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Review article

Contrast mechanisms in MR imaging

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Abstract. This paper is a brief introduction to tissue-specific parameters and the utilization of various MR imaging sequences to display these parameters in order to differentiate normal from pathologic tissue and function. The three dominant tissue-specific parameters discussed are proton density, longitudinal relaxation time T1, and transverse relaxation time T2. For the utilization of gradient-echo sequences, transverse relaxation time T2* is introduced, more dependent on the environment or tissue interfaces than on the tissue itself. Another tissue-specific parameter is the concentration of macromolecules and their hydration layers as targeted with magnetization transfer imaging. Still another tissue-specific parameter is the chemical environment. Functional parameters that influence the contrast are diffusion, perfusion, flow, or motion. The sequence-related utilization of these tissue-specific parameters start with magnetization preparation as in spectral suppression of fat signal, relaxation-dependent elimination of fat or cerebrospinal fluid (CSF) signal, simple inversion pulse, magnetization transfer saturation, or diffusion weighting. Possible contrast mechanisms for the tissue-specific parameters are discussed for each of the commonly used sequences, whether of spin-echo type or of gradient-echo type, with or without magnetization preparation, conventional single-echo acquisition, or contemporary multiecho acquisition.

Key words: MR imaging – Contrast mechanisms – Proton density, T1, T2 – Spin echo – Gradient echo – Turbo spin echo – Echo-planar imaging

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Introduction

Contrast mechanisms in MR imaging are based on tissue-specific parameters, utilized with the appropriate imaging technique, sometimes in conjunction with a preparation of the magnetization or application of a contrast agent.

Tissue-specific parameters

The primary sources of inherent tissue contrast in MRI are threefold: the proton density (PD), the longitudinal relaxation time T1, and the transverse relaxation time T2. Exposed to an external field, a macroscopic magnetization builds up within soft tissue, since the parallel alignment of the spins with the magnetic field corresponds to a lower energy state of the proton. The larger the macroscopic magnetization, the stronger the induced signal of the tilted magnetization and the brighter the pixel intensity displayed on the monitor.

Proton density, PD

The macroscopic magnetization building up within a voxel of tissue is a function of the number of spins involved and the tissue temperature. The tendency of spins to occupy the lower energy level is opposed by thermal motions that tend to equalize the two energy levels. The contribution of both phenomena is usually referred to as proton density (PD) of a given tissue (Fig. 1).

Longitudinal relaxation time T1

An MR signal is generated by turning the longitudinal magnetization into the transverse plane, where it rotates with the Larmor frequency, inducing a signal in a nearby coil. After being turned into the transverse plane, the magnetization tends to realign itself again parallel to

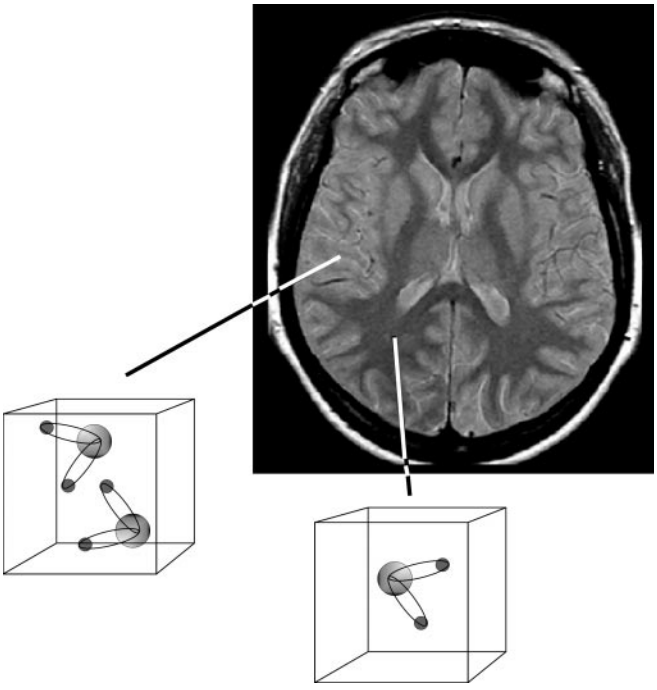


Fig. 1. A proton-density image represents the number of participating spins within a voxel. A proton-density-weighted image is an approximation of that representation

the main field, corresponding to the original occupation of the two possible energy levels. This longitudinal regrowth requires a transfer of energy from the nuclear spin system to its environment. The process is called relaxation and the time needed for the recovery is called relaxation time, in this case T1 relaxation time (Fig. 2). In the early days of nuclear magnetic resonance the environment was usually the crystalline lattice of molecules, and the T1 relaxation time has since then been referred to as spin-lattice relaxation time or, based on the recovery of longitudinal magnetization, as longitudinal relaxation time. The T1 relaxation requires a dipole–dipole interaction of fluctuating field, typically originated in electrons or other adjacent protons. The fluctuating has to occur close to the Larmor frequency. A tumbling molecule could be the basic source of such a fluctuation. A small water molecule tumbles much too rapidly to contribute effectively to this T1 relaxation. This is the reason why T1 values of free water are up to 4 s. Where the water is partially bound or motion restricted, T1 values are between 400 and 800 ms. Operating at a higher field strength does mean a higher resonance or Larmor frequency. The T1 relaxation process is based on fluctuating fields caused by tumbling of molecules close to the Larmor frequency. With the molecular environment still being the same, but the tumbling frequency now requested to be higher, the T1 relaxation process is observed to be less effective at high field strength as compared with a lower magnetic field. Therefore T1 is a function of field strength. The exception is highly mobile molecules, such as free water, where the fraction of molecules tumbling within the appropriate frequency range is nearly constant for lower as well as higher field strengths.

Transverse relaxation time T2

Turning the longitudinal magnetization 90° it becomes the transverse magnetization, which rotates in the transverse plane with the Larmor frequency and induces the MR signal. This macroscopic magnetization is a compo-

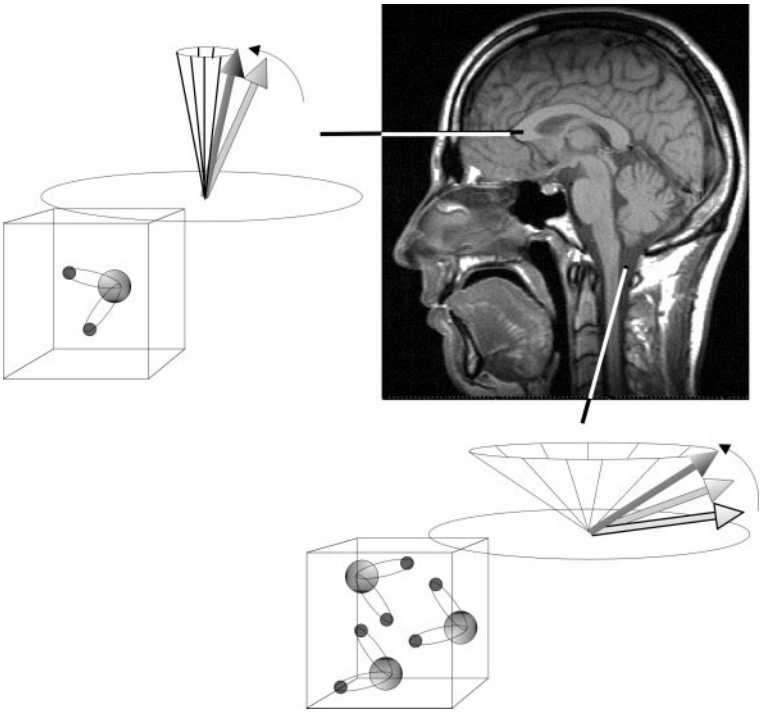


Fig. 2. A T1 image characterizes the time needed for the magnetization of the specific tissue to realign itself with the main magnetic field. A T1-weighted image is an approximation, contaminated by the proton density

Table 1. Relaxation parameters for various tissues. *GM* gray matter; *WM* white matter; *CSF* cerebrospinal fluid

Region	Longitudinal relaxation time T1 (ms)			Transverse relaxation times T2 (ms)
	1.5 T	1.0 T	0.2 T	
Brain				
GM	921	813	495	101
WM	787	683	390	92
CSF	2650	2650	2650	280
Edema	1090	975	627	113
Meningioma	979	871	549	103
Glioma	957	931	832	111
Astrocytoma	1109	1055	864	141
Miscellaneous tumors	1073	963	629	121
Liver				
Normal tissue	493	423	229	43
Hepatomas	1077	951	580	84
Miscellaneous tumors	905	857	692	84
Spleen				
Normal tissue	782	683	400	62
Pancreas				
Normal tissue	513	455	283	
Miscellaneous tumors	1448	1235	658	
Kidney				
Normal tissue	652	589	395	58
Miscellaneous tumors	907	864	713	83
Muscle				
Normal tissue	868	732	372	47
Miscellaneous tumors	1083	946	554	87

