Pushing the Limits of Accuracy in MRI – A Perspective

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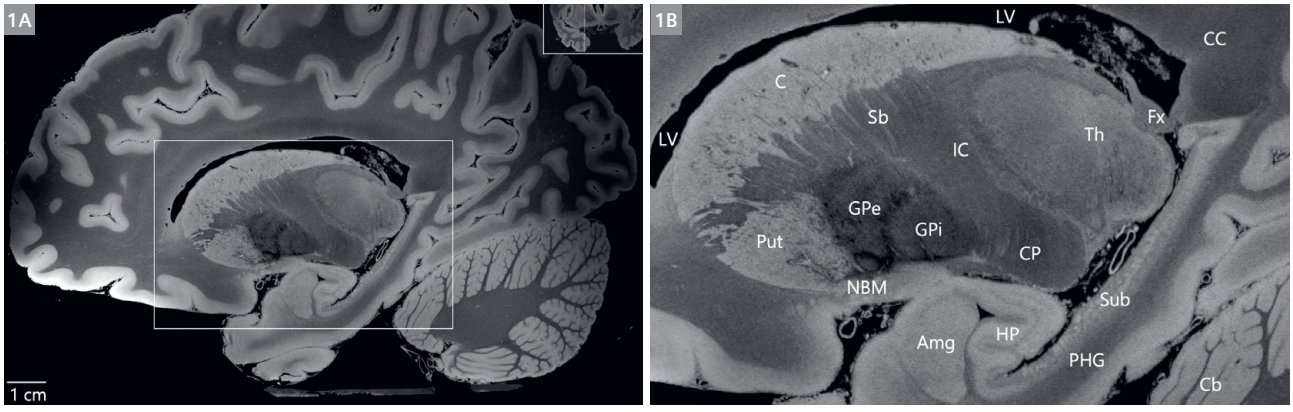
Introduction

I am pretty sure that magnetic fields were never intended to be perfectly homogeneous or to vary precisely linearly in space at exactly a certain moment in time. At the very least, it is probably plausible to say that it was not what James Clerk Maxwell was thinking when he formulated his famous equations. Yet in 2021, magnetic resonance imaging (MRI) is used to do just about everything in healthcare, including guiding the placement of an electrode deep into the interior of the human brain at better than 1 mm accuracy to help patients with epilepsy, or producing exquisite anatomical information at 100 micron isotropic resolution (Fig 1).

MRI is based on magnetic fields throughout the entire measurement and imaging process, starting with a static external magnetic field that magnetizes the hydrogen nuclei in the body and ending with producing an image from that magnetization. The accuracy of those fields therefore ultimately determines the precision of the image outcome. The position of a voxel in a digital image representation of the anatomy is based on the singular assumption that the magnetic fields are precisely known everywhere in space and time. Deviation from this and there will be a proportional inaccuracy associated with the position of that voxel.



1 100 micron thick sagittal slice through an ex-vivo human brain acquired with the MAGNETOM 7T Classic showing delineation of basal ganglia, diencephalon, and medial temporal neuroanatomy at 100 micron resolution **(1A)**. A zoomed view of the striatum, amygdala (Amg), and hippocampus (HP) (within the white rectangle in 1A) is shown in **(1B)**.
Neuroanatomic abbreviations: C = caudate; Cb =cerebellum; CC = corpus callosum; CP = cerebral peduncle; Fx = fornix; GPe = globus pallidus externa; GPi = globus pallidus interna; IC = internal capsule; LV = lateral ventricle; NBM = nucleus basalis of Neynert; PHG = parahippocampal gyrus; Put = putamen; Sb = striatal bridges; Sub = subicular cortices; Th = thalamus.
With permission: Brian L Edlow, MD, Massachusetts General Hospital. BL Edlow, A Mareyam, A Horn, et al., 7 Tesla MRI of the ex vivo human brain at 100 micron resolution. Sci Data 6, 244 (2019). https://doi.org/10.1038/s41597-019-0254-8.

