure the BOLD activity that the researcher is trying to

detect. In addition, monitoring physiological rates can help as secondary reaction measures (such as monitoring the cardiac rate variability during a stress experiment).

5.3 Cardiac Monitoring

Monitoring the cardiac waveform can be achieved in several ways. The most common solutions are pulse oximeters or ECG patches. The primary cardiac harmonic frequency lies in the 0.5–2.0 Hz range, with both the first and secondary harmonics shown to affect the fMRI signal [31].

Pulse oximetry refers to indirectly monitoring the oxygen levels in the extremities to monitor the cardiac waveform. This is most often accomplished in fMRI labs by using an LED and photodiode that clips to the subject's finger, connected to a data acquisition board (see Fig. 17). Several MR scanner vendors offer this as part of the MR system (GE, Siemens), and stand-alone monitoring units from commercial vendors are also available (Invivo, Biopac). Normal setup with compliant subjects allows adequate sampling of cardiac rhythm, as seen in Fig. 18. Drawbacks include the fact that



Fig. 17 Pulse oximeter for indirect measure of cardiac waveform

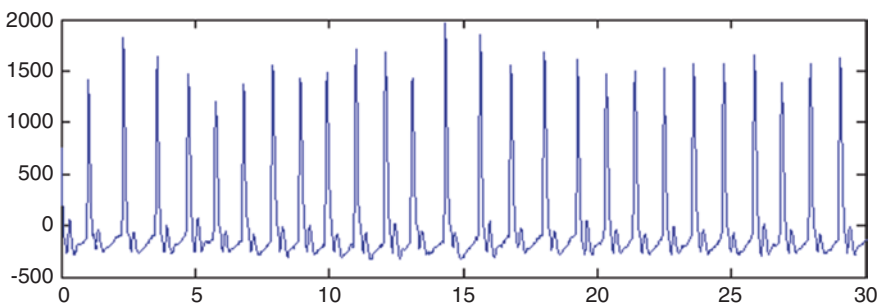


Fig. 18 Cardiac waveform acquired during an fMRI scan. (Data acquired on a 3.0 T GE scanner, using a pulse oximeter with a sampling rate of 40 Hz)

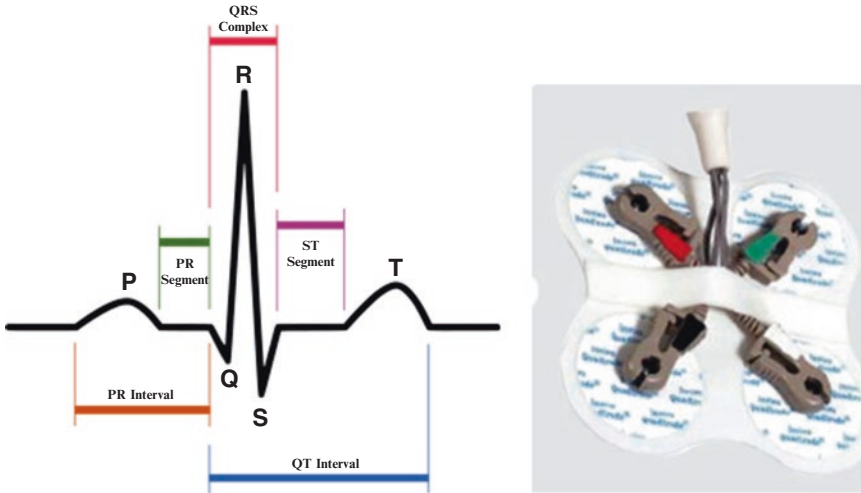


Fig. 19 Example of ECG patch (Courtesy of Invivo, www.invivocorp.com). With a schematic of a typical QRS waveform

subject motion may corrupt the signal, and motor tasks may be impeded with the oximeter placed on the finger (alternative placement on the ear or toe is possible).

ECG patches located over the heart allow high-fidelity monitoring of cardiac electrical activity. This allows identification of features beyond the simple cardiac peaks, such as the QRS complex during the depolarization of the ventricles (Fig. 19). Disadvantages of ECG recording include increased setup complexity, and patient comfort.

