ULTRAFAST MAGNETIC RESONANCE IMAGING

A New Window on Brain Research

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TECH VIEW

Driven by faster imaging methods, magnetic resonance imaging (MRI) is maturing into a valuable tool for brain research. As a benchmark, the first clinical scanners produced a typical image in 20 min. Thanks to hardware improvements and new imaging software, a similar scan today takes a fraction of a second. The impact of fast MRI on brain research and medical treatment has been dramatic.

Traditional Fourier transform MRI methods collect one signal (echo) for each radio frequency (RF) excitation pulse. Fast MRI breaks the one-excitation one-signal link (Fig. 1). Instead, subsecond, ultrafast MRI acquires all image data after a single RF excitation pulse. This is referred to as "single shot" imaging. Echo planar imaging (EPI), the first ultrafast sequence, forms an image using a series of reversals of the imaging gradient to create a gradient echo train (*1*). An EPI acquisition takes only about 100 ms. Accomplishing this feat stresses the limits of the scanner hardware. The MR scanner must have strong imaging magnetic field gradients capable of switching quickly and a static magnetic field that is very homogeneous. On this foundation, a set of instructions—the pulse sequence—controls the scanner during the data collection.

Advances in MRI pulse sequence design have produced an impressive collection of methods capable of single-shot imaging. These include EPI, rapid acquisition with relaxation enhancement (RARE), spiral trajectory imaging (Spiral), burst excitation pulse imaging (Burst), and gradient-and-spin echo imaging (GRASE) (*2*). Nearly 50% faster scan time is achieved in each of these pulse sequences by incorporating the half Fourier technique (*3*). Each method has its benefits and tradeoffs depending on the specific physiologic application.

Armed with rapid MR pulse sequences, investigators have taken aim at functional and structural analysis previously beyond the scope of conventional MR imaging. Fast imaging has enabled the detection of the small fluctuations in the MR signal resulting from changes in the blood oxygen level–dependent (BOLD) contrast associated with brain activation (*4*). This so called functional MR imaging (fMRI) has been embraced by the neuroscience community and used for the study of the visual, auditory, sensory/motor, language, and memory systems. Exploiting the spatial resolution of functional MRI, surgeons map and avoid vital brain regions during neurosurgical procedures. Functional MRI is arguably the most important application of ultrafast imaging, and its value to the neuroscientist has been detailed elsewhere (*5*).

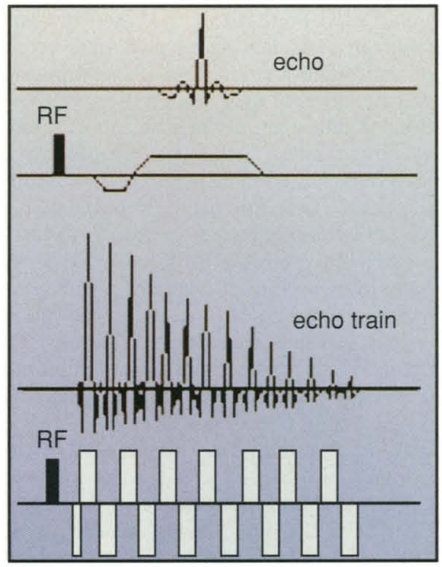

Fig. 1. Comparison of a conventional MRI sequence (top) with one signal per RF pulse and (bottom) an ultrafast MRI sequence with several signals per RF pulse. In the latter case, the gradient polarity is reversed quickly after the RF pulse to create the echo train.

Ultrafast imaging also opened a new window on cerebral hemodynamics. Rapid sampling following contrast agent injection allows for characterization of susceptibility-related signal changes. Application of intravascular tracer kinetic models to these images yields maps of relative cerebral blood volume (*6*). Alternatively, water can be used as an intrinsic contrast agent. With special RF pulses designed to "label" arterial blood, fast MRI enables characterization of cerebral blood flow (*7*). Animal studies have shown that diffusion-weighted imaging (DWI) is a sensitive indicator of acute stroke. In humans, artifacts caused by physiological motions are eliminated by ultrafast DWI thus permitting detection of acute cerebral ischemia in critically ill patients (*8*).

