Echo planar imaging on high field microimaging systems

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Echo planar imaging (EPI) is one of the most efficient magnetic resonance imaging (MRI) techniques. It is also a technically demanding experiment and is prone to severe artifacts. The artifacts can be caused by various factors related to the hardware, the experiment or the sample. In this article, the nature of the artifacts commonly encountered in EPI is presented. Various experimental methods used to minimize these are also discussed.

ECHO planar imaging (EPI) is one of the early magnetic resonance imaging (MRI) techniques proposed by Peter Mansfield[1,2]. EPI is a unique imaging method because it can collect an MR image, from a single free induction decay signal (FID), in about 40 to 100 ms. Such a rapid imaging technique has many advantages in MRI, such as the vast improvement in efficiency. The faster scans help to reduce motion-related artifacts and problems in MR images. The speed at which images are obtained can gives us unique insight into dynamic processes. One of the most intriguing applications of this technique is in the dynamic study of the brain activity related to blood volume changes (BOLD)[3–5].

EPI has not been widely used in research or clinical settings until recently because of technical limitations. EPI is very demanding on the imaging hardware because large field gradients have to be generated and switched rapidly at the rate of about 1 kHz. Another serious drawback of the method is its susceptibility to artifacts which can often result in severe distortions in the images.

The importance of functional studies in neuroscience is the primary reason for the rapid development in the EPI technology. Over the last decade, significant improvements have been made in the gradient hardware. Similarly, a number of new ideas related to the experiment and data analysis for dealing with artifacts have been published[6]. The advances in EPI research have made it possible to conduct useful experiments even in a clinical setting. Currently, state-of-the-art clinical MRI systems are being operated at 4 to 8 tesla and are capable of producing EPI images with sub-millimeter in-plane resolution.

In magnetic resonance microscopy (MRM), images with an in-plane resolution of about 10–100 microns are obtained. The sample size is usually limited to about 1 to 50 mm in diameter because of practical considerations. The small voxel sizes are also associated with lower signals and therefore it is advantageous to operate at high field strengths (7 tesla or higher). Operating at high fields could pose a challenge because field inhomogeneity effects can adversely affect the images, often distorting them beyond recognition. The smaller size of the samples used in MRM allows one to build smaller gradient coils. Fortunately, the smaller coils are more efficient and less demanding on the amplifier hardware. Implementing EPI experiments on a spectrometer is not trivial and therefore it is important to understand the limitations of EPI and the possible artifacts that can be generated. Most of the EPI-related research efforts have been directed towards overcoming these difficulties and are the subject of the current article.

The pulse sequence

The basic EPI pulse sequence is shown in Figure 1. It is based on the spin-warp and Fourier imaging methods used in MRI[2,7,8]. In fact, the initial part of the sequence is very similar to the conventional gradient recalled echo sequence. In the EPI sequence, however, all the signal information needed to reconstruct the image is obtained in a 'single shot', thus improving the efficiency significantly. The slice selection pulse selectively excites the signals from a plane in the object. The slice gradient G_s, and the shaped RF pulse determine the location. The phase encoding gradient G_p, and the readout gradient G_r, are used to resolve the spatial distribution of the spins along orthogonal directions in the selected slice. The initial readout gradient is used to dephase the spins that were excited by the RF pulse. The dephasing process can be reversed by applying a readout gradient of opposite polarity resulting in the gradient echo. By repeating this process (Figure 1) a train of echoes can be generated. The signal intensity will eventually decay to zero because of T_2 (spin–spin relaxation) and T_2^* (field inhomogeneity and magnetic susceptibility) effects. The field of view or length along the read dimension is given by