5.4 Respiratory Monitoring

The respiratory rhythm has a normal frequency range of 0.1–0.5 Hz. Motion of the chest during respiration combined with the changes in oxygen saturation in the lungs lead to a modulation of the local magnetic field that can affect the phase of the MR signal at the position of the head during scanning (Fig. 20), which can lead to modulation of the recorded MR signal intensity. Mitigation of respiratory effects on the MR signal can include scanning during breath-holds, modified pulse sequences to sample and account for the modulation in magnetic field [32] and recording of the respiratory signal to use as nuisance covariates in post-processing analysis [33].

Monitoring respiratory rhythm can be accomplished by using a plethysmograph (pressure belt) around the waist of a subject, like the one shown in Fig. 21, or by using a nasal cannula to monitor expired CO₂ concentration. A sample respiratory waveform is shown in Fig. 22.

5.5 Galvanic Skin Response (GSR)

Galvanic skin response (GSR) is a measure of the electrical resistance of the skin, a physical property that has been shown to increase in response to subject arousal, mental effort, or stress. It is monitored



Fig. 20 Phase difference between inspiration and expiration for a coronal slice



Fig. 21 Plethysmograph belt for measuring respiration

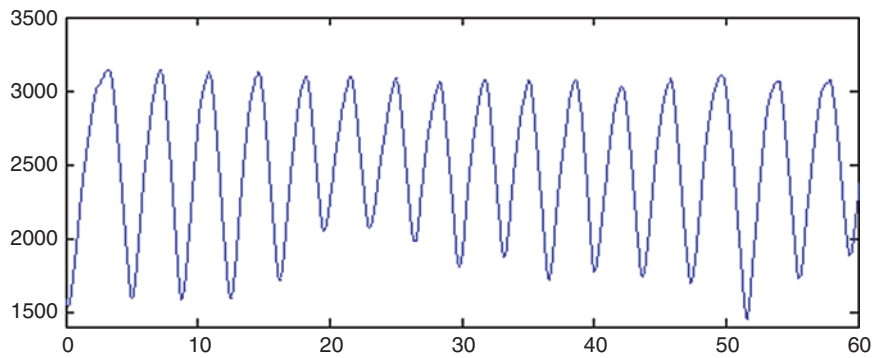


Fig. 22 Respiratory waveform acquired during an fMRI scan. (Data acquired on a 3.0 T GE scanner, using a pulse oximeter with a sampling rate of 40 Hz)

by measuring a voltage drop across the skin using paired electrodes. This can have the same motion sensitivity and motor task complication as the pulse oximeter if the electrodes are placed on the fingers. These problems are usually reduced by placing the electrodes between the second and third knuckles, instead of on the fingertip.

5.6 Head Motion Tracking

Severe head motion during an fMRI scan can severely corrupt the data. Besides minimizing patient motion using cushioning and restraints, a measure of head motion may also be collected to help correct data in post-processing. This may be done using modified pulse sequences (PACE), or by using external motion tracking [33–35]. Again, patient comfort and visual path should be taken into consideration.

5.7 Eye Tracking

Patient gaze and fixation time is important for several types of fMRI paradigms and pathological types. In addition, eye motion can be a source of variance in fMRI scans [36]. Thus, tracking eye position can be desirable. The common method is to monitor the position of infrared (IR) light that is reflected off the eye of the subject. This involves transmitting IR light to the subject's eye, and then recording it, using MR-compatible equipment. Several vendors provide hardware solutions including both long-range and short-range cameras. These systems typically have on the order of $0.1\text{--}1^\circ$ spatial resolution and accuracy, with working ranges of $10\text{--}25^\circ$ horizontally and vertically, and 60–120 Hz sampling rate.

In acquiring a physical eye-tracking system for an fMRI lab, consideration should be given to the optical path for the eye-tracking system, taking into account the MR bore, head coil, and visual stimulus presentation system; signal integrity of the MR data; ease of setup for the MR techs and scanners. This will also involve peripheral equipment located in the scanner room or control room: usually a camera, power supply, video monitor for real-time display of the subject's eye, and a PC.

6 Multimodal fMRI

Acquiring other neurophysiological measures with fMRI data can complement the excellent spatial resolution and depth penetration of fMRI with modalities that have superior temporal resolution and different sensitivities to the underlying neuronal activity. In the following sections, we will expand upon complementary modalities that allow investigations of response (e.g., EEG, fNIRS) and stimulation (e.g., TDCS, TMS).