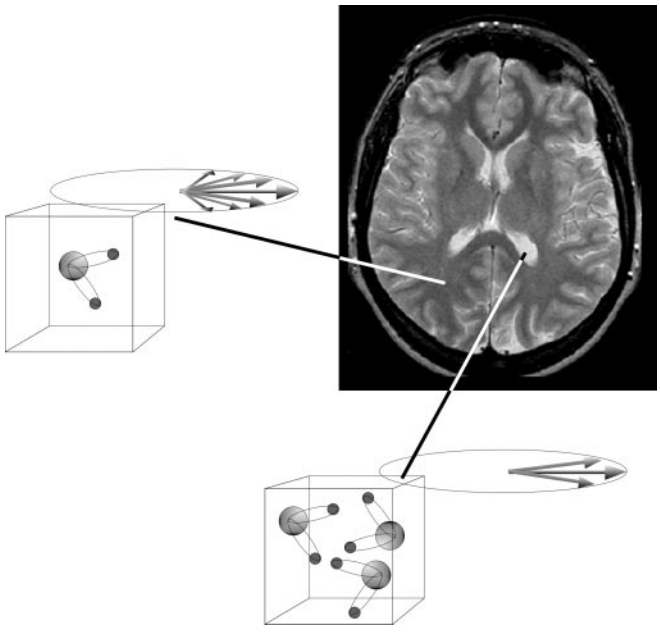


Fig. 3. A T2 image represents the speed of dephasing for the transverse magnetization. In order to calculate the T2 value multiple echoes are necessary documenting the signal course. A T2-weighted image is an approach for a fast illustration of different T2 values, contaminated by the proton-density influence

sition of individual spins, exposed to static or slowly fluctuating local magnetic field variations. Temporary small field changes will cause a different resonance frequency for that moment. The result is that part of the magnetization still rotates with the same frequency but no longer has the same phase position in the transverse plane. The magnetization diminishes as illustrated in Fig. 3 causing the signal to decay. This process is called T2 relaxation. Since it is related primarily to the intrinsic field caused by adjacent spins, it is also referred to as spin-spin relaxation time or, since it takes place in the transverse plane, as transverse relaxation time T2. The transverse relaxation process T2 relies primarily on static or slowly fluctuating fields and is therefore not a function of field strength. Table 1 gives an overview of T1 and T2 values for human soft tissues [1–5].

*Transverse relaxation time T2**

In addition to the transverse decay of the macroscopic magnetization due to T2 relaxation, there are other dephasing mechanisms that are consistent over time and fixed in location. Any field variation across a voxel causes a difference in resonance frequencies, latter resulting in a dephasing of the transverse magnetization (Fig. 4). Main-field inhomogeneities can cause such dephasing, but also tissue-related susceptibility-induced field distortions. In spin-echo imaging this dephasing is refocused with the 180° radio-frequency (RF) refocusing pulse. In gradient-echo imaging, where this RF pulse is omitted, the T2*-dictated free induction decay is observed [6].

Magnetization transfer, MT

Macromolecules have a layer of "bound" water. Since static or slow changing magnetic fields are dominant in the vicinity of macromolecules, the associated hydrogen pool has a very short T2. The T2 is usually so short that this hydrogen pool is not directly observable, and the signal vanishes faster than the ability to acquire some data. The short T2 corresponds to a significant difference in resonance frequencies causing the rapid dephasing. A significant difference in resonance frequencies is a synonym for a very broad resonance of these unobservable protons. The magnetization of these invisible protons can be transferred to the visible "free" water via a chemical exchange or cross-relaxation, which is a special form of dipole–dipole interaction [7].

Chemical shift

The resonance frequency of a nuclear spin depends on the locally experienced magnetic field. This field is a composition of the externally applied magnetic field and the magnetic field generated by the circulating electrons. The field generated by the electrons always opposes the applied field. A proton with a circulating electron in close vicinity is therefore called shielded. It experiences an effective lower field than the externally ap-

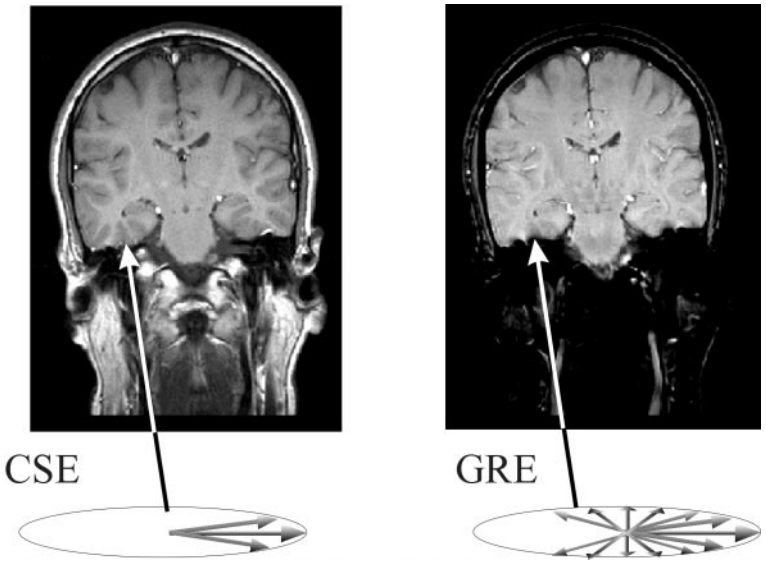


Fig. 4. **a** Image acquired with a conventional spin-echo *(CSE)* sequence. **b** Image acquired with a gradient-echo *(GRE)* method. All parameters were selected to be identical, except for the missing 180° refocusing pulse for the GRE sequence. The comparison is a drastic example of how the susceptibly difference at bone–soft tissue interfaces dictates the T2* dephasing

plied. In water molecules the hydrogen nuclei are almost stripped of their electron due to the strong electronegativity of the oxygen atom. Aromatic hydrogens with fatty compounds, on the other hand, experience a localized augmented field, they are more shielded, and they have a lower resonance frequency than water protons. Since the difference in resonance frequencies is caused by induced secondary fields, the magnitude of this so-called chemical shift is proportional to the strength of the externally applied field and is approximately 3.5 ppm of the Larmor frequency at that field strength [8].

Diffusion, perfusion, MR contrast agents, in-flow, motion

Random translational motion of molecules, also called Brownian motion, results in molecular diffusion. The ability of molecules within a given tissue to do so is described by the diffusion coefficient. Magnetic resonance imaging applies field gradients for the purpose of spatial encoding. Dephasing gradients are usually associated with rephasing gradients. If the magnetization moved due to diffusion, the rephasing will be incomplete and the detected signal will be diminished [9]. Perfusion relates to blood delivery to tissues and refers to the circulation of blood in tissue capillaries. Perfusion is also important in conjunction with the application of an MR contrast agent. Using a gadolinium chelate as contrast agent, where the interaction between nearby protons and the electrons of gadolinium allow a more rapid T1 relaxation, requires a delivery via perfusion to the targeted tissue. T1-shortening agents are also used to dramatically reduce the T1 relaxation time of the blood within the vasculature for MR angiography. Even without contrast administration, the blood signal is increased at locations where unsaturated blood is flowing into the repeatedly excited slice. This phenomenon is called “inflow” and is utilized in MR angiography. A temporary change in field causes a shift in position of the transverse magnetization within the transverse plane, also called phase position. For tissue that is moving, and for blood that is flowing, phase positions can be used for characterizing or quantifying these motions [10].

Imaging of tissue-specific parameters

Magnetization preparation

In order to modify the contrast, magnetization can be prepared prior to imaging, almost independent of the type of imaging sequence that is to be applied. The commonly used preparation schemes include suppression of signal from fat, signal nulling of tissue using an inversion pulse, improvement in T1-weighting using an inversion pulse, magnetization transfer saturation, and diffusion weighting.