$$lro = 2 \cdot \pi \cdot sw/(\gamma \cdot gro), \quad (1)$$

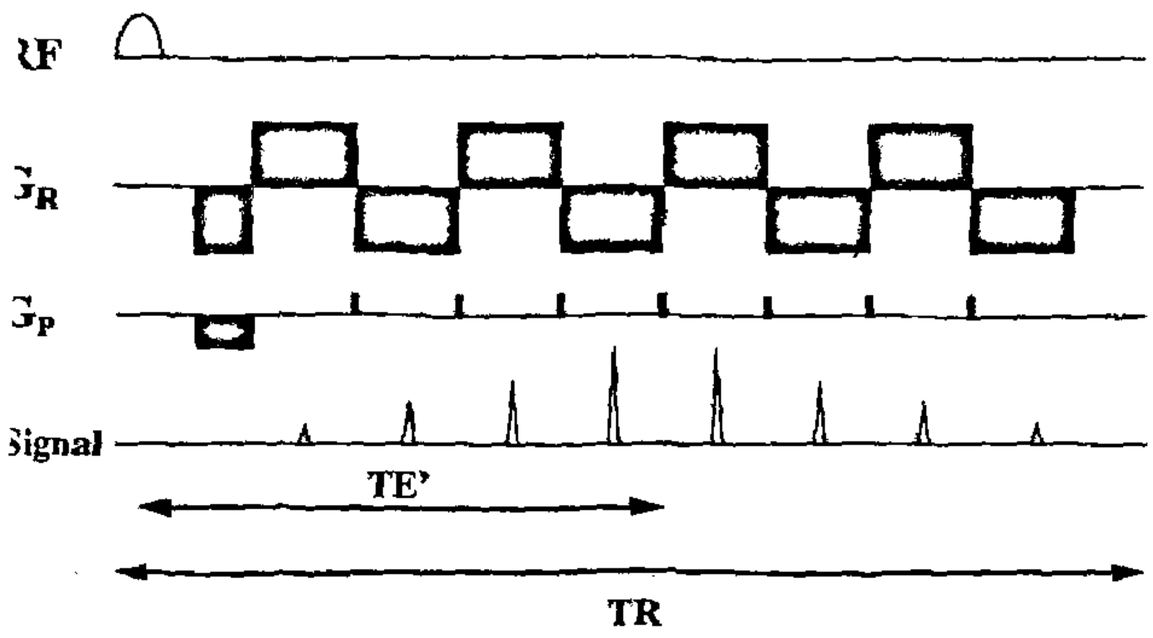

Figure 1. The gradient-echo version of the EPI pulse sequence. The RF pulse represents a 90° slice selective pulse. The read gradients generate a series of gradient echoes which dephase due to T_2 and T_2^*. Each echo is phase encoded in a linear fashion. TE' refers to the effective echo time.

where *gro* (Gauss/cm) is the read gradient amplitude, *sw* (Hz) is the spectral bandwidth, and γ the gyromagnetic ratio (rad/Gauss/cm). The spectral width *sw*, is related to the number of complex points *nr*, and the acquisition time per echo *at* (sec), and is given by:

$$sw = nr/at. \tag{2}$$

It is clear from eqs (1) and (2) that the appearance of the image along the read dimension is governed by a number of interrelated parameters. For example, the resolution along the read dimension can be enhanced by reducing the field of view *lro*, and/or by increasing the number of sampling points *nr*. Similarly, the loss of signal due to T_2 and T_2^* can be minimized by reducing the acquisition time *at*. Another benefit of reducing the acquisition time is the improvement in efficiency resulting from the shorter overall scan time. The efficiency and appearance of the EPI images ultimately depends on the maximum (readout) gradient strength available.