6.1 fMRI-EEG

The simultaneous acquisition of electroencephalography (EEG) data with fMRI data allows the higher temporal sampling rate of EEG (~ 5000 Hz) to be combined with the superior resolution (\sim mm) and depth penetration of fMRI.

Several factors must be accounted for when setting up a simultaneous EEG/fMRI acquisition, chief among them safety and signal quality. In the following, we will try to touch on most of the considerations one will make when selecting and setting up EEG-fMRI hardware.

Several companies have MR-compatible EEG hardware commercially available (Brain Products, Neuroscan, EGI). A common EEG setup includes an electrode cap, connected to a signal amplifier and recording device. Any part of this setup that is inside the MR scanner room within the 5 G line must be nonferrous, and the amount of metal must be kept to a minimum, with care exercised around all metallic components (this includes electrode leads on the cap and skin, batteries in amplifiers, etc.). Fiber optics can be used for signal transmission after amplification, with recording devices located in the scanner control room.

Much planning is required to integrate the EEG with the MR. The head coil used for MR acquisition may affect the physical setup. For instance, an open birdcage coil may allow placement of the EEG cap cord and amplifier above the head of the subject, with no obstruction of the subject's field of view. With an alternative phased-array coil that is closed at one end, this setup may not be possible.

Also, for time synchronization, it may be necessary to use the TTL pulse from the scanner (mentioned in Sect. 5.1) to trigger the EEG recording device at each TR.

Finally, for fusion of the fMRI and EEG data, accurate electrode locations on the head should be recorded and transferred to the structural MR images to be used as references for localization. Commercial head position recording systems are available (Brainsight). These systems can record points on the subject's head using infrared positional markers, and coregister these coordinates with the structural MR scans of the subject. Subsequent coregistration of the fMRI and structural MR data allows direct overlay and source localization using both between the MR, fMRI, and EEG data.

The EEG equipment should not adversely affect the MR data, if proper materials and shielding are used. Images with and without the EEG equipment should be inspected for any introduction of AC line noise (~60 Hz) or localized variance in the structural and fMRI images.

The MR equipment will affect the EEG recording, due to the high-field environment, and the application of gradients during the MR acquisition (Fig. 23). However, the MR gradient artifact can be corrected for in post-processing, using either available software (EEGLAB, <http://www.sccn.ucsd.edu/eeqlab/>) or adapting techniques such as PCA or ICA.

6.2 Functional Near-Infrared Spectroscopy (fNIRS)

Functional MRI allows investigation of the hemodynamic response to neural activity, thus allowing localization of brain regions involved in a cognitive task. However, fMRI is not a naturalistic setting.