There are many applications now that rely on the informational accuracy of MRI, whether it be with its signal amplitude, phase, or position in space. Nowhere is this more evident than when using MRI for stereotactic planning, where spatial accuracy is paramount. High resolution isotropic 3D MR imaging has become the modality of choice for radiation treatment planning or surgical implantation procedures. Inaccuracies in the spatial position of the anatomy with respect to external fiducial markers can lead to potentially catastrophic outcomes. Spatial precision is also a requirement for personalized prosthetic modeling, where localized errors in position can cause painful misalignment for the recipient. Tissue morphometry and segmentation are being used more and more for medical and therapeutic evaluation that relies heavily on the volumetric precision not only in a given dataset but also longitudinally over time.

But spatial accuracy is not the only thing that relies on magnetic fields. In recent years, MRI is becoming more quantitative where accuracy in its signal amplitude and phase are necessary as well. Flow quantification in vascular and cardiac applications relies heavily on the precision of the signal phase, as does high-intensity focused ultrasound (HIFU) and other therapeutic procedures that use the phase information for MR thermometry to monitor tissue response. MR elastography requires the phase information to measure tissue stiffness in liver disease. Applications that demand accuracy and reproducibility in the signal amplitude also exist. Quantitative biomarkers such as the Apparent Diffusion Coefficient (ADC) in diffusion-weighted MRI rely on the signal amplitude decay associated with diffusion sensitization of water motion to probe tissues on a microscopic scale. And, fMRI requires extreme temporal stability of the signal magnitude to detect the statistical significance of the blood oxygen level dependence (BOLD) response in brain activity.

In the early days of MRI, we pretty much focused on just trying to maximize the signal-to-noise ratio (SNR) and simply hoped that after a 15-minute acquisition the scan would yield a reasonable facsimile of the human anatomy, whether it be of the brain, a knee, or the liver. But in this age of precision medicine, MRI is becoming much more quantitative, requiring equally greater accuracy. Just getting an image is no longer a reasonable expectation. MRI is now expected to be perfect in every way. Let us take a brief look into just how perfect, or not-so-perfect, it is.

Signal encoding

MRI of course begins with an external static B_0 magnetic field to create the initial magnetization. The MR signal that eventually is generated will possess characteristics of amplitude, phase, and frequency. Essentially, all three of these features are based on magnetic fields as described by the Larmor equation. For them to be accurate, this means that the magnetic fields that they are based on must also be accurate. Note that there are three magnetic fields that we deal with in MRI: B_0, B_1^+, and B_1^-. B_1^+ and B_1^- are the transmission and reception fields, respectively, and are perpendicular to the B_0 field in order to rotate the magnetization and detect it. Although the B_1 fields are clearly important and deserving of discussions about their accuracy, it is the B_0 field that is the focus here since it is ultimately what encodes the MR signal that gets detected and generates the image. Therefore, for the remainder of this paper only the B_0 magnetic fields will be discussed.

The MR experiment can be viewed as having four basic time-sequential elements – preparation, excitation, encoding, and readout. During preparation, the initial state of the magnetization for the experiment becomes defined. This may be an inversion preparation that might be applied for a specific type of tissue contrast, or it might be a type of saturation to suppress the magnetization from a specific tissue such as fat. In this stage, the accuracy of the B_0 field could be argued as playing a lesser role, primarily associated with the spatial uniformity of the outcome.

After the initial preparation, excitation is then carried out to rotate the magnetization out of the B_0 direction to create a transverse component which eventually becomes detected. This process relies on the resonance condition between RF transmission and magnetization, whereby their frequencies must be matched to produce the action of excitation and the rotation of the magnetization. By applying a spatially varying gradient field (G) during excitation one can then selectively excite a specific region in space. Here, the total magnetic field, $B_{0,tot}$ (comprised of the summation of the main magnetic field, B_0, and the gradient field, G) plays a significant role, since a one-to-one relationship will exist between the excitation of a physical location in space that matches the resonance condition according to the Larmor equation. Transmission at a specified frequency and bandwidth will produce excitation anywhere in physical space with a given slice thickness where it matches the Larmor frequency of the magnetization. For this to be accurate requires precision of $B_{0,tot}$ and therefore the main magnetic field, B_0, and the gradient field, G.