The second orthogonal, image dimension is resolved using the principle of *two-dimensional* NMR spectroscopy[2]. The echo is 'phase encoded' using a series of gradient pulses along the second dimension. Note that each of the alternate echoes must be reversed because they are acquired with the G_r of opposite polarity. The resulting 2D *k*-space data matrix containing $nv \times nr$ complex points is Fourier transformed to yield the image. The field of view along the phase encoding direction is given by,

$$lpe = 2 \,.\, \pi/(\gamma \,.\, gpe \,.\, tpe), \tag{3}$$

where *gpe* (Gauss/cm) refers to the amplitude of the stepped gradient pulse and *tpe* (sec) the duration of the pulse. The initial dephasing gradient pulse is usually adjusted so that the effective phase encoding gradient goes from a negative value to a positive value. Therefore the central echoes experience the least phase encoding gradient. The total scan time is governed mainly by the acquisition time *at*, and the number of echoes *nv*. The resolution along the phase dimension is given by *lro*/*nv*. Therefore any attempts to improve the resolution along the phase encode direction will result in an increased scan time.

Artifacts in EPI

Setting up and implementing EPI experiments is difficult because the images are prone to severe artifacts. Special precautions must be taken to avoid them or else the images can be distorted beyond recognition. Artifacts can arise due to factors related to (i) the hardware, (ii) the imaging sample, and (iii) the type of experiment.

Hardware-related factors

Gradient strength and rise-time. The most critical parts of the hardware for EPI are the gradient coils and the amplifiers used to drive them. Their importance in determining the resolution and scan times has already been mentioned in the previous section. Large gradient strengths and short rise times are desirable for EPI. In clinical scanners the gradient strength is limited to about 10–50 mT/m. The smaller bore gradient coils used in small and medium sized MRI systems can generate about 100–4000 mT/m. The gradient amplifiers supply the voltage *V*, and current *I*, to the gradient coils. The voltage across the coil with an inductance *L*, and resistance *R* is given by,

$$V = R \,.\, I - L \,.\, \mathrm{d}I/\mathrm{d}t. \tag{4}$$

Because of the inductive nature of the gradient coil there will be a finite time before the gradient field reaches its set value. Therefore the actual gradient pulses will exhibit a finite rise and fall time. The rise and fall times in conventional clinical scanners can be of the order of 1 to 5 ms. In high performance gradients, these times are reduced to less than 300 μs. Considerable amount of research and development has been done in the gradient coil and amplifier design for clinical research. The small bore gradient coils used for microscopy are more efficient and capable of performing EPI experiments more readily. For example, a typical gradient coil with a 40 mm bore size can generate a field up to about 1000 mT/m and switch to maximum gradient values in about 50 μs or less.

Field inhomogeneity. One of the most serious artifacts in EPI is caused by field inhomogeneity related effects.

These effects are exaggerated at higher field strengths. The field inhomogeneity can result from imperfections in the magnet and magnetic susceptibility effects caused by the sample. The variation in the field causes the signals to resonate at different frequencies resulting in broadening of the NMR line. Its effect along the read dimension is less severe because of the large read gradients usually employed in EPI. However, along the phase encode dimension, the off-resonance effects are more severe resulting in a considerable shift in pixel position given by,

$$s = f \,.\, t \,.\, lpe, \tag{5}$$

where f (Hz) is the frequency offset from resonance and t (sec) is the inter-echo spacing. There is also another serious problem related to field inhomogeneity – the irreversible loss of signal due to T_2^* dephasing. The T_2^* loss limits the number of echoes that can be acquired and hence the achievable resolution along the phase encode dimension.

Eddy current fields. During MRI experiments the rapidly switched gradients induce eddy currents in conductive materials in the vicinity resulting in a residual eddy current field (ECF). The effect of the ECF on the image is difficult to predict because it is complex and time-dependent[9]. The problem is even more complicated in the case of EPI experiments involving multiple gradient pulses.

Sample-related factors

T_2 and T_2^*. Many samples cannot be studied using EPI because of their physical characteristics and NMR properties. One of the important factors to consider is the T_2 and T_2^* properties of the sample, which cause asymmetric decay of the echoes resulting in blurring of the image. T_2^* effects are mainly caused by magnetic susceptibility field gradients because of the heterogeneous nature of imaging samples. For example, the air–tissue interfaces in head imaging studies can result in very large, localized field gradients due to susceptibility effects. The T_2^* effects are often large resulting in severe distortions and even complete loss of signal intensity.