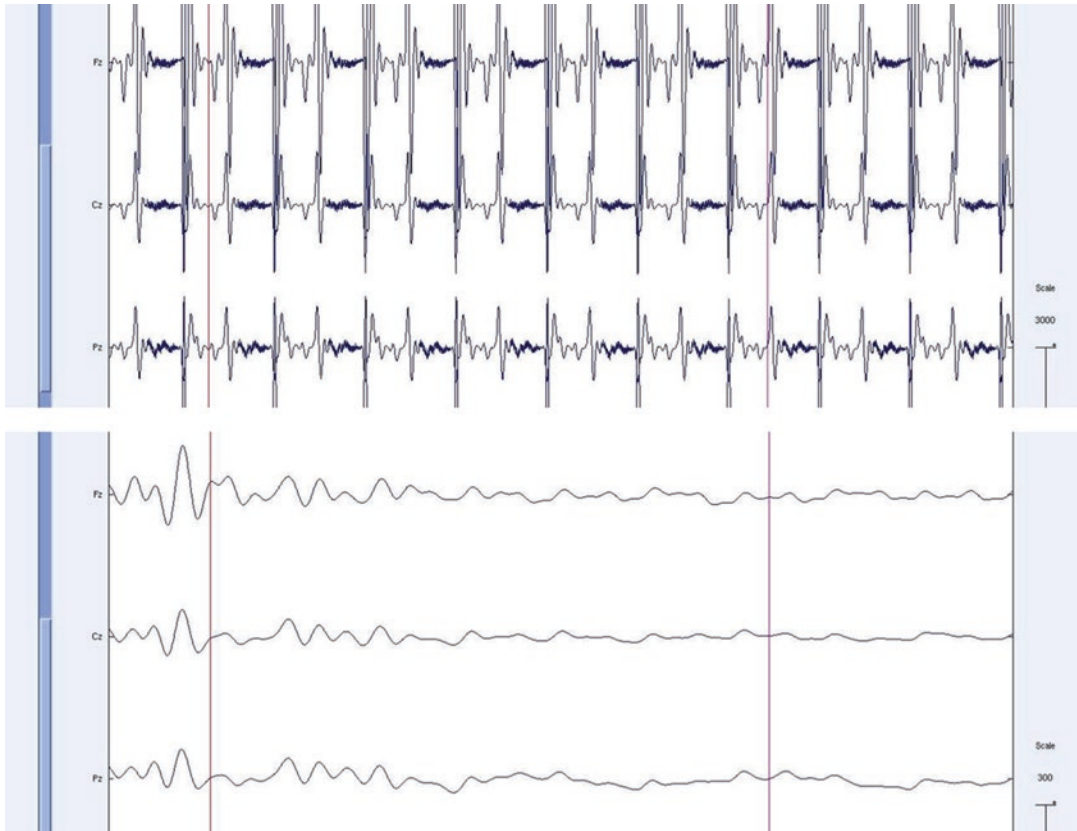


Fig. 23 EEG recorded during fMRI acquisition, before (*top*) and after (*bottom*) MR artifact correction

Functional near-infrared spectroscopy (fNIRS) offers a possible solution for portable neuroimaging in the field. It offers subsecond temporal sampling, with spatial resolution on the order of centimeters. For multimodal work with fMRI, it is attractive as it samples the same hemodynamic changes as BOLD fMRI imaging, namely the change in relative levels of oxygenated and deoxygenated blood, using the differential absorption of infrared laser light. An image of a commercially available fNIRS system can be seen in Fig. 24.

Generally, fNIRS operates by using infrared light source and detector pairs. While the light used is in the infrared range, and thus the majority of the setup may be thought of as fiber-optic and largely MR compatible, the internal construction of the probes may contain non-MR compatible materials (such as metal coatings in reflectors). Careful consideration must thus be used for a fNIRS-fMRI combined experiment. Several vendors offer MR-compatible probes (EGI, Imagent), or custom setups can be constructed in-house [37]. In terms of induced noise, attention must be paid to induced MR artifacts due to probe construction. However, due to



Fig. 24 Example MRI compatible fNIRS setup (Cortech Solutions, www.cortech-solutions.com/Products/NI/NI-OM), showing light guides, example subject setup configuration, and receiving equipment

the optical nature of the fNIRS signal, it is not affected by the MR environment, offering one advantage over EEG-fMRI acquisition.

6.3 Brain Stimulation and fMRI

A fundamental strategy used in cognitive neuroscience is to stimulate the brain in some way and then observe how it responds. Functional MRI provides such observations of the brain's responses. While most studies use sensory (audio, visual, tactile ... etc.) cues and cognitive tasks as a form of stimulation, one can also stimulate human brains directly and noninvasively inside an MR scanner.

One such technique is transcranial magnetic stimulation (TMS), which has great potential not only as research tool but also as a therapeutic device [38–40]. The principle behind TMS is that a large current waveform is driven through a coil placed adjacent to the tissue of interest. The current in turn induces an electromagnetic field depending on the rate of change of the current, as predicted by classical electrodynamics. The induced electric field penetrates the tissue and induces eddy currents on conductors, such as nerve fibers. When a nerve fiber is aligned with the direction of the electric field, a large current is induced in the axon which causes its membrane to depolarize, effectively causing the transmission of an action potential [41–43]. After depolarization of the axonal membrane, the sodium–potassium pumps rebuild the membrane potential and the nerve fibers return to their original state within seconds.

The effects of these induced discharges are complex, depending upon the magnitude and timing of the TMS pulse affecting inhibitory and/or excitatory neuronal populations (for recent reviews, see [44–46]). If a single TMS pulse is applied in the hand

region of the motor cortex, for example, motor neurons depolarize and the hand will twitch ('motor evoked potential', or MEP). Subthreshold stimulation, followed by supra-threshold stimulation, can inhibit or facilitate the MEP, which varies with the distance and location of the subthreshold stimulus [47].