The encoding process is facilitated by applying G magnetic fields that spatially vary the B_0 magnetic field in a well-behaving manner so that signal can be mapped uniquely to different points in physical space. Gradient pulses of a given direction, amplitude, and duration encode the signal in *k*-space, the Fourier counterpart of image space, with the coordinates of k_x, k_y, and k_z. The action of the encoding process is to define the starting point coordinates in *k*-space for the readout process to follow, and the value of *k* will be based on the time

integration of the gradient pulsing. That said, the accuracy of the *k*-space encoding will therefore be defined by the accuracy of the gradient pulsing. In addition, however, since the transverse magnetization experiences the *total* magnetic field $B_{0,tot}$, the uniformity of the main magnetic field B_0 also plays an important role in the accuracy.

The final step of the MR experiment is the signal readout when the magnetization is detected and digitally sampled. *k*-space gets sampled according to the gradient pulsing that is applied simultaneously during the detection process. The *k*-space trajectory in readout will be based on the direction, amplitude, and duration of the gradient pulsing. Therefore, the trajectory will be determined by the precision of the gradient pulsing. And, as with the encoding process, the transverse magnetization experiences $B_{0,tot}$, so the readout accuracy will also depend on the uniformity of B_0 as well.

Historical progression

The spatial accuracy and temporal stability of the main static B_0 magnetic field and the pulsed G gradient magnetic fields has gone through different progression through the years. Early magnets were very large and heavy, and their spatial uniformity, or homogeneity, was in general quite poor. As the engineering design and manufacturing improved, magnet homogeneity also improved. However, other factors did not necessarily always allow continual improvement in the homogeneity. For example, a demand existed for wider and shorter bore designs to increase patient comfort, and siting requirements became more challenging for installing magnets in much smaller footprints. As a result, even though magnets progressively have become higher in field strength and more reliable and efficient, attaining the greatest homogeneity across a large imaging volume is not the only factor that is considered in present magnet technology.

Some amount of compensation for this can come from the implementation of active shimming with coils that generate 2nd-order spatial – or more recently even 3rd-order – harmonic correction of the static B_0 field. But it takes space to accommodate these extra shim coils in the bore, and this may be counterproductive with the ever-increasing demand for wider bore systems. For accuracy and precision, magnet homogeneity is what matters. But the final design will ultimately consider these other factors as well.

Probably what has progressed the most in the past decades is the gradient performance (on this point, readers can refer to the recent comprehensive historical summary *"An Attempt to Reconstruct the History of Gradient-System Technology at Siemens"* by Franz Schmitt et al. in the 2020 ISMRM issue of MAGNETOM Flash (77) 2/2020). In the early- to mid-1980s, gradient coils were unshielded, which meant that without compensation the field errors were on the order of 20% of the nominal amplitude of the gradient pulsing. Performance-wise, pulse rise times were typically 1500 µsecs or even longer in duration, and the maximum gradient amplitudes were no greater than about 3 mT/m. Since that time, continual improvements in power amplifiers, gradient coil design, and manufacturing have led to actively shielded configurations that have force compensation to minimize mechanical torque and vibrations, as well as counter windings to minimize higher-spatial-order eddy currents. Errors are reduced by several orders of magnitude or more, and gradient performance on contemporary whole-body clinical systems now have 200 T/m/s slew rates that allow pulse rise times of less than 100 µsecs and amplitudes up to 80 mT/m amplitudes. Digital precision to control arbitrary and complex gradient waveforms and their pre-emphasis to minimize eddy currents has steadily improved over the years, from 12 bits, to 16 bits, and up to 20 bits or higher.

Specialized gradient coil designs have most recently dramatically increased performance to as high as an astonishing 600 T/m/s and 500 mT/m. However, such fantastic improvements have not come without some compromises as well. In order to achieve these levels and stay within safe limits of peripheral nerve stimulation in the human body, the accuracy and extent of the spatial linearity of such gradient fields can be constrained.

The steady improvements in magnet, shim, and gradient coil design over the decades have allowed for rapid expansion of the types of acquisitions and applications that are now achievable with MRI. However, spatial and quantitative accuracy has not necessarily been the only metric by which contemporary systems are judged. Yet it can be considered just as critical and just as important.

Confounding factors (and where things can go wrong)

To have an appreciation for what it actually means to achieve better than 1 mm spatial accuracy or to produce an image with 100 micron resolution is to also have a realistic appreciation for what can go wrong. This became readily apparent to me very early in my career as an MRI scientist. My first role was to develop new applications, and what I found more times than not was that theory rarely behaved the same way in actual practice. And when it comes to the magnetic fields there are many things that can occur to cause these fields to distort in the real world, as shown in Table 1.