Chemical shift. In conventional MR images, chemical shift components in tissue samples generate a chemical shift artifact along the readout dimension. For example, water and fat images are chemically shifted with respect to each other. The shift is greater at higher field strengths. The chemical shift artifact along the read dimension is minimized when relatively large readout gradients are used. This results in large artifacts along the phase encoding dimension. The phase modulation of the echoes caused by multiple resonances causes another undesirable side-effect. Post-processing routines that are used to correct for image artifacts resulting from experimental timing errors will fail (to be discussed later). If multiple resonances are present in the sample, the EPI sequence must be modified to select and image only the chemical shift component of interest.

Experiment-related factors

Odd–even echo mismatch. The sign of the readout gradient in the EPI sequence is alternated (Figure 1). Therefore every alternate echo signal must be time reversed prior to the Fourier transform along the phase encode dimension. Any mismatch in either amplitude or phase between odd and even echoes will cause a characteristic artifact (ghost) which is shifted with respect to the main image by *lpe*/2 (half-field of view, half-FOV). Small errors in gradient amplitudes and pulse sequence timings can result in half-FOV 'ghost' artifacts. Any small error in timing can cause a phase mismatch between the odd and even echoes resulting in the ghost artifact. The half-FOV ghost can also be caused by factors such as, eddy current effects, timing and amplitude errors related to the gradient hardware, and receiver anti-aliasing filter delays. The influence of the above factors can be more difficult to handle because they affect the odd and even echo differently. Another effect that can cause differences between the odd and even echoes are the off-resonance effects caused by local susceptibility gradients within the sample. The positive and the negative read gradients result in different local fields at a specific location within the sample further complicating the problem.

A simplistic way to remove the half-FOV ghost is to acquire the odd echoes only. However, the resolution and the efficiency of the image is reduced by a factor of two. The efficiency can be somewhat improved by replacing the read gradient corresponding to the even echo with a shorter gradient pulse[10].

Sampling errors. The discussions so far assumed that the readout gradient was constant during acquisition resulting in linearly arranged k-space data points. Some EPI experiments use complex gradient patterns resulting in nonlinear k-space trajectories[11]. The nonlinear trajectories are usually designed to overcome limitations in the gradient hardware. The k-space trajectory can be optimized to suit a given amplifier. For example, a sinusoidal or trapezoidal read gradient is less demanding on the gradient amplifier. The data points must be sampled in a nonlinear fashion so that the k-space data is redistributed in a rectilinear grid. Any distortion in the field caused by imperfections in the imaging gradients leads

to errors in sampling and in the 'gridding' routines leading to artifacts. Field inhomogeneity can also cause off resonance artifacts[12,13].

Artifact reduction in EPI

Gradient hardware

Most of the efforts in EPI research have been directed towards minimizing image artifacts. Major advances in gradient coil and gradient amplifiers have allowed EPI experiments to be performed on clinical scanners. Actively shielded gradient technology is a major breakthrough in MRI because it reduces the eddy current effects by two orders in magnitude. Eddy current fields can be further minimized by pre-conditioning (pre-emphasis) the gradient waveform signal[9]. There have also been major advances in gradient amplifier designs. Sufficiently high gradient strengths and fast response times can now be achieved in large sized gradient coils. For example, the current head gradient coils used in clinical scanners can generate upto about 50 mT/m with rise-times under 300 μs. The larger gradient strengths and shorter rise/fall times allow shorter acquisition time and minimize signal losses and artifacts due to T_2* effects. Fortunately, the smaller (actively shielded) gradient coils and gradient amplifiers used in MR microscopy systems are more efficient. Most commercially available microscopy systems are capable of performing EPI experiments.

