Sequenze di impulsi base in MRI
Contrasto e pesatura delle immagini

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In order for a structure (physiological or pathological) to be clearly visible in a magnetic resonance image there must be a difference in signal intensity (i.e. a contrast) between it and the adjacent tissues.
Contrast-to-noise ratio (CNR)

Measure of the ability to differentiate between two adjacent anatomic structures in an MR image on the basis of their signal intensities in relation to image noise.

\[ CNR = \frac{S_A - S_B}{\sigma_{noise}} \]
Three intrinsic features of a biological tissue contribute to its signal intensity or brightness on an MR image and hence image contrast:

- The proton density $\rho$, i.e. the number of excitable spins per unit volume, determines the maximum signal that can be obtained from a given tissue. Images with contrast that is mainly determined by proton density are called proton density-weighted or simply proton density images.

- The spin-lattice relaxation time $T_1$ of a tissue which is the time it takes for the excited spins to recover and be available for the next excitation. $T_1$ affects signal intensity indirectly. Images with contrast that is mainly determined by $T_1$ are called $T_1$-weighted images ($T_{1w}$).

- The spin-spin relaxation time $T_2$ of a tissue which mostly determines how quickly an MR signal fades after excitation. $T_2$ affects signal intensity indirectly. Images with contrast that is mainly determined by $T_2$ are called $T_2$-weighted images ($T_{2w}$).

Proton density, $T_1$ and $T_2$ may vary widely from one tissue to the next. Depending on which of these parameters is emphasized in an MR sequence, the resulting images differ in their tissue-tissue contrast. This provides the basis for the soft-tissue discrimination and diagnostic potential of MR imaging.
Other parameters that are sequence specific contribute to the observed contrast:

- **Repetition Time (TR):** is the interval between two successive excitations of the same slice. It determines the amount of $T_1$ relaxation that is allowed to occur.

- **Echo Time (TE):** is the interval between application of the excitation pulse and collection of the MR signal. It determines the amount of transverse ($T_2$) relaxation that is allowed to occur before the signal is read.
The shorter the TR, the smaller the component of longitudinal magnetization that is restored and is available for subsequent excitation. As a consequence, the MR signal decreases as well. This process is known as saturation.
T₁ contrast (T₁ weighted images)

With short values of TR the signal coming from regions with short T₁ will be more intense (image more white) than that coming from regions with long T₁ (image mostly black)
T₁ contrast (T₁ weighted images)

Increased T₁ weighting
With long values of TE the signal coming from regions with short $T_2$ will be less intense (image more black) than that coming from regions with long $T_2$ (image mostly white)
**T$_1$ and T$_2$ weighted Images : Effect of TE**

T$_2$ contrast (T$_2$ weighted images)

- TE = 1 ms, TR = 5000 ms
- TE = 20 ms, TR = 5000 ms
- TE = 50 ms, TR = 5000 ms
- TE = 100 ms, TR = 5000 ms
- TE = 200 ms, TR = 5000 ms

Increased T$_2$ weighting
Long values of TR together with short values of TE give raise to images in which the signal is proportional to the amount of spins inside the region.

A proton density image: everything is almost the same color, except for the skull.
The different steps that make up an *MR pulse sequence* are:

- **Excitation of the target area**
  - Switching on the *slice-selection gradient*,
  - Delivering the *excitation pulse* (RF pulse),
  - Switching off the *slice-selection gradient*.

- **Phase encoding**
  - Switching on the *phase-encoding gradient* repeatedly, each time with a different strength, to create the desired number of phase shifts across the image.

- **Formation of the echo or MR signal**
  - *Generating an echo*

- **Collection of the signal**
  - Switching on the *frequency-encoding or readout gradient*,
  - *Recording* the echo.

These steps are repeated many times, depending on the desired image quality.
Multislice Imaging

- Conventional imaging with “inactive” repetition times (TR) between two successive excitation pulses is highly inefficient, especially when using sequences with long scan times and long TR (e.g. scan time of more than 4 min for acquisition of a $T_{1w}$ SE image with 256 excitations and a TR of 1000 ms).

- The “wait times” or “dead times” can be put to good use by exciting and recording signals from other slices during this period. In this way, more slices instead of only one can be acquired in the same time.
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- Gradient echo (GRE) sequences.
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In SE sequences the spin-echo sequence $90^\circ - \tau - 180^\circ - \tau - \text{echo}$ is applied.

In GRE an echo is generated by the inversion of the frequency-encoding gradient.

These sequences are the basic MR pulse sequences.
Spin Echo (SE) Sequences

- Spin echo sequences use a *slice-selective 90° RF pulse* for excitation.

- Then *dephasing occurs* because some spins precess faster than others as a result of the *static magnetic field inhomogeneities*.