Spectral suppression of fat signal

Lipid protons in adipose tissue are contained in molecules of intermediate size, allowing motions close to the Larmor frequency – thus enabling an effective T1 relaxation. On the other hand, there are only few static contributions to cause a rapid dephasing of the transverse magnetization. Fat has a short T1 relaxation time and relatively long T2 values. The hyperintense signal of fat may reduce the dynamic range for windowing images or may obscure lesions. Artifacts due to respiratory motion usually originate within the subcutaneous fat. These are reasons why it is often desirable to eliminate or reduce the signal from fat. The magnetization can be prepared utilizing the chemical shift property of adipose tissue. Lipid protons have a resonance frequency approximately 3.5 ppm lower than the resonance frequency of water-bounded hydrogen, i. e., 210 Hz for a 1.5-T

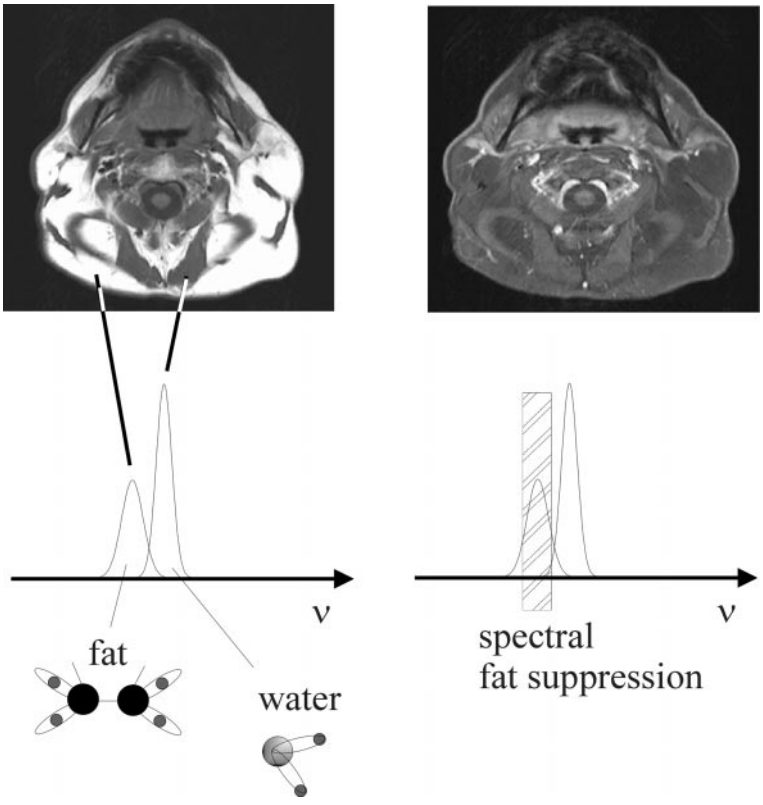


Fig. 5. Spectral fat suppression: Fat has a resonance frequency approximately 3.5 ppm lower than the Larmor frequency of free water, due to the different electronic environments. With an RF saturation pulse placed around the resonance frequency of adipose tissue it is possible to saturate the fat and to reduce the signal from fat

system or 147 Hz for a 1.0-T magnet. Applying a spectral saturation pulse prior to the imaging sequence, as indicated in Fig. 5, will suppress the signal from fat.

Relaxation-dependent elimination of fat signal

After application of a 180° RF inversion pulse, the magnetization of all tissue will be aligned antiparallel to the main field, and will over time recover and align itself back to the parallel position. The time needed depends on the longitudinal relaxation time T1. An imaging sequence starts with the projection of the existing longitudinal magnetization onto the transverse plane. If there is no longitudinal component, there will also be no transverse component to generate a signal. Fat has a very short T1 relaxation time. Using an inversion pulse prior to the measurement, it is possible to apply the excitation pulse of the imaging sequence at the time the recovering longitudinal magnetization of fat is passing through the transverse plane as illustrated in Fig. 6. This technique is called short tau inversion recovery (STIR). The inversion time for fat suppression on a 1.5-T system is approximately 150 ms. A disadvantage of this technique is that the inversion pulse affects all tissues, often reducing the signal-to-noise ratio dramatically. The theoretical solution to this problem is a spectral inversion pulse. Since the majority of contrast agents used in MR are T1-shortening agents, STIR may lead to tissue nulling for an otherwise enhancing lesion.

Relaxation-dependent elimination of cerebrospinal fluid signal

For periventricular lesions the pathology is often obscured or masked by the adjacent hyperintense cerebrospinal fluid (CSF). It has been suggested to eliminate this signal with a technique called fluid-attenuated inversion recovery (FLAIR) [11]. Because CSF has a very long T1 relaxation time, an inversion time of 1.9 s is needed to wait for the longitudinal component of the magnetization to be zero and to start an imaging sequence that will not contain any signal from CSF. Due to the long inversion time, this technique is only suitable in conjunction with faster spin-echo imaging such as turbo spin echo (TSE) or fast spin echo (FSE; Fig. 7).

Radio-frequency inversion as a tool to increase T1-weighting

The contrast between two adjacent tissues is defined as the signal difference. The signal is proportional to the rotating transverse magnetization; the latter is generated by projecting the current longitudinal magnetization onto the transverse plane. Using an RF inversion pulse prior to starting an imaging sequence, the longitudinal magnetization depends on the time between inversion and the excitation pulse of the imaging sequence, the inversion time. This inversion time can be utilized to maximize the signal difference, the contrast, between tissues with a small difference in T1 values, as indicated in Fig. 8.

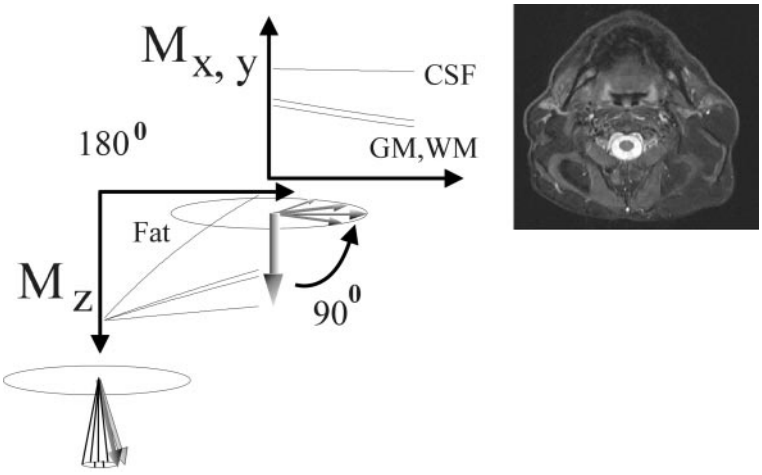


Fig. 6. The short tau inversion recovery approach (STIR). Fat has a short longitudinal relaxation time. The longitudinal magnetization (M_z) is inverted prior to imaging. During the subsequent inversion time the magnetization within various types of tissue undergo a longitudinal relaxation with the aim of realigning parallel to the main magnetic field. Starting the imaging sequence turns any longitudinal magnetization in the transverse plane, where it will become the transverse magnetization (M_{xy}), responsible for the signal induction. If there is no longitudinal component, there will be no signal generated. With an inversion time of approximately 150ms, the magnetization of adipose tissue passes through the transverse plane and does not have a longitudinal component. Starting the sequence at that time will generate an image without a fat-signal contribution

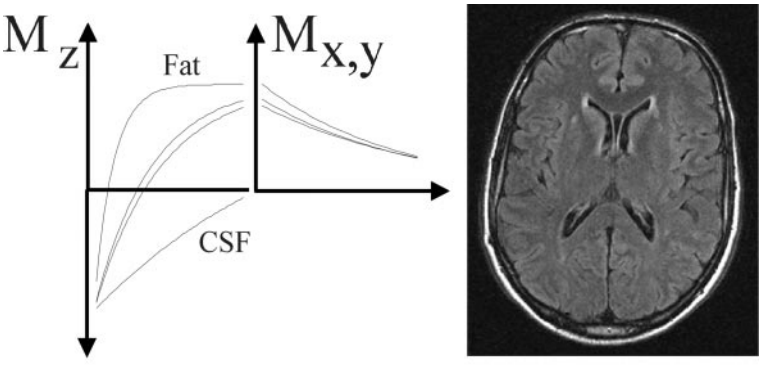


Fig. 7. The fluid-attenuated inversion recovery (FLAIR) approach: With faster spin-echo techniques it becomes feasible to select inversion times as long as 1.9 s. In so doing, the signal from the cerebrospinal fluid *(CSF)* can be suppressed in a fashion similar to that of fat with the STIR technique

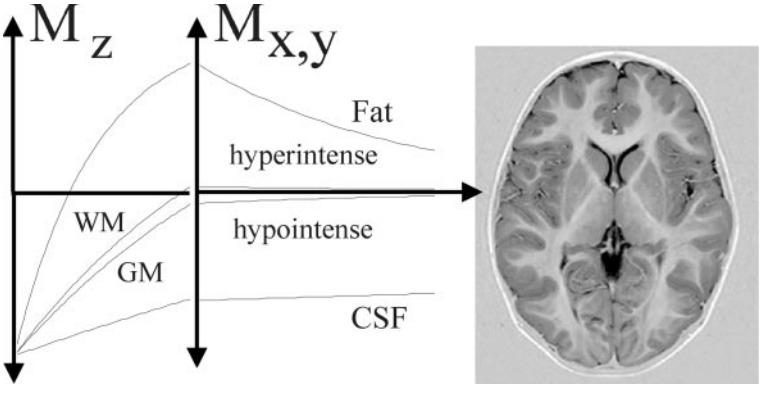


Fig. 8. The true inversion recovery technique for visualizing small differences in T1 values. The magnetization is inverted prior to imaging. No signal is presented as intermediate gray. The transverse magnetization generated by the tilting of the antiparallel longitudinal magnetization is represented with a hypointense signal. The signal generated by the already recovered realigned longitudinal magnetization is hyperintense

Magnetization transfer contrast

The protons within a macromolecular reservoir as well as the associated water protons in their hydration spheres have a very short T2 and are not observable. A short T2 corresponds to a broad range in the resonance frequency. A presaturation pulse with a bandwidth of a few hundred Hertz and a center frequency shifted from the water resonance by 1000–2500 Hz saturates protons in the immobile pool without affecting the protons within free water. The theory is that the magnetization of this invisible proton pool is transferred to the visible pool with corresponding exchange mechanisms. A reduced signal in tissues in which macromolecular–water interactions are expected is observed. The first and very effective application of MTS pulses was for magnetic resonance angiography, in which the stationary background is suppressed with this approach (Fig. 9). A second potential use is the utilization in conjunction with gadolinium-enhanced imaging (especially at low field), since the MT pulse has no effect on the gadolinium–water interaction and suppresses the signal from background tissues. In diseased tissue, where the protein–water content is altered, the MT pulse may render demyelination earlier than conventional T2-weighted imaging.