The primary objective of the magnet static B_0 magnetic field is to possess perfect uniformity everywhere in space. Since the B_0 field defines the initial state of the magnetization and its encoding, spatial non-uniformities and imperfections are a fundamental source of error. The

magnet itself is of course finite in size. As such, it will possess a nominal field strength in the middle of the bore and zero field strength at some distance far away. Therefore, at some point as you move away from the isocenter yet still are within the imaging field of view of spatial encoding, the B_0 field will taper off and the required homogeneity is lost. There exists a so-called "sweet spot" where the uniformity of the field is the highest.

One of the most common things that can lead to errors in the static magnetic field are the spatial distributions of the different magnetic susceptibility (χ) that exist in tissues and objects (Fig. 2). This physical property determines the B_0 magnetic field that that medium experiences. Most soft tissues are quite similar, so the distortions of the field are negligible. However, the χ of bone and air are quite different from soft tissue and their presence can cause significant local distortions in B_0. And of course, foreign objects such as surgical or therapeutic implants that might be made of a type of metal possessing very different properties of χ can produce very large spatial distortions of B_0 near the object.

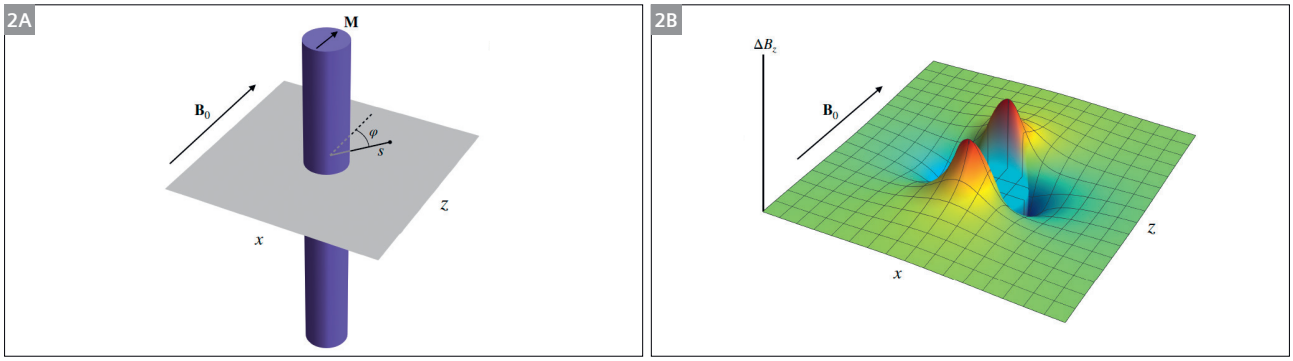
Static and dynamic B_0 magnetic field	Dynamic G magnetic field
Finite shim volume	Eddy currents
Magnetic susceptibility	Concomitant fields
Chemical shift	Finite spatial linearity
External influences	Calibration and regulation
	Mechanical vibration
	Heating and drift

Table 1: Some of the sources of static B_0 and dynamic G errors.

The molecular environment that surrounds hydrogen nuclei causes small but observable changes in the microscopic magnetic field environment known as chemical shift. Because fat and water in tissues have a frequency shift that equates to roughly 3.5 ppm of magnetic field difference, this means that the signal from each will originate from different locations in space. The most common example of this is pixel misregistration where fat will be located at slightly different positions in the field-of-view from water. Excitation of fat will also occur at different positions from water.

These are static B_0 factors. But what about dynamic errors that are caused by external influences or the pulsing of the gradient G fields necessary to encode the MR signal? In urban areas like New York City, the environment can be a "firestorm" of magnetic fields that are constantly fluctuating all around you. A common source are subways, not so much because of the moving metallic trains but because of power lines that can produce strong magnetic fields from surges needed to move the trains. Although Siemens Healthineers has a unique solution for protecting the magnet from such external B_0 perturbations, if an MRI scanner is simply too close it can lead to measurable errors if it occurs when a scan is being done at that time.