Half-FOV artifact reduction

The half-FOV ghost artifact can be minimized by careful adjustment of the timing and gradient amplitudes. This is usually done empirically by observing the image while adjusting the read gradient amplitude. Another effective method involves post processing of the EPI data using the phase information obtained from a reference scan[13,14]. A reference scan is collected with the phase encode gradients turned off. The reference scan is used to determine the phase errors corresponding to each echo signal along the read dimension. The phase error in the EPI echo train is then corrected during the data processing step. Factors related to eddy current effects, field inhomogeneity, gradient response times, anti-aliasing filters, etc. affect the odd and even echoes differently leading to mismatch in both amplitude and phase. In the latter case, more elaborate correction schemes must be employed to minimize the artifacts[14,15].

Chemical shift artifact suppression

The correction scheme mentioned in the previous section does not work if the NMR signals contains multiple resonances. For example, it is not possible to distinguish the phase shifts caused by chemical shifts from those that are caused by timing errors. Therefore whenever multiple resonances are present it is essential that the unwanted signals be suppressed. Some of the commonly used techniques in MRI[8] for CS artifact removal are CS selective excitation, T_1-null, and CS selective suppression (CHESS).

T_2 related artifact reduction*

Any spurious field gradients such as those caused by magnet field inhomogeneity effects and susceptibility effects can seriously distort EPI images and cause signal loss. Some approaches to minimize these artifacts are: (i) improve the field homogeneity by shimming; (ii) refocus the T_2* related dephasing; (iii) reduce the acquisition time; and (iv) unwind the dephasing effects by post processing.

Shimming is an important part of the experimental set-up for EPI. Conventional shimming methods can be slow and tedious. Image (field-map) based automatic shimming methods are effective in shimming some MRI samples. They are fast and can be used to shim an arbitrary region of the sample. However, one must exercise caution when using the image-based shimming methods because they are prone to errors in regions with poor S:N ratio and short T_2*.

The T_2* dephasing in a sample can be reversed by applying a 180° refocusing pulse. The spin-echo version of the EPI sequence (SE–EPI) can be represented by: 90-TE′/2-180-[EPI], where TE′ refers to the effective echo time which is the time between the initial 90° pulse and the center of the echo train. In the above sequence, the duration of pulse sequence will be increased by TE′/2, and cause some signal loss due to T_2. However the T_2* losses are refocussed at the center of the echo train. A variant of the above sequence (GRASE) uses multiple 180° pulses to further reduce T_2* related artifacts[18]. Adding more slice selective 180° pulses increases the scan time compared to the GE–EPI sequence. Note that any imperfection in the 180° pulses can generate stimulated echoes which can lead to additional artifacts. Phase alternation and crusher pulses are usually employed to minimize artifacts caused by stimulated echoes.

By limiting the number of echoes in the EPI echo train one can significantly reduce T_2* related artifacts. But reducing nv, results in the loss of resolution in the phase dimension. The resolution can be regained by repeating the EPI sequence in a 'multi-shot' or interleaved mode at the expense of increased scan time. In the interleaved mode sufficient time (TR) must be allowed before repeating subsequent scans. In the case of GE–EPI, a small flip angle excitation pulse can be used and the sequence repeated more rapidly.