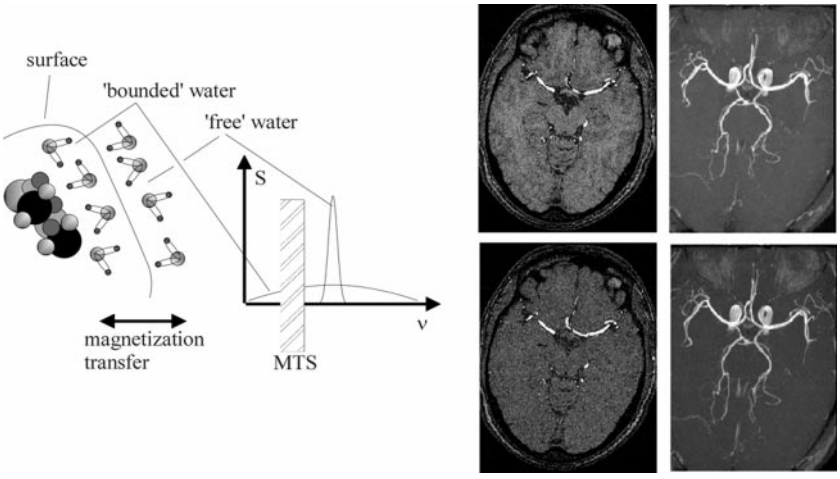


Fig. 9. Magnetization transfer. Water molecules close to macromolecules are called 'bounded.' They have a very short T2 value, corresponding to a broad resonance spectrum. Placing a saturation pulse 1000–2500 kHz below the Larmor frequency of free water will saturate this pool of invisible bounded water. Certain mechanisms, such as chemical exchange and cross relaxation, transfer this saturation to the visible free-water pool

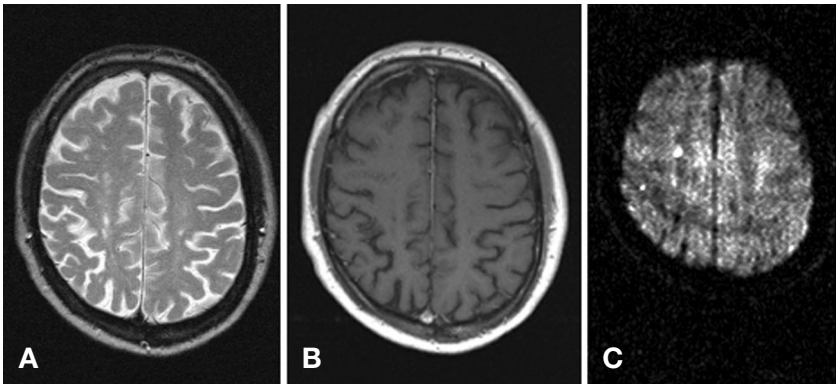


Fig. 10 A–C. Diffusion imaging. **A** T2-weighted spin echo; **B** contrast-enhanced T1-weighted spin echo; and **C** diffusion-weighted echo-planar images of a patient with clinical history of repetitive cerebral infarcts. The most recent 48-h-old infarct within the right hemisphere is visible only in the diffusion-weighted echo-planar image **(C)** with a b-value of 1000 *(white spot)*

Diffusion weighting

The application of a field gradient causes the resonance frequency to be a function of location with the corresponding dephasing of the transverse magnetization within a voxel. Applying the same gradient with identical amplitude and duration, but with opposite polarity, refocuses the dephasing as if nothing had happened. Diffusion characterizes the arbitrary motion of water molecules within a given tissue. A molecule experiences a certain magnetic field, depending on the position within a gradient field. The corresponding transverse magnetization will speed ahead or fall behind in comparison to the transverse magnetization of neighbouring molecules. The transverse magnetization is dephased. A gradient of the same amplitude and duration but of opposite polarity will rephase the transverse magnetization – as long as the molecules are still at the same locations. If that is not the case, i. e. if the molecules moved due to diffusion, the rephasing will be incomplete and a residual dephasing of the transverse magnetization for that region will remain, causing a loss in signal intensity. The residual dephasing corresponds to the diffusion coefficient. Areas with a diffusion deficit will remain hyperintense after the application of a diffusion weighted preparation (Fig. 10). Since bulk motion obscures the smaller change due to diffusion weighting, the preparation is commonly used in conjunction with an ultrafast readout module.

Conventional spin-echo imaging

Pathology is identified by screening for morphologic changes, for an altered dynamic behavior, and for a change in the observable parameters of a diseased location as compared with the adjacent healthy environment. Depending on which tissue parameter is aimed at, the images are PD weighted, T1-weighted, T2-weighted, or diffusion weighted.

Proton-density weighting

In order for the signal intensity to be dominated by the influence of the proton density, contamination of the signal with T1 or T2 relaxation processes have to be avoided. As illustrated in Fig. 11, the repetition time (TR) has to be long enough that most of the longitudinal magnetization is relaxed as to minimize the difference due to T1 recovery. The echo time (TE), the time at which the data are collected, has to be as short as possible, so as to avoid a contamination by the immediate onset of T2 decay following excitation. The TR in routine clinical PD-weighted imaging is usually not selected to achieve a maximum contrast, but to get a reasonable PD-weighting in an acceptable measurement time. The minimum TE is usually given by the intrinsic constraints of Fourier imaging: The slice-selective RF pulse needs a

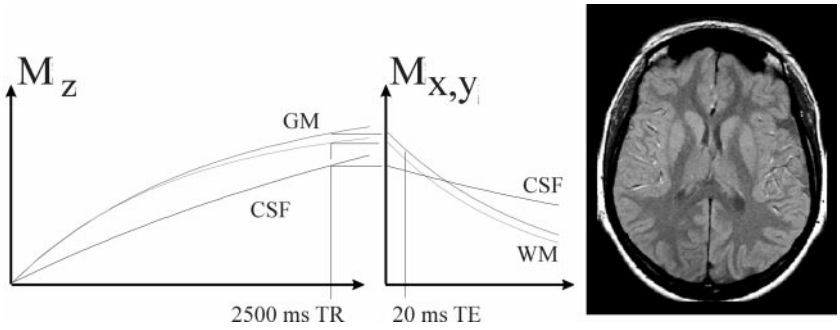


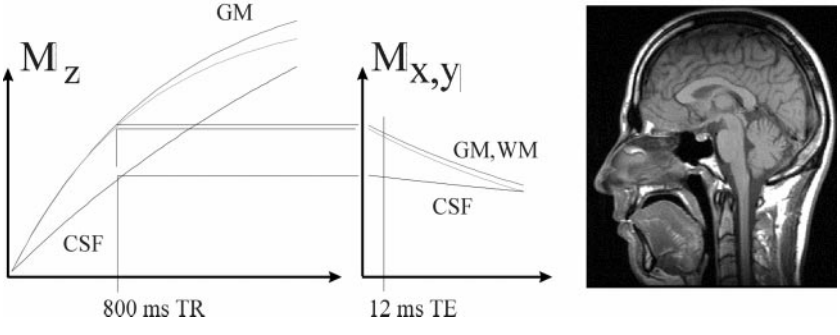
Fig. 11. Proton-density-weighted CSE image. The *left graph* illustrates the recovery of longitudinal magnetization (M_z) following excitation. The speed of this relaxation is characterized by the tissue-specific longitudinal relaxation time T1. In order to minimize the T1 influence, the TR has to be of sufficient duration. The *right graph* demonstrates the dephasing of the generated transverse magnetization ($M_{x,y}$) due to T2 decay. In order to minimize the contamination of the proton-density weighting with any T2 influence, the selected TE has to be as short as possible

few milliseconds, the phase encoding takes a few milliseconds, the selective RF refocusing pulse needs a few milliseconds, and the length of the data acquisition window is dictated by the desired bandwidth of the measurement, with the echo time being defined for the center of the acquisition window, at least for conventional spin-echo (CSE) imaging.