Faraday's law tells us that a magnetic field that changes in time will generate an electric field. When a gradient is pulsed, it changes the total magnetic field $B_{0,tot}$ dynamically over time at a given point in space. This will therefore produce a countering eddy-current induced magnetic field on conductive surfaces that can then distort G and in turn $B_{0,tot}$ dynamically. Such eddy-current fields can come from implants or objects that have conductive components



2 Localized magnetic susceptibility induced B_0 distortion in the presence of a cylinder containing uniform susceptibility that is greater than the surrounding external environment. **(2A)**: mathematical model showing the orientation of the cylinder relative to the main static B_0 magnetic field. **(2B)**: theoretical simulation of the distortion of the B_0 field. This model demonstrates the origins of the Blood Oxygen Level Dependent (BOLD) effect in the microvasculature in regions of brain activation.
With permission: Bradley R Buchbinder, MD, Massachusetts General Hospital. BR Buchbinder. Chapter 4: Functional magnetic resonance imaging. Handbook of Clinical Neurology. Vol 135. Neuroimaging, Part I. pp 61-92, JC Masdeu and RG Gonzalez, Editors, Elsevier BV (2016). https://doi.org/10.1016/B978-0-444-53485-9.00004-0

and surfaces, but the dominant source is from the conductive cryoshields within the magnet itself. As previously mentioned, actively shielded gradient coils are designed to minimize this, but the high performance of modern systems will still generate measurable errors within the imaging volume caused by these eddy currents.

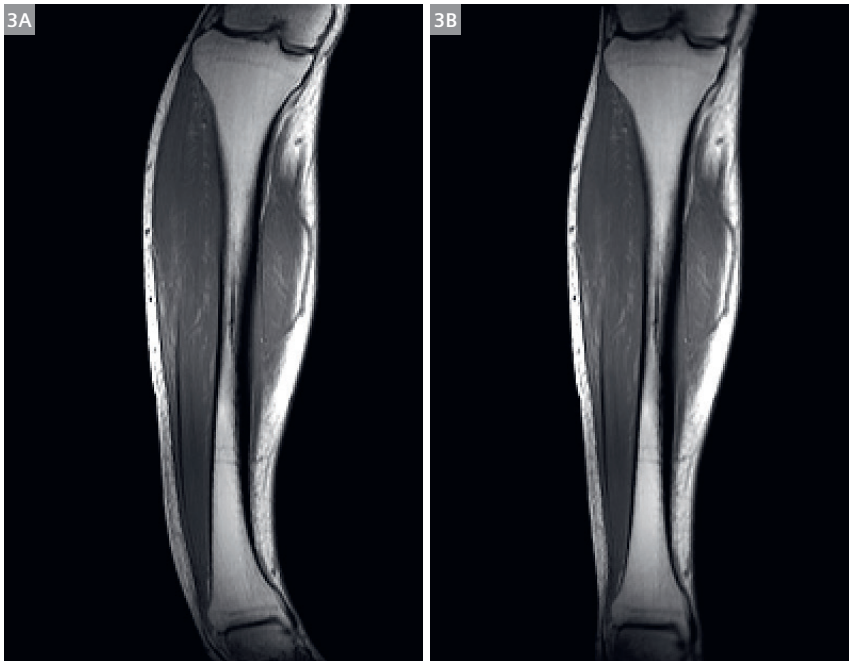
Another source of error caused by pulsing the gradients is the additional terms commonly referred to as Maxwell concomitant gradients. According to Maxwell's equations, it can be shown that when producing a spatially varying gradient field, the actual total effect contains higher-spatial-order mathematical terms that are secondary or "concomitant" fields over and above the spatial linear term we wish to produce for encoding purposes. The extent of their contribution to errors are primarily proportional to the square of the magnitude of the gradient strength, the square of the position away from isocenter, and are inversely proportional to the main magnetic field strength. Therefore, large-gradient amplitudes of pulsing such as what are used in diffusion applications can produce appreciable errors from this source.

Aside from these physics-based phenomena, there are also several engineering factors that also can contribute to the overall errors associated with the gradient fields. First, like the magnet, the gradient coil is finite. As such, this will mean that the fields that it generates will eventually fall off away from the isocenter. Additionally, with the increased performance of modern gradients it is necessary to consider peripheral nerve stimulation and other safety constraints that will limit the extent of spatial linearity of the gradient fields. Figure 3 demonstrates how significant the spatial distortion can be if corrections of these errors are not applied.