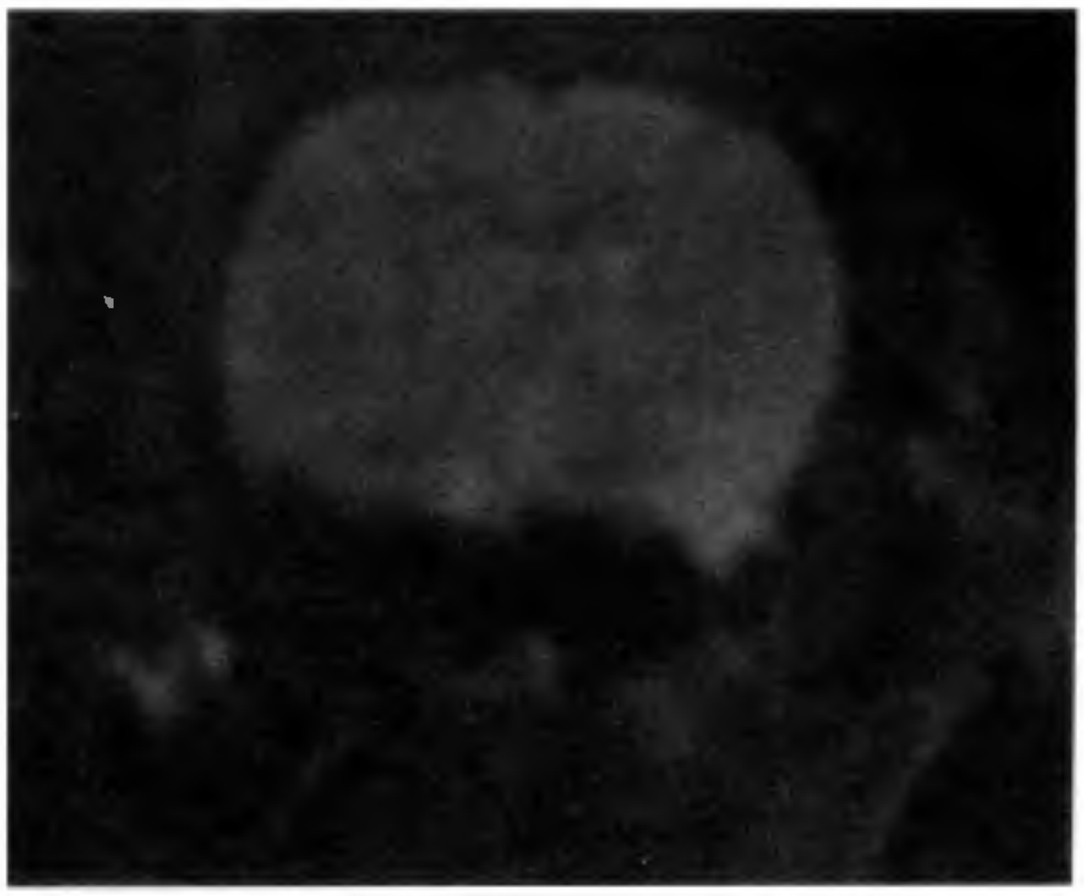

Figure 2. A single-shot, spin-echo, EPI image of a rat brain taken using a 7T vertical bore system. Some of the distortions seen at the base of the brain are due to susceptibility and field inhomogeneity effects. Manual shimming was employed by monitoring the signals from the slice. A reference scan was used to eliminate for half-FOV ghosts. Experimental parameters: FOV 30 mm; matrix size 64 × 64; scan time about 48 ms; slice thickness 1 mm.

Summary

EPI is a fast and efficient MRI technique. The increasing interest in functional neuroscience has helped in the rapid progress of EPI. Recent advances in gradient hardware design and in EPI techniques have allowed researchers to carry out useful experiments even in clinical settings. However EPI has several limitations. It is not easy to set-up and run an experiment routinely on arbitrary objects. Some of the limitations can be overcome by using modifications of the EPI pulse sequence and by various artifact reduction schemes. Most of the artifact reduction experiments require multiple scans leading to loss in efficiency. The T_2 and T_2* related problems are perhaps the most serious because they limit the type of objects that can be studied. The T_2* effects get progressively worse at higher field strengths. Figure 2 shows EPI images from the brain of a live rat obtained at 7 tesla. During the above experiment, however, a few hours were spent optimizing the field homogeneity. The problems associated with T_2* effects are probably the main reason for the limited number of publications on EPI using high field microimaging systems.

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ACKNOWLEDGEMENT. I thank Dr S. Naruse, Kyoto University Medical School, for assistance with the rat EPI experiments.