T1-weighting

Immediately after the excitation, the longitudinal magnetization recovers with the tissue-specific relaxation rate. With the repetition of the next Fourier line, that recovered magnetization will be turned into the signal-inducing transverse magnetization, as illustrated in Fig. 12. There is an optimum TR, where the signal difference, the contrast of tissues with a slightly different T1 value, is maximal. The contrast has to be put into perspective with the expected noise. The contrast-to-noise ratio is usually higher for half the optimum TR and two acquisitions as compared with the optimum TR executed with only one acquisition (Fig. 13). Since T1 is a function of field strength, the optimum TR is field-strength dependent as illustrated in Fig. 14. Repetition times in clinical routine imaging are in general larger than the optimum TR in order to get a sufficient number of slices in multislice imaging.

Fig. 12. A T1-weighted CSE image. Depending on the T1 relaxation times that are to be compared, there is one specific TR that produces the largest difference. For a 1.5-T system and for a protocol that utilizes only one acquisition, the optimum TR for a gray matter–white matter differentiation is 800 ms. The selected TE has to be sufficiently short in order to minimize any T2 contamination of the signal



T2-weighting

In order to avoid any contamination with effects from T1 relaxation, the TR selected has to be long enough, as for PD-weighted imaging. Contrary to the short echo time utilized in PD-weighted imaging, a long echo time is utilized in order to achieve a maximum contrast between tissues with differences in T2 values. There is again an optimum echo time as illustrated in Fig. 15, but the maximum is flat and the difference between an 80-ms echo time or a 140-ms echo time is barely noticeable.

Fast imaging with spin-echo sequences

Fast-spin-echo or TSE techniques are based on the idea first mentioned by Henning et al. [12] that multiple echoes can be used, with each echo phase encoded, in order to reduce the measurement time.

Proton-density weighting

There is no change in argument with respect to conventional spin-echo imaging. In order to get a PD-weighted

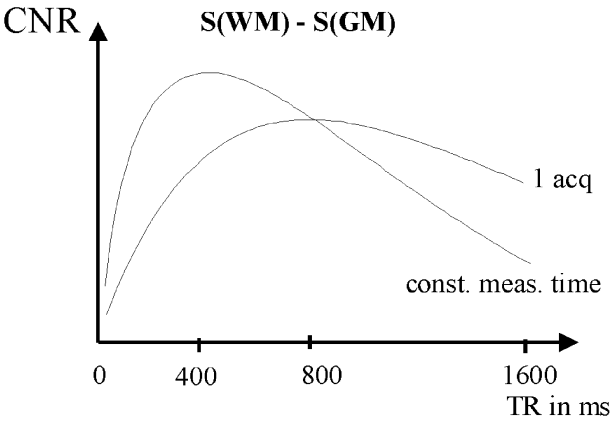


Fig. 13. The contrast-to-noise ratio *(CNR)* in T1-weighted CSE imaging is a function of the TR and the number of averages. A 400-ms TR with two acquisitions leads to a better CNR than selecting the optimum TR of 800 ms with only one acquisition (1.5 T)

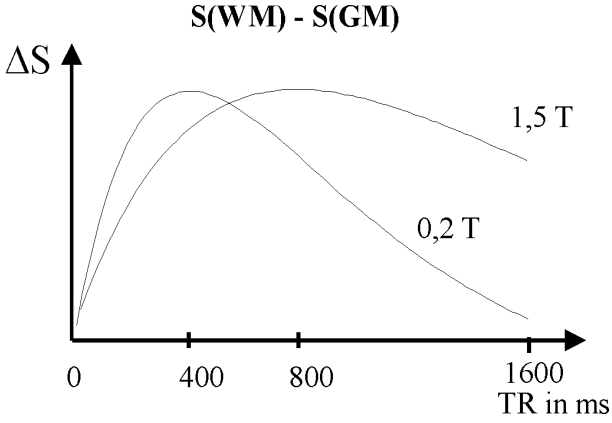


Fig. 14. The optimum TR is field-strength dependent. For a 1.5-T system the optimum TR for GM–WM differentiation is 800 ms, whereas at 0.2 T a TR of 400 ms should be selected

image the TR needs to be as long as is reasonable and the echo time to be as short as possible. With respect to the TR, TSE imaging performs exceptionally well, since the time penalty of selecting a long TR is offset by the turbo factor, which is, the number of phase-encoded echoes per excitation that are used to fill the raw data matrix. The turbo factor is directly proportional to the potential reduction in measurement time for a given TR. As for the short TE, the TSE technique is slightly limited. Since multiple echoes are used to fill the raw data matrix, the first echo is utilized to measure the low spatial frequencies, whereas higher spatial frequencies are measured with later echoes. As a consequence, the contrast has a moderate T2-weighting as a function of object size. The hyperintense appearance of CSF in PD-weighted TSE imaging as compared with PD-weighted conventional SE imaging is based solely on the improvement in PD-weighting by selecting a longer TR (Fig. 16).

T1-weighting

On top of the short echo time, the request for a short TR in order to achieve a T1-weighting further reduces the advantages of TSE imaging. It has to be recalled that the signal changes due to T2 decay are significant for shorter echo times. Signal variations within the raw data matrix causes image blurring. The slice loop time that is the minimum TR per slice is also much longer for TSE imaging as compared with conventional spin-echo sequences, restricting the number of possible slices in a multislice measurement.

T2-weighting

A long TR and a long TE are perfect parameters for TSE imaging. Signal variations between 80- and 140-ms echo times are small, and multiple echoes with a different phase encoding can be read into the raw data matrix without causing image blurring. The TRs for TSE protocols used in clinical routine are usually longer compared with CSE imaging, and therefore tissues with long T1 values show an increased signal contribution as compared with CSE imaging (Fig. 17). Due to generated stimulated echoes, the signal-to-noise ratio in TSE imaging is actually better than expected [13–15], considering the primary echo only. The RF pulses of adjacent slices operate as off resonance pulses on the invisible macromolecule-associated protons leading to a further reduction in signal of tissues with an already short T2 and therefore to an improvement in contrast [16]. There are only two disadvantages, one minor and one major. The minor disadvantage is that the J-coupling pattern is broken, fat appears hyperintense as compared with conventional spin-echo imaging [17]. The J-coupling of fat-bounded hydrogen leads to an additional signal decay in conventional spin-echo imaging. With closely spaced 180° refocusing pulses as used in TSE imaging, this J-coupling pattern is broken, causing a hyperintense appearance of fat on TSE images. The major disadvantage of TSE imaging is the decreased sensitivity to susceptibility differences due to the short spacing of RF refocusing pulses: The signal void observed in the vicinity of hemorrhagic blood products are slightly less obvious on TSE images as compared with the appearance on conventional spin-echo imaging [18–22]. The application of breath-held TSE sequences in areas of shorter T2 times, such as liver pathologies, has to be used sparingly, since the contrast is reduced as compared with conventional SE imaging. The reduction in contrast in this case is proportional to the increase in echo-train length. The TSE sequences that utilize a short echo-train length are reported to provide a liver-to-lesion contrast comparable to that of CSE images [23].

Conventional gradient-echo imaging

The fast low angle shot (FLASH) and gradient echo (GRE) imaging techniques are the early results in an attempt for faster imaging. The 180° refocusing pulse is omitted, allowing a faster TR, and a low flip angle is