The advent of single-shot imaging techniques, free from the artifacts related to brain motion and CSF pulsations, allow for measurement of the brain diffusion tensor. This analysis unravels the details of water mobility in the brain. With this novel contrast property, anisotropic diffusion in white matter reveals information about the microstructure and orientation of the fiber tracts (*9*). Just as ultrafast MRI observes dynamic physiological processes, it can be used to track surgical interventions in "real time." MR "fluoroscopy" tracks catheters and devices as they are positioned and monitors the progress of therapy (*10*).

Ultrafast MRI offers clear benefits for neuroimaging research. For studies of cerebral activation, MRI has intrinsically higher spatial and temporal resolution than does positron emission tomography (PET), which detects the annihilation quanta emitted by trace amounts of labeled water or glucose. Furthermore, MRI evaluation of brain perfusion is attractive relative to PET and xenon-enhanced computed tomography, because there is no radiation exposure. Magnetoencephalography (MEG), which measures the weak magnetic fields generated by neuronal firing, has unequaled temporal resolution. However, MEG data are enhanced significantly when combined with the high spatial resolution of MRI.

Ultrafast MRI is not a panacea, however, because there are potential biohazards and safety issues related to the experiment. The RF pulses essential for imaging deposit power in the tissues: this energy manifests as heating. The U.S. Food and Drug Administration (FDA) sets strict limits on RF power deposition on human scanners. Heating is the fundamental limitation of echo train imaging with spin echoes (such as single-shot RARE). Also integral to ultrafast imaging is rapid switching of strong magnetic field gradients. Time varying magnetic fields, in the extreme case through Faraday's law of induction, can produce peripheral nerve stimulation and muscle spasms. Care must be taken in the experimental design to stay within FDA limits. Finally, anyone who has volunteered for a functional MRI study is aware of the most obvious drawback of ultrafast imaging, acoustic noise. Rapid gradient switching generates Lorentz forces, which in turn produce uncomfortably loud tones that can exceed 100 dB.

Even after addressing safety issues, there are many problems and limitations with different approaches to fast MRI. The

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EPI gradient reversal technique suffers from rapid signal decay, which permits, at most, 100 ms for data acquisition. This necessitates high signal bandwidth that reduces the signal-to-noise ratio. The limitation on the number of signals acquired also limits spatial resolution. Moreover, the "blind spots" and distortions in EPI due to susceptibility artifacts at interfaces of bone, air, and brain are particularly bothersome (*11*). The newer fast MRI pulse sequences reduce susceptibility artifacts, as demonstrated by a comparison of EPI with GRASE (Fig. 2). By incorporating spin echo and stimulated echo processes to reduce signal decay and phase errors, GRASE also achieves higher spatial resolution than EPI. It is possible that methods such as single-shot GRASE and RARE will replace EPI for the study of dynamic physiologic processes because of the superior resolution and reduced artifacts. Alternatively, EPI (GRASE, and so on) can be improved with the use of several RF excitations and shorter echo trains to form an image. However, these "multishot" techniques suffer from decreased temporal resolution and loss of phase coherence between signals.