By selectively applying a TMS pulse during the performance of a task, neural circuits are effectively jammed, and performance interruptions can be observed. In effect, one creates a controlled, completely reversible "lesion," enabling the study of brain function through perturbation of neuronal activity [44, 48]. Although these studies have rapidly become a popular investigative tool for cognitive neuroscientists, one important limitation stems from inadequate knowledge about the shape and magnitude of the induced current fields that introduce the perturbation. Hence, TMS and fMRI can be complementary for the study of brain function. TMS can interfere, or modulate the cognitive process under scrutiny by locally altering the responsiveness of the tissue, while fMRI can allow the investigators to precisely map out these effects. While TMS and fMRI experimental data can be coregistered and integrated after each experiment has been carried out separately [49], it is desirable to be able to observe the BOLD responses to TMS.

However, there are some clear challenges to carrying out joint TMS and fMRI experiments. Such experiments require TMS coils that contain no ferromagnetic parts and extra long cabling so that the amplifier/capacitor bank can be kept outside of the 5 G line. Specialized holders must be constructed to hold the TMS coil in the appropriate position during the duration of the scanning session (Fig. 25). Like all electronic equipment, the TMS hardware

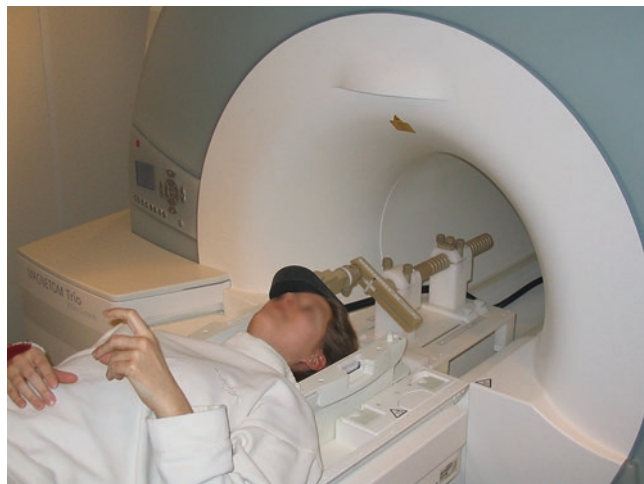


Fig. 25 MRI compatible TMS coil and holder apparatus (image courtesy of Dr. A. Thielscher of the Max Plank Institute for Biological Cybernetics <http://www.kyb.mpg.de/>)

must be shielded in a faraday cage to prevent RF contamination of the MRI signal [50]. Commercial TMS coils currently have these characteristics as optional features.

Another important aspect is the synchronization of TMS pulses and image acquisition. It is very important that the scanner's RF receiver chain be switched off while the stimulator is pulsing in order to protect it from the large signals that may severely damage it. At the same time the scanner's pulses may induce currents in the TMS hardware (although these are reportedly not harmful to the hardware). Isolation between the two is achieved by synchronizing the TMS pulses with the MRI scanner via TTL pulses. The imaging pulse sequence is typically designed with long gaps for the TMS pulses. These gaps include about 0.1 s to allow TMS induced eddy currents inside the bore to decay. There is also the challenge of the large torques that a large, sudden dipole exerts when in the presence of a large magnetic field. However, in the case of figure-eight coils, those torques cancel since the two "wings" of the coil are torqued in opposite directions. Furthermore, rapid bi-phasic pulses also cancel those torques and the subject does not perceive any such effects. The coil, however, experiences internal stresses from the magnetic forces [50–52].

Recently, transcranial direct current stimulation (TDCS) has been adopted by neuroscientists as a method to manipulate the excitability of neurons [53–56]. The technique is very simple and can be easily combined with functional MRI with minor safety concerns. In a nutshell, TDCS works by running a small direct current (1–2 mA) from an anode to a cathode placed across brain. While the mechanism is not entirely understood, the neurons beneath the anode experience enhanced excitability because of a shift in the transmembrane potential, and the opposite is true at the cathode [57]. At the time of writing, TDCS and its mechanism are a very exciting and active area of research. Indeed it is often combined with BOLD and ASL fMRI to study its effects [58, 59].