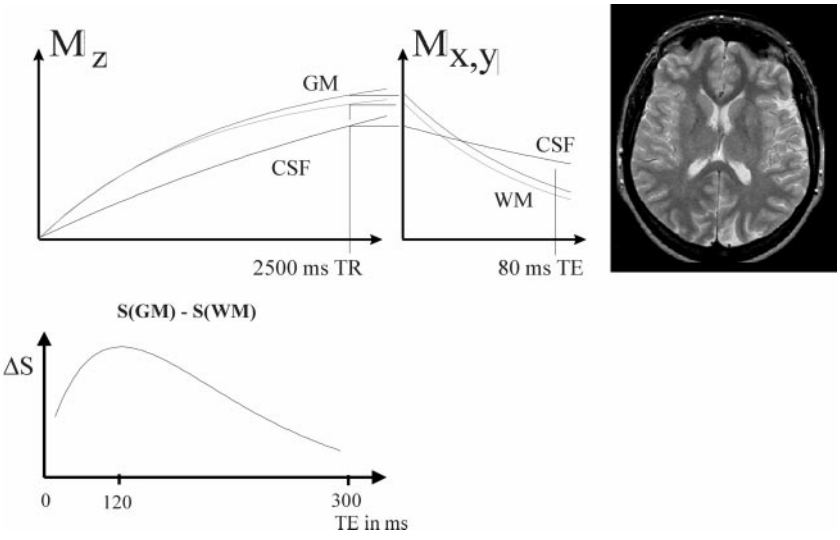


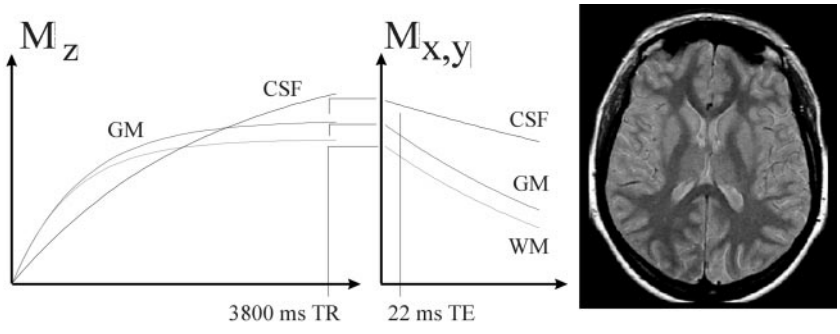
Fig. 15. A T2-weighted CSE image. The *left graph* illustrates the recovery of longitudinal magnetization (M_z) following excitation. The *right graph* demonstrates the dephasing of the generated transverse magnetization (M_{xy}) due to T2 decay. There is an optimum TE which depends on the difference of T2 values for the tissues to be studied

used in order to increase signal efficiency. The majority of routine clinical applications using GRE techniques utilize short repetition times for T1-, T2*-, or T2-weighted imaging. There are three fundamental principles that need to be discussed in conjunction with the contrast achieved in GRE imaging. Firstly, due to the omitted 180° refocusing pulse, the signal follows the T2* relaxation curve, with a few exceptions which are mentioned later. Secondly, the signal contribution is a function of the excitation angle, as illustrated in Fig. 18. Since the flip angle varies across the slice profile, the achieved contrast corresponds to the integration, which is the summation of all these contributions across the excited slice. Thirdly, chemical shift becomes an issue. As mentioned previously, the resonance frequency of fat-bounded hydrogen protons is lower than that of water-bounded hydrogen protons. In conventional spin-echo imaging the faster water component is placed behind the slower fat component with the 180° refocusing pulse and at the time of data collection all components are back in phase. With GRE imaging the magnetization of the slower fat component continues to fall behind the magnetization of the water fraction, and there is a situation in which fat-related magnetization is in phase with water-related magnetization – and the other extreme, in which the two magnetizations are of opposed phase. These combinations are listed in Table 2. In opposed-phase situations, the voxel that contains fat and water provides a low signal intensity, since the opposing magnetizations interfere with each other destructively (Fig. 19).

Fig. 16. A T2-weighted TSE image. The *left graph* illustrates the recovery of longitudinal magnetization (M_z) following excitation. The TRs in TSE imaging are usually larger as compared with CSE techniques for the purpose of improving the contrast. This is the main reason for the bright appearance of CSF on proton-density-weighted TSE images, demonstrating the "better" suppression of the T1 influence still apparent on routine proton-density-weighted CSE images (see Fig. 11)

T1-weighting

The TRs in GRE imaging range from as short as possible for 3D approaches to almost similar to conventional spin-echo approaches for multislice abdominal imaging. They are usually applied together with a low-flip-angle excitation in order to optimize the signal-to-noise ratio. Even for MR angiography the approach is called T1-weighted, since the short TRs in conjunction with a relatively large flip angle and a spoiling of any residual transverse magnetization at the end of one Fourier line leads to a suppression of signal with long and even moderate T1 values. Signal is supposed to come from the inflow phenomenon, from the unsaturated blood flowing into the volume or slice, or from the blood with a dramatically reduced T1 relaxation time due to an appro-



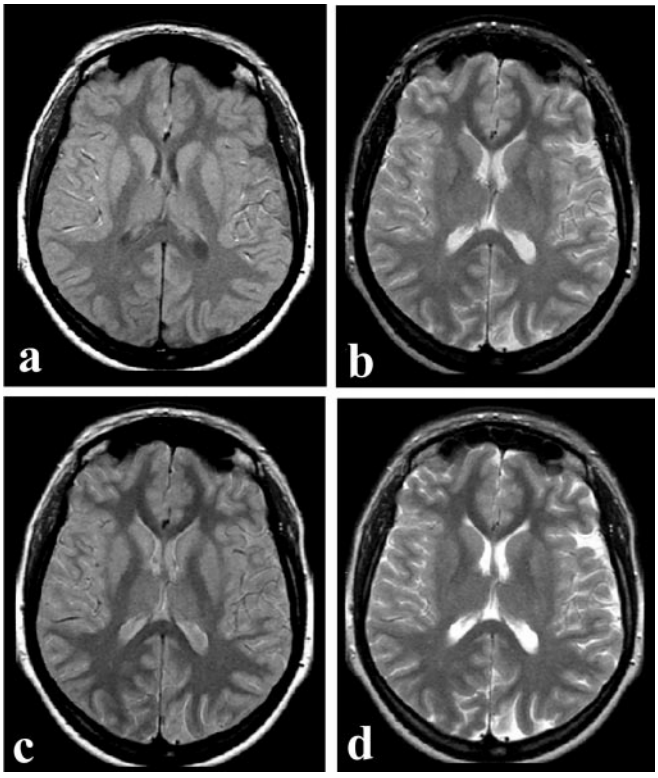


Fig. 17 a–d. Difference between CSE and TSE double-echo imaging. **a, b** An 8-min (TR/TE = 2500/20/80 ms) CSE image acquisition. **a** Proton-density-weighted image; **b** T2-weighted image; **c, d** A 3-min (TR/TE = 3800/22/90 ms) TSE image acquisition [proton-density-weighted **(c)** and T2-weighted **(d)** image]. The increase in contrast is due primarily to the selection of a longer TR and due to the MTS effect of the multiple 180° RF pulses used in this multislice acquisition

Table 2. Depending on the selected echo time, the magnetization of adipose tissue and water may be parallel to each other, a situation called in-phase, or antiparallel, called opposed phase. The in-phase situation results in a maximal signal contribution of voxel containing adipose tissue as well as water, whereas in an-opposed phase situation the magnetizations destructively interfere with each other causing a signal void or signal loss. The theoretical values are based on a water–methylene two-component system. For some fat molecules and fat-infiltrated tissue there may be a slight difference compared with these theoretical values leading to a imperfect in-phase or opposed-phase situation with increasing echo time, and this may require some tests for selecting the optimal echo time. The first in-phase situation is the time immediately following the excitation, at a theoretical echo time of 0 ms

Field strength (T)	Difference frequency (Hz)	First opposed-phase situation at TE (ms)	Second in-phase situation at TE (ms)	Second opposed-phase situation at TE (ms)
0.2	29	17.3	34.5	51.8
0.35	51	9.85	19.7	29.6
0.5	72	6.9	13.8	20.7
1.0	144	3.45	6.9	10.4
1.5	217	2.3	4.6	6.9

priate contrast agent as used in contrast-enhanced MR angiography (Fig. 20).

T2-weighting*

In addition to T2 decay, those dephasing mechanisms that are stable over time and fixed in location, usually refocused with the now-missing 180° refocusing pulse, contribute to the contrast. The new faster decay rate is characterized with T2*, which includes T2, the interaction at the atomic and molecular levels, and the dephasing mechanisms due to local field inhomogeneities. T2*-weighting refers to two types of protocols. Susceptibility differences cause local field inhomogeneities and contribute to T2*. Dephasing starts with the excitation and the later the echo is acquired, the more severe the signal void due to these dephasing mechanisms. Selecting a low bandwidth which requires a long data-acquisition window, and is correlated with a prolonged echo time, increases this sensitivity and increases T2* weighting. The T2* sensitivity is utilized in demonstrating the intracellular paramagnetic deoxyhemoglobin, methemoglobin, or hemosiderin in hemorrhagic lesions [24]. The same sensitivity is utilized in functional MR imaging for all techniques that rely on BOLD (blood oxygenation level dependent), where the oxygen delivery exceeds the blood oxygen extraction in activated areas, causing a decrease in paramagnetic blood deoxyhemoglobin content and therefore an increase in MR signal [25]. This kind of T2* sensitivity is also utilized for cerebral perfusion imaging. Gadolinium chelates are traditionally thought of as being T1 agents used to increase the signal intensity of tissues on T1-weighted images. However, when used as cerebral perfusion agents, gadolinium chelates are used primarily as susceptibility agents, decreasing the signal intensity on T2*-weighted images [26]. The other type of protocol also declared as being T2*-weighted aims for hyperintense signal for tissue with a relatively long T2*, similar to the definition of T2-weighting in conventional spin-echo imaging. Utilizing a very low-flip-angle excitation, the longitudinal magnetization remains close to the fully relaxed state. In such a situation the recovery due to T1 relaxation is very small and the difference between tissue with slightly different T1 values is even smaller. The influence of T1 relaxation is suppressed, similar to the situation for long TR protocols in conventional spin-echo imaging. Since the T1 influence is suppressed, the influence of T2* differences becomes dominant, so the protocol can be called T2*-weighted (Fig. 21).