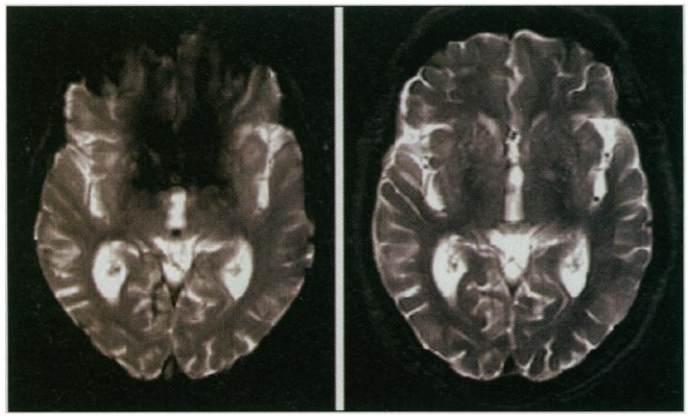

Fig. 2. Comparison of optimized, single-shot imaging sequences. (Left) EPI has signal loss, distortions, and artifacts characteristic of gradient echo train imaging. (Right) GRASE, a newer technique, achieves higher spatial resolution without artifacts, using a gradient-and-spin-echo train. Both images were acquired on the same state-of-the-art MRI scanner. Figure courtesy of D. Feinberg and G. Johnson at NYU Medical Center.

Although ultrafast MRI is a powerful tool for brain research, it is not the only game in town. PET offers sensitive evaluation of cerebral activation, metabolism, perfusion, and receptor binding. Furthermore, PET does not have the "blind spots" characteristic of EPI. Although magnetoencephalography and electroencephalography detect changes closely associated with neuronal activation, this is not yet within the realm of MRI, but it may not be far off. MRI researchers have discovered and now imaged a small signal drop within 500 ms of brain activation, more than a second before the BOLD signal increase (*12*). This "fast response" mirrors the results of optical imaging studies; however, its physiologic mechanism is a topic of much debate. Perhaps, the fast response in the BOLD experiment will bring us closer to neuronal activity and improve the temporal resolution of functional MRI.

Fast MRI has opened up new windows into the structure and function of the brain. For example, recent work combining ultrafast measurement of the BOLD signal and changes in cerebral perfusion is improving knowledge of the relationship between perfusion and oxygen consumption during cerebral activation (*13*). Functional MRI methods can be used in conjunction with pharmacological activation to improve understanding of mechanisms of drug action (*14*). Through the combination of ultrafast evaluation of contrast agent perfusion and water diffusion, researchers may soon be able to characterize the elusive ischemic penumbra, the region of viable brain at risk for infarction following cerebral vascular occlusion (*15*). With such information, it may be possible to triage patients for a host of interventions emerging from the laboratory that may ultimately lead to improved patient outcome following stroke. Echo train imaging can be used to obtain three-dimensional (3D), high-contrast, high-resolution images of the temporal lobes useful for the study of epilepsy. In the neurosciences, these high-resolution 3D maps can be analyzed with "cortical unfolding" algorithms to produce "flat maps" of the cerebral cortex (*16*).

Rapid imaging will also allow for observation of biophysical processes such as the propagation of acoustic waves through the brain (MR elastography) and the velocity of brain motion (*17*). Velocity images have already allowed the observation of normal physiological pulsations and internal displacements of the brain during cardiac and respiratory cycles (*18*). Analysis of these velocity and elastography images may improve our understanding of the brain's response to trauma.

Development of single-shot 3D ultrafast scans will improve temporal resolution for events occurring simultaneously in different brain regions. This may elucidate dynamic cerebral physiology obscured by current temporal sampling rate limitations. Stronger magnets (3 to 4 Tesla) are being widely distributed to research laboratories with the expectation of improved sensitivity for brain activation studies. Magnetic field inhomogeneity and susceptibility artifacts, however, increase with higher field strength, so well-tailored pulse sequences will be needed to realize the full benefit of higher fields.

Rapid improvements and novel applications have occurred in MRI as the instrument itself is a platform for creative experimentation. Without changing a single wire, a scientist can reconfigure the entire design of MRI image acquisition. By analogy to new compositions for musical instruments, the new pulse sequence software redesigns the experiment played out by the hardware. Coupled with the inevitable hardware advances characteristic of our time, ultrafast MRI will certainly quicken its pace and drive neuroimaging research into the next millennium.

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