The main issues that must be addressed when conducting TDCS-fMRI experiments are the heating of the electrodes and wires by currents induced by the scanner's oscillating magnetic fields (RF and gradients). A solution to this problem is to increase the impedance of the electrodes and wires by placing resistors (>5 kOhm) in line. One must also be careful of the presence of the ancillary equipment, such as the power supply to the TDCS device, in the magnet room. In general it is good to keep that part outside the scanner room and feed the cabling through a penetration panel. In that case, the wires are likely to act as an antenna and bring in RF noise from outside the magnet room, which is detrimental for image quality. A solution to this problem is to also place a low-pass filter in line (between the power supply and the electrodes) to eliminate the RF noise in the system. One example of this approach can be seen in [58], where the investigators placed a

5.6 kOhm resistor on MR compatible rubber electrodes, and filters in line with the power supply that were rated to attenuate 60 dB between 20 and 200 MHz.

7 Conclusions

The hardware used in magnetic resonance imaging is quite extensive and we hope to have provided an adequate overview of the subsystems involved in the generation of MRI images. Functional MRI requires additional hardware for collection of behavioral data and stimulation of the subject while collecting the functional images. The greatest challenge is perhaps to coordinate all these devices while being mindful of the interactions between the devices and the MRI scanner. Failure to do so often results in severe artifacts in the desired measurements, or worse, the subject could be severely injured. In this chapter we have also explored the hardware requirements for multimodal imaging, such as EEG-fMRI or TMS-fMRI.

References

1. Shellock FG (2002) Reference manual for magnetic resonance safety, implants, and devices. Saunders, Oxford, UK
2. Shellock FG, Cruess JV 3rd (2002) MR safety and the American College of Radiology white paper. *AJR Am J Roentgenol* 178:1349–1352
3. Train JJ (2003) Magnetic resonance compatible equipment. *Anaesthesia* 58:387, Author reply 387
4. Durand E, van de Moortele PF, Pachot-Clouard M, Le Bihan D (2001) Artifact due to B0 fluctuations in fMRI: correction using the k-space central line. *Magn Reson Med* 46:198–201
5. Tinkham M (2004) Introduction to superconductivity, 2nd edn, Dover Books on Physics. Dover Publications, Mineola, NY
6. Radebaugh R (2009) Cryocoolers: the state of the art and recent developments. *J Phys Condens Matter* 21:164219
7. Williams DS, Detre JA, Leigh JS, Koretsky AP (1992) Magnetic resonance imaging of perfusion using spin inversion of arterial water. *Proc Natl Acad Sci U S A* 89:212–216
8. Yang QX, Wang J, Zhang X et al (2002) Analysis of wave behavior in lossy dielectric samples at high field. *Magn Reson Med* 47:982–989
9. Collins CM, Liu W, Schreiber W, Yang QX, Smith MB (2005) Central brightening due to constructive interference with, without, and despite dielectric resonance. *J Magn Reson Imaging* 21:192–196
10. Tropp J (2004) Image brightening in samples of high dielectric constant. *J Magn Reson* 167:12–24
11. Schneider E, Glover G (1991) Rapid in vivo proton shimming. *Magn Reson Med* 18:335–347
12. Dylan Tisdall M, Witzel T, Tountcheva V, McNab JA, Adad JC, Kimmlingen R, Hoeft P, Eberlein E, Heberlein K, Schmitt F, Thein H, Wedeen Van J, Rosen BR, Wald LL (2012) Improving SNR in high b-value diffusion imaging using $G_{max}=300$ mT/m human gradients, *Proc ISMRM* 2012
13. Gach HM, Lowe IJ, Madio DP et al (1998) A programmable pre-emphasis system. *Magn Reson Med* 40:427–431
14. Wysong RE, Madio DP, Lowe IJ (1994) A novel eddy current compensation scheme for pulsed gradient systems. *Magn Reson Med* 31:572–575
15. Mansfield P, Chapman B (1986) Active magnetic screening of coils for static and time-dependent magnetic field generation in NMR imaging. *J Phys E Sci Instrum* 19:540–545
16. Edelstein WA, Kidane TK, Taracila V et al (2005) Active-passive gradient shielding for MRI acoustic noise reduction. *Magn Reson Med* 53:1013–1017
17. Pruessmann KP et al (1999) SENSE: sensitivity encoding for fast MRI. *Magn Reson Med* 42(5):952–962