T2-weighting

In order to get a T2-related contrast in GRE imaging, the influence of the T2 relaxation time has to exceed the dephasing mechanisms included in T2* relaxation. There are two possibilities usually combined depending on the applied sequence. One possibility is the generation of spin echoes, the refocusing of magnetization with the next excitation. A typical example of such a se-

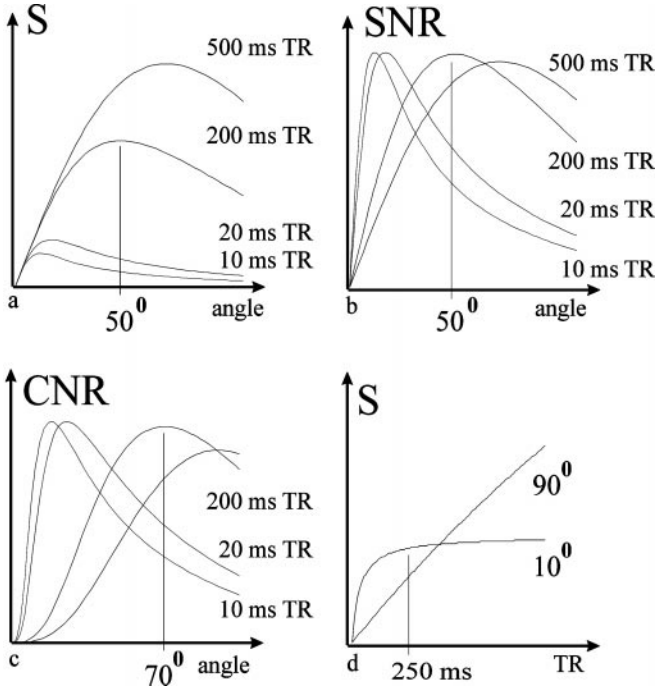


Fig. 18 a–d. Signal *(S)*, signal-to-noise *(SNR)*, and contrast-to-noise *(CNR)* courses in low-flip-angle gradient-echo imaging. **a** The signal course is representative for a 782-ms T1 relaxation time (spleen at 1.5 T) and is proportional to the excitation angle: The lower the excitation angle, the lesser the transverse magnetization generated. If the excitation angle is too large, the tissue becomes saturated and the generated signal is again diminished. The theoretically optimal angle is called the Ernst angle and is 50° for a TR of 200 ms (for a T1 of 782 ms). **b** Normalizing to a constant measurement time (e. g., one acquisition 200 ms TR vs ten acquisitions 20 ms TR) and calculating the SNR, the optimum angle is again 50° for a 200-ms TR. **c** Maximizing the difference between, for example, liver and spleen (782 ms T1 vs 493 ms at 1.5 T) leads to an optimum excitation angle of 70° for a TR of 200 ms. **d** Operating with very low flip angle suppresses the T1 influence even at short TRs, allowing short-TR T2-weighted imaging

quence is the backward running fast imaging with steady precession (FISP), the PSIF, where the transverse magnetization is generated with the first excitation, refocused with the second excitation, and then read out. The effective echo time for such an approach is almost two TRs. These techniques are also known as contrast-enhanced fast imaging techniques. The other method relies on refocusing of the transverse magnetization at the end of the measurement. Doing so will increase the signal contribution from tissue with a long T2. This is the case for sequences such as fast imaging with steady precession (FISP), gradient-recalled acquisition in the steady state (GRASS), fast field echo (FFE), and Fourier acquired steady-state technique (FAST). Of course it is possible to combine both methods as is the case in double-echo steady state (DESS), constructive interference in steady state (CISS), and trueFISP approaches. Figure 22 gives a demonstration of the signal evolution for FLASH, FISP, and DESS.

Flow sensitivity and phase contrast

It has been shown that with a specific gradient arrangement, the phase position of the transverse magnetization can be made insensitive or sensitive to flow and motion [10]. Choosing a flow-sensitive sequence, the phase difference between an insensitive scan and a sensitive scan can be utilized to quantify flow velocities, as illustrated in Fig. 23. Taking the vector between the transverse magnetizations of the two measurements leads to the so-called phase-contrast technique used in MR angiography (Fig. 24).

Fast gradient-echo imaging

In order to reestablish contrast in short TR low-angle GRE imaging, an inversion pulse preceding the whole measurement has been suggested [27]. The recovering of the longitudinal magnetization is a function of the tissue-specific T1 value. Thus the preparation pulse introduces a T1-weighting. Other preparation pulses are also possible and have been tried, but the preparation with an inversion pulse is the only technique that has established itself in routine clinical protocols.

T1-weighting

The T1-weighting in fast GRE imaging is achieved in a fashion similar to that in spin-echo imaging; however, instead of having an inversion pulse prior to the measurement of a single Fourier line, in this magnetization-prepared rapid-GRE approach, the inversion pulse is placed prior to the whole measurement. The signal contribution slides along a relaxation curve as illustrated in

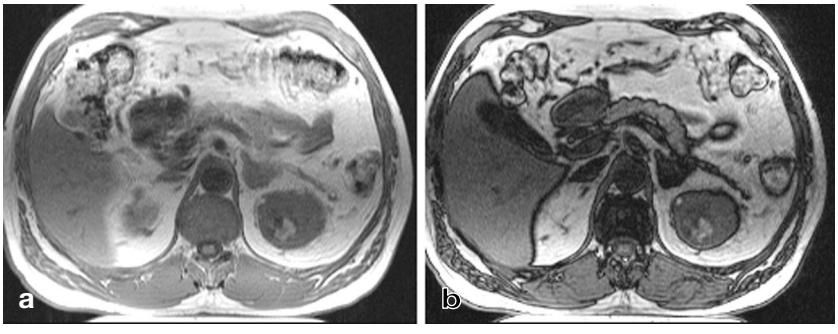
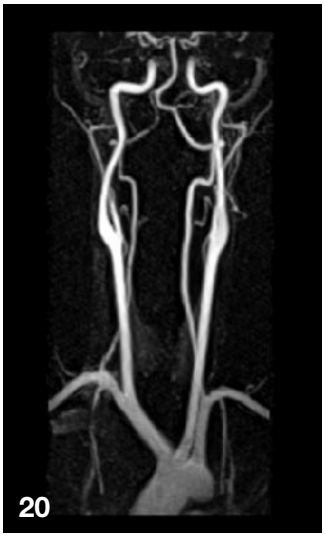


Fig. 19 A, B. Adrenal gland adenoma. **A** In-phase and **B** opposed-phase FLASH images of a left adrenal gland adenoma show a significant decrease in signal intensity on the opposed-phase image as compared with the in-phase image due to the fat content of the adenoma



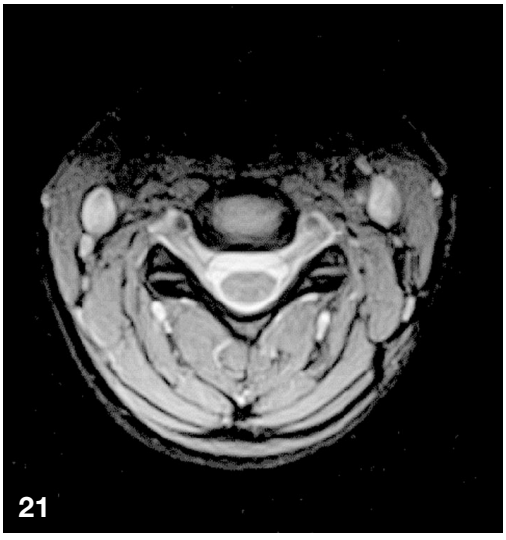


Fig. 20. Contrast-enhanced MRA of carotid arteries. Contrast is achieved solely by administration of a paramagnetic T1-shortening agent leading to a hyperintense appearance of a vascular tree at the time the contrast bolus is passing through an otherwise saturated surrounding. The selected sequence is usually of FISP type with a TR of 3.8 ms, a TE of 1.49 ms, an excitation angle of 25°, a spatial resolution of 1.43 × 1.09 × 1.33 mm, and a measurement duration of 10 s

Fig. 21. T2*-weighted transverse cut of the cervical spine at 0.2 T with FLASH. A low-flip-angle excitation of, for example, 10°, in conjunction with a relatively long TR of 120 ms suppresses the influence of different T1 relaxation times and thus allows short-TR T2(*)-weighted imaging

Fig. 25 and can vary within the k-space. The dominant contrast is given for the time on the relaxation curve where the low spatial frequencies of the object are acquired. The initial magnetization is dictated by the inversion time and the T1 values of the tissues. The available magnetization throughout the measurement is a function of this initial magnetization, the TR selected, the flip angle utilized, and the duration of the measurement. The 2D version of this sequence is called snapshotFLASH, turboFLASH, (fast spoiled gradient recalled acquisition into steady state) FSPGR, or TFE and is generally used as a fast localizer or for dynamic contrast-enhanced studies. The 3D version, the MPRAGE [28], almost replaced conventional T1-weighted imaging within the brain, but did show some inconsistent enhancement pattern when used in conjunction with a gadolinium chelate as a contrast agent [29, 30]. Since then it is commonly used as a supplement in routine brain studies and in pediatric patients for 3D reformatting of developmental disorders or in epilepsy.