Calibration and regulation of the amplifier output that drives the production of the gradient field are important aspects of accurate field generation. When a pulse sequence instruction specifies the amplitude and duration of a gradient pulse, this information is sent to the amplifier to convert the digital instruction to an analog electrical current which then drives the gradient coil generating the requested G field. Too much current will produce a G that is higher than what the instruction calls for. Calibrating this is therefore necessary to ensure accurate field generation (Fig. 4). And proper regulation is required to make sure that the baseline current always remains zero when no gradient field is being pulsed.

Rapidly changing magnetic fields associated with gradient pulsing also induce Lorentz forces that in turn produce mechanical vibrations. This of course also leads to the quite familiar knocking sounds associated with all MRI scanners. But it also can produce physical displacement. Although minor in most cases now that modern gradient coils are designed with force compensation to mitigate these vibrations, it cannot be completely ruled out as a potential factor.

The amount of current required to generate the gradient fields can be quite large, which over time produces a lot of heat that must be mitigated with cooling. However, state-of-the-art applications that exploit the maximum gradient performance over longer periods of time can lead



3 Large FOV coronal T1-weighted spin echo slice through the lower leg and calf muscle. Without correcting for the spatial nonlinearity of the gradient field, the image is geometrically distorted **(3A)**. Gradient related nonlinearity distortion is completely predictable if the gradient field is known and can therefore be corrected by pixel reformatting/ remapping **(3B)**.

to gradual drifting of the total B_0 field over the duration of the MR experiment.

And finally, with all these things that can go awry, when it is all said and done, Siemens Healthineers continues to strive to improve and perfect things, and we are therefore able to achieve some of the most astounding diagnostic images and remarkable outcomes with MRI, that continues to significantly make a positive impact on healthcare.

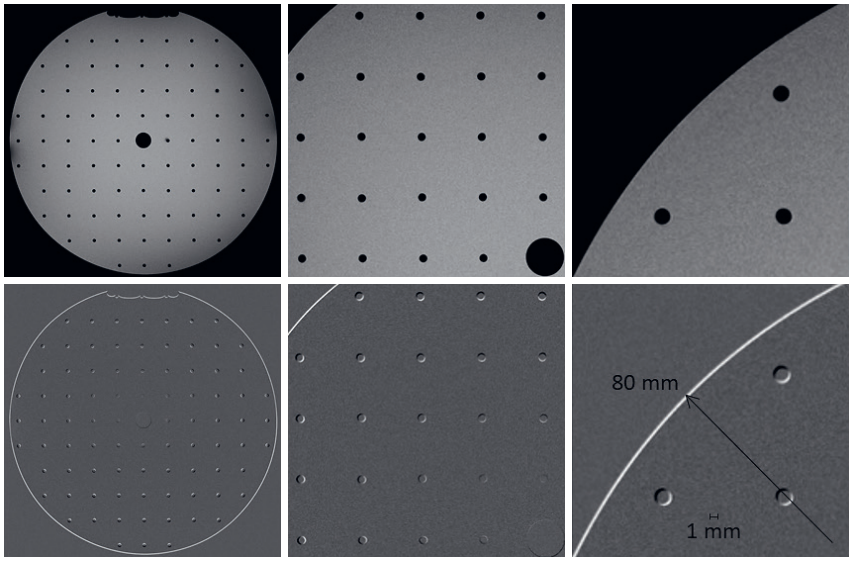
MRI applications

Once magnetization is transverse after the excitation process, it becomes vulnerable to all the inaccuracies of the B_0-related magnetic fields, whether from the main static magnetic field or from the pulsing of the gradients. This will be true regardless of the application. However, it is the application and what information it is trying to extract from the human body that ultimately determines whether the errors in $B_{0,tot}$ make a difference or not. For a given B_0 error somewhere in space, the spatial distortion or signal phase deviation may be large or small at that location based on the technique of measurement and its application.

Specific details of the myriad of MRI applications that now exist on modern scanners are beyond the scope of this paper. But there are several basic aspects that can make an application more or less sensitive to the $B_{0,tot}$ field and its errors. One of these is the MR signal readout. How fast one samples the signal and encodes it in *k*-space defines the field sensitivity of the MR experiment. The longer this duration, the more time passes for the transverse magnetization to evolve in the $B_{0,tot}$ field that it experiences. Errors in the field increase the magnitude of the error in the signal, as the magnetization continues to evolve during the sampling process.