18. Blaimer M, Breuer F, Mueller M et al (2004) SMASH, SENSE, PILS, GRAPPA: how to choose the optimal method. *Top Magn Reson Imaging* 15:223–236
19. Hoult DI, Chen CN, Sank VJ (1984) Quadrature detection in the laboratory frame. *Magn Reson Med* 1:339–353
20. Roemer PB, Edelstein WA, Hayes CE, Souza SP, Mueller OM (1990) The NMR phased array. *Magn Reson Med* 16:192–225
21. Griswold MA et al (2002) Generalized auto-calibrating partially parallel acquisitions (GRAPPA). *Magn Reson Med* 47:1202–1210
22. Larkman D, Hajnal J, Herlihy A, Coutts G, Young I, Ehnholm G (2001) Use of multicoil arrays for separation of signal from multiple slices simultaneously excited. *J Magn Reson Imaging* 13(2):313–317
23. Setsompop K, Gagoski BA, Polimeni JR, Witzel T, Wedeen VJ, Wald LL (2012) Blipped-controlled aliasing in parallel imaging for simultaneous multislice echo planar imaging with reduced g-factor penalty. *Magn Reson Med* 67:1210–1224
24. Feinberg D, Moeller S, Smith S, Auerbach E, Ramanna S, Glasser M, Miller K, Ugurbil K, Yacoub E (2010) Multiplexed echo planar imaging for sub-second whole brain fmri and fast diffusion imaging. *PLoS One* 5(12), e15710
25. Zhang Z, Yip CY, Grissom W, Noll DC, Boada FE, Stenger VA (2007) Reduction of transmitter B1 inhomogeneity with transmit SENSE slice-select pulses. *Magn Reson Med* 57(5):842–847
26. Stenger VA, Boada FE, Noll DC (2000) Three-dimensional tailored RF pulses for the reduction of susceptibility artifacts in T2*-weighted functional MRI. *Magn Reson Med* 44(4):525–531
27. Yip CY, Fessler JA, Noll DC (2006) Advanced three-dimensional tailored RF pulse for signal recovery in T2*-weighted functional magnetic resonance imaging. *Magn Reson Med* 56(5):1050–1059
28. Jakob PM et al (1998) Functional burst imaging. *Magn Reson Med* 40:614–621
29. Edmister WB, Talavage TM, Ledden PJ, Weisskoff RM (1999) Improved auditory cortex imaging using clustered volume acquisitions. *Hum Brain Mapp* 7:89–97
30. Noll DC, Schneider W (1994) Theory, simulation, and compensation of physiological motion artifacts in functional MRI. Image processing, 1994. Proceedings ICIP-94. IEEE Int Conf 3:40–44
31. Hu X, Le TH, Parrish T, Erhard P (1995) Retrospective estimation and correction of physiological fluctuation in functional MRI. *Magn Reson Med* 34:201–212
32. Pfeuffer J, Van de Moortele PF, Ugurbil K, Hu X, Glover GH (2002) Correction of physiologically induced global off-resonance effects in dynamic echo-planar and spiral functional imaging. *Magn Reson Med* 47:344–353
33. Tremblay M, Tam F, Graham SJ (2005) Retrospective coregistration of functional magnetic resonance imaging data using external monitoring. *Magn Reson Med* 53:141–149
34. Zaitsev M, Dold C, Sakas G, Hennig J, Speck O (2006) Magnetic resonance imaging of freely moving objects: prospective real-time motion correction using an external optical motion tracking system. *Neuroimage* 31:1038–1050
35. Thesen S, Heid O, Mueller E, Schad LR (2000) Prospective acquisition correction for head motion with image-based tracking for real-time fMRI. *Magn Reson Med* 44:457–465
36. Chen W, Zhu XH (1997) Suppression of physiological eye movement artifacts in functional MRI using slab presaturation. *Magn Reson Med* 38:546–550
37. Harrivel AR et al (2009) Toward improved headgear for monitoring with functional near infrared spectroscopy. *NeuroImage* 47:S141
38. Barker AT (1991) An introduction to the basic principles of magnetic nerve stimulation. *J Clin Neurophysiol* 8:26–37
39. Barker AT (1999) The history and basic principles of magnetic nerve stimulation. *Electroencephalogr Clin Neurophysiol Suppl* 51:3–21
40. Jalinous R (1991) Technical and practical aspects of magnetic nerve stimulation. *J Clin Neurophysiol* 8:10–25
41. Ruohonen J, Ravazzani P, Tognola G, Grandori F (1997) Modeling peripheral nerve stimulation using magnetic fields. *J Peripher Nerv Syst* 2:17–29
42. Ilmoniemi RJ et al (1997) Neuronal responses to magnetic stimulation reveal cortical reactivity and connectivity. *Neuroreport* 8:3537–3540
43. Berne RM, Levy MN (1993) Physiology, Mosby year book. Mosby, St. Louis
44. George MS et al (2003) Transcranial magnetic stimulation. *Neurosurg Clin N Am* 14:283–301
45. Paus T (2005) Inferring causality in brain images: a perturbation approach. *Philos Trans R Soc Lond B Biol Sci* 360:1109–1114
46. Pascual-Leone A, Walsh V, Rothwell J (2000) Transcranial magnetic stimulation in cognitive neuroscience—virtual lesion, chronometry, and functional connectivity. *Curr Opin Neurobiol* 10:232–237