Gradient- and spin-echo imaging

The idea was to reduce the measurement time in TSE imaging even further by introducing gradient echoes into the sequence structure [31]. Instead of measuring the one spin echo generated with a 180° refocusing pulse, multiple switching of the readout gradient at that location will generate multiple gradient echoes under the given spin-echo envelope.

T2-weighting

The echo-train length in TGSE imaging is usually long, indicating that the only useful application is the generation of T2-weighted images. Since the RF spacing is now increased, the J-coupling pattern is unbroken, and fat appears similar as in conventional spin-echo imaging. With the introduction of gradient echoes the hope had been that also the sensitivity to hemorrhagic lesions had been reestablished. Thus far the new technique has not fulfilled that expectation [32].

Ultrafast gradient-echo imaging

Using a single excitation and multiple phase-encoded gradient echoes to fill the raw data matrix has been suggested by Mansfield and is called echo-planar imaging (EPI) [33]. This technique and derivatives are considered ultrafast GRE imaging. Derivatives means leaving the pure single-shot technique and doing multishots, or

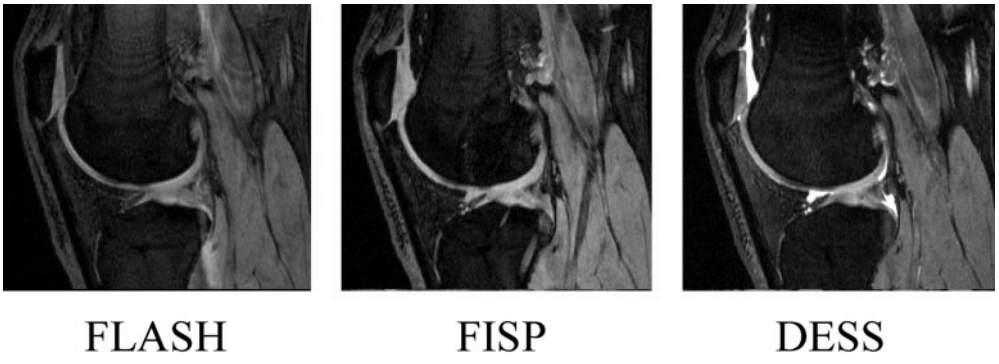


Fig. 22. Sagittal images of the knee acquired with FLASH, FISP, and DESS. The transverse steady-state component generated with FISP adds up to the FLASH signal intensity for tissue with long T2* values. With DESS a T2 component is added on top of the FISP signal

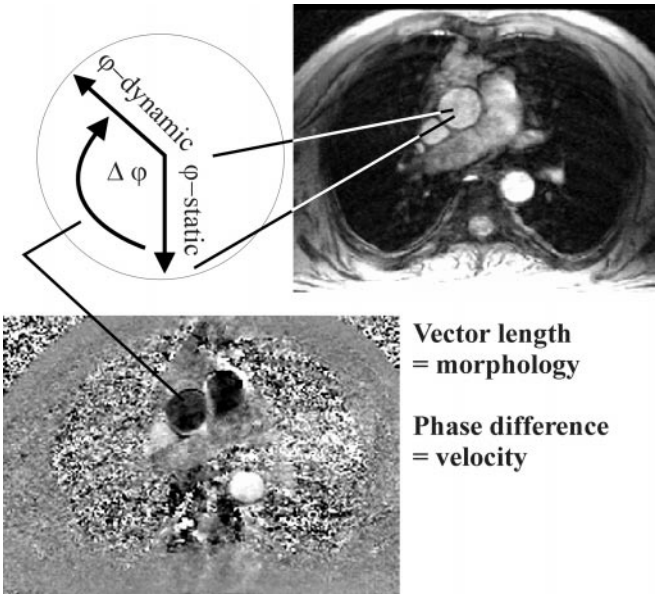


Fig. 23. Flow quantification with flow-sensitive GRE imaging. In addition to the magnitude information of the transverse magnetization assigned to the signal intensity within the morphologic image, the phase position relative to a reference scan is indicative for the velocity. The phase difference can be assigned to a signal intensity leading to a gray-scale proportional to velocity

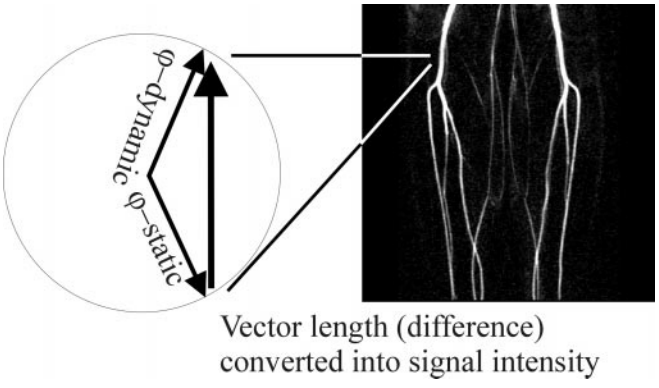


Fig. 24. Phase-contrast MRA with flow-sensitive GRE imaging. The difference (vector) between the reference scan and the flow-sensitized scan is converted to a signal intensity leading to the so-called phase-contrast display of the studied vascular tree

filling the raw data matrix on a spiral trajectory. All these techniques have in common that they utilize a certain number of phase-encoded gradient echoes for data collection.

T1-weighting

The T1-weighting is established identical to the approach mentioned for fast GRE imaging. An inversion pulse is placed prior to the whole measurement, making the recovering longitudinal magnetization a function of inversion time and tissue-specific T1 relaxation time. Shifting the acquisition of the low spatial frequencies at

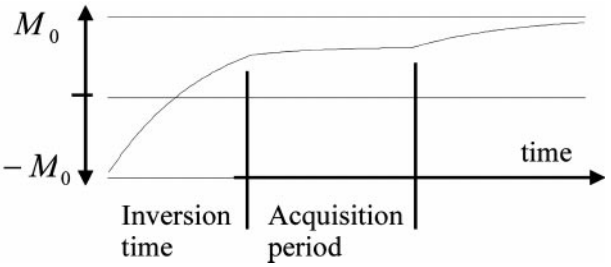


Fig. 25. The behavior of the longitudinal magnetization following inversion, the onset of a module of rapidly acquired gradient echoes with low-angle excitation, and the final recovery in turbo FLASH imaging

the beginning of the echo train may also provide a reasonably short effective echo time.

T2-weighting*

Echo-planar imaging does not have a TR, with the exception of dynamic imaging of the same slice. With no preceding inversion pulse and no previous excitation the longitudinal magnetization fully relaxed and does not depend on the tissue-specific T1 relaxation. The application of multiple phase-encoded gradient echoes provides a T2*-weighted contrast. The effective echo time is the time after the excitation at which the low spatial frequencies are acquired. T2*-weighted echo-planar imaging samples the so-called free induction decay (FID–EPI).

T2-weighting

The effect of static dephasing mechanisms contributing to the contrast can be reduced by placing the echo-planar-imaging readout module under a spin-echo envelope (SE–EPI).

Diffusion weighting

In the first article on spin-echo imaging in 1950, long before spatial localization was available, Hahn described the loss of signal that would result from diffusion through an inhomogeneous magnetic field during a spin-echo measurement [34]. The phenomenon was later utilized to generate diffusion weighting by placing two identical large gradients around a 180° RF refocusing pulse, the so-called Stejskal-Tanner approach [35]. A field gradient will cause a dephasing due to the resonance frequency being a function of location. The phase position is inverted with the 180° RF refocusing pulse and by applying the identical field gradient again, the magnetization is rephased under the assumption that the affected protons are still at the same place. If this is not the case, i.e., if they moved due to motion, perfusion, or diffusion, the rephasing will be incomplete and the large gradients will cause a decreased sig-

nal. Since bulk motion exceeds the effect of diffusion by several magnitudes, a diffusion-weighted preparation followed by a rapid echo-planar-imaging readout module is the method of choice to image this tissue-specific parameter. The technique is currently an important element in the work-up of patients with cerebral ischemia, in conjunction with perfusion studies and MRA.

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