Single-shot echo-planar-imaging (EPI) applications such as functional MRI (fMRI), diffusion tensor imaging (DTI), and dynamic susceptibility contrast (DSC) are at one extreme of the sensitivity spectrum where the entire readout of the MRI signal and complete sampling of *k*-space is done with a single magnetization preparation. Ironically, although this provides the ability to produce rapid "freeze-frame" results in a matter of 20 or 40 ms per image, on the scale of evolution of the transverse magnetization this is quite slow. These techniques are therefore extremely sensitive to B_0 errors leading to substantial spatial distortions, and signal magnitude and phase deviations.

In the more traditional steady-state Cartesian sampling used in gradient echo (GRE), spin echo (SE) or turbo spin echo (TSE) techniques, the duration of the readout of a line in *k*-space, and thus the sensitivity of the scan, is determined by different factors. On the one hand, high-bandwidth sampling associated with short readout durations offers the ability to shorten timing such as echo time (TE) or echo spacing with less sensitivity to B_0 errors, but is accomplished at the expense of increased noise and thus lower SNR. On the other hand, longer durations of lower bandwidth sampling improve the SNR but at the



4 Effect of gradient calibration. A high resolution image of a phantom specially designed to assess spatial accuracy is shown in the upper row at various magnifications. The bottom row is a difference map between two slightly different calibrations. Note that since calibration is relative, the absolute spatial error will depend on the distance away from isocenter.

expense of increased sensitivity to B_0 errors. And, what fights against this is that higher spatial resolution necessitates higher *k*-space sampling of the information requiring larger gradient pulsing which can introduce greater error. So, although one may spatially encode an image with high resolution, the inaccuracy in the spatial position may also be higher.

Cartesian sampling is not the only method used to sample and fill *k*-space. Depending on the application, spiral or radial sampling trajectories can be of benefit. For example, ultrashort echo times are necessary to catch the MR signal before it rapidly decays away in solids such as cortical bone, or regions of interest that contain large localized susceptibility-based B_0 inhomogeneities, such as lung parenchyma. Each sampled data point in *k*-space will only be as accurate as the gradient pulsing that is required to encode that sample with the correct *k*-space coordinates. The more complex the *k*-space trajectory and the longer the readout of the sampling, the greater the potential for error in the mapping.

And finally, as perfect as we might strive to make the magnetic fields and signal encoding, the cooperation of the subject may end up being the single most important confounding factor. The longer the scan is, the greater the probability that the patient will move during the scan which can compromise the accuracy of the outcome. Navigator signals and tracking devices are prospective strategies used to attempt to mitigate some of these inevitable errors due to motion, but these as well ultimately rely on the accuracy of the B_0 fields to correct things.

On the not-so-distant horizon

As the MRI applications become more sophisticated, so do the ways to produce more accurate and reliable results. Clearly, engineering and manufacturing continues to improve the performance of MRI scanners, and Siemens Healthineers leads the way on this front. The scanner is no longer just a diagnostic device that produces images, but is a quantitative measurement system of biomarkers in the age of precision medicine.

In a different approach that accepts the premise that complicated four-dimensional B_0 errors will always exist, dynamic field cameras are devices that measure these complicated fields and either retrospectively or prospectively correct for such errors so that the result is completely corrected of the deviations that occur during the measurement process.

And of course, artificial intelligence (AI) has made great strides in recent years to become integrated in healthcare, radiology applications, and workflow. MRI is not excluded from this. AI is being assessed across a broad range of applications from improving lesion conspicuity, to increasing SNR without the typical compromise in spatial resolution, and using deep-learning algorithms to correct for B_0-related errors and producing super-resolution results.

Concluding remarks

At the beginning of my career, it was extremely important to me that I never stop learning in whatever field I chose. If I stopped learning, I vowed that I would change my direction. I never anticipated that when I chose to be a scientist in the field of magnetic resonance imaging that I would still be here today 35 years later where never a day passes that I am still fascinated by what can be accomplished with this incredible technology.

James Clerk Maxwell may not have ever expected that magnetic fields would be exploited in this way, but I am pretty sure he would be quite pleased to see what we have done with them.

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