47. Rothwell JC (1999) Paired-pulse investigations of short-latency intracortical facilitation using TMS in humans. *Electroencephalogr Clin Neurophysiol Suppl* 51:113–119
48. Ilmoniemi RJ, Ruohonen J, Karhu J (1999) Transcranial magnetic stimulation—a new tool for functional imaging of the brain. *Crit Rev Biomed Eng* 27:241–284
49. Bastings EP et al (1998) Co-registration of cortical magnetic stimulation and functional magnetic resonance imaging. *Neuroreport* 9:1941–1946
50. Bohning DE et al (1998) Echoplanar BOLD fMRI of brain activation induced by concurrent transcranial magnetic stimulation. *Invest Radiol* 33:336–340
51. Bohning DE et al (1999) A combined TMS/fMRI study of intensity-dependent TMS over motor cortex. *Biol Psychiatry* 45:385–394
52. Bohning DE et al (2000) BOLD-fMRI response to single-pulse transcranial magnetic stimulation (TMS). *J Magn Reson Imaging* 11:569–574
53. Nitsche MA, Paulus W (2000) Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *J Physiol* 527(Pt 3):633–639
54. Fregni F, Boggio PS, Nitsche M, Bermpohl F, Antal A, Feredoes E, Marcolin MA, Rigonatti SP, Silva MT, Paulus W, Pascual-Leone A (2005) Anodal transcranial direct current stimulation of prefrontal cortex enhances working memory. *Exp Brain Res* 166(1):23–30
55. Dieckhöfer A, Waberski TD, Nitsche M, Paulus W, Buchner H, Gobbelé R (2006) Transcranial direct current stimulation applied over the somatosensory cortex – differential effect on low and high frequency SEPs. *Clin Neurophysiol* 117(10):2221–2227
56. Wagner T, Valero-Cabre A, Pascual-Leone A (2007) Noninvasive human brain stimulation. *Annu Rev Biomed Eng* 9:527–565
57. Radman T, Ramos RL, Brumberg JC, Bikson M (2009) Role of cortical cell type and morphology in subthreshold and suprathreshold uniform electric field stimulation in vitro. *Brain Stimul* 2:215–228
58. Antal A et al (2011) Transcranial direct current stimulation over the primary motor cortex during fMRI. *Neuroimage* 55(2):590–596
59. Weber MJ et al (2014) Prefrontal transcranial direct current stimulation alters activation and connectivity in cortical and subcortical reward systems: A tDCS-fMRI study. *Hum Brain Mapp* 35(8):3673–3686



<http://www.springer.com/978-1-4939-5609-8>

fMRI Techniques and Protocols

Filippi, M. (Ed.)

2016, XIII, 911 p. 248 illus., 112 illus. in color.,

Hardcover

ISBN: 978-1-4939-5609-8

A product of Humana Press