- A *180° RF pulse* is then delivered to reverse and refocus the spins.

- It serves to eliminate the effects of static magnetic field inhomogeneities but cannot compensate for *variable field inhomogeneities* that underlie spin-spin interaction (T₂).
Spin Echo Pulse Sequence Diagram

1) Steady state: no magnetization in xy-plane
2) After 90° RF pulse: all magnetization precessing in xy-plane
3) Decay of signal due to spin dephasing (T2 and T2*)
4) 180° refocusing pulse after 1/2 TE interval: spin reversal
5) After full TE interval: spin rephasing and full recovery of magnetization (echo)
Spin echo sequences are characterized by an excellent image quality because the effects of static field inhomogeneities are eliminated by the 180° RF pulse.

The tradeoff is a fairly long scan time (because of the 90° excitation pulse).

SE sequences are used as the standard sequences for acquiring $T_{1w}$ or $PD_w$ images.

**$T_1$ weighting:**
- Short TE: 10-20 ms
- Short TR: 300-600 ms
- Typical scan time: 4-6 min

**$PD/T_2$ weighting:**
- Short TE: 10 ms / long TE: 80+ ms
- Long TR: 2000+ ms
- Typical scan time: 7-15 min

True $T_2$ weighting
Gradient Echo (GRE) Sequences

- They are also known as gradient-recalled echo or fast field echo (FFE) sequences.

- The frequency-encoding gradient coils are used to produce an echo rather than a pair of RF pulses. This is done by first applying a negative pulse to destroy the phase coherence of the precessing spins (dephasing). Subsequently, the gradient is reversed and the spins rephase to form a gradient echo.

- Flip angles different than 90° can be used.
Gradient Echo Pulse Sequence Diagram

1) Steady state: no magnetization in xy-plane
2) After excitation RF pulse (α): all magnetization processing in xy-plane
3) Spin dephasing through frequency-encoding gradient
4) Spin rephasing through frequency gradient reversal
5) Rephasing (echo) after TE interval: full recovery of transverse magnetization
Since the flip angle can be set to less than 90° it does not take too much for the magnetization to recover, so very short repetition times (TR) can be achieved.

Faster imaging is possible compared with SE.

Static field inhomogeneities are not compensated for and the signal decays with $T_{2^*}$. The image contrast is called $T_{2^*}$ contrast.

Since some GRE sequences are very fast (very short TR), part of the signal will be “left over” from cycle to cycle. This signal must be destroyed when $T_{1w}$ images are acquired. The destruction of the residual MR signal is called spoiling and is accomplished by turning on the slice-selection gradient to dephase the spins before the next RF pulse is applied. Popular spoiled GRE sequences are SPGR (spoiled gradient echo) and FLASH (fast low angle shot).
**Gradient echo**

**$T_1$ weighting:**
- Large flip angle: 70-110°
- Short TE: 5-10 ms
- Short TR: <50 ms
- Typical scan time: seconds to minutes

**$T_2^*$ weighting:**
- Small flip angle: 5-20°
- Longer TE: 15-25 ms
- Short TR: full recovery possible because flip angle is small
- Typical scan time: seconds to minutes

**PD weighting:**
- Small flip angle: 5-20°
- Short TE: 5-10 ms
- Short TR: full recovery possible because flip angle is small
- Typical scan time: seconds to minutes
An Inversion Recovery (IR) sequence is a sequence with an additional 180° inversion pulse that precedes the usual excitation pulse.
Inversion Recovery

- The inversion pulse flips longitudinal magnetization from the positive z-direction into the negative z-direction.

- No signal forms after delivery of the $180^\circ$ RF pulse.

- The inverted longitudinal magnetization vector moves through the transverse plane to return to its original orientation. After some relaxation has occurred, the RF pulse is applied. The time between the $180^\circ$ pulse and the RF pulse is the *inversion time (TI)*.

- Image contrast can be manipulated by changing the TI.

- Two IR techniques are widely used in routine clinical applications: the Short TI Inversion Recovery (STIR) sequence and the Fluid-Attenuated Inversion Recovery (FLAIR) sequence.
STIR Sequences

- STIR (Short TI Inversion Recovery) sequences are widely used for fat suppression because they reliably eliminate the signal from fat at all magnetic field strengths.

- A standard STIR SE sequence inverts the longitudinal magnetization of both fat and water by delivery of the 180° pulse, which is followed by a TI of some hundred milliseconds.
The TI is adjusted such that the 90° RF pulse is emitted exactly at the moment when fat passes through zero.

The TI for fat suppression is about 150 ms at a field strength of 1.5 T and about 100 ms at 0.5 T.
FLAIR Sequences

- FLAIR (Fluid-Attenuated Inversion Recovery) is an inversion recovery technique that differs from STIR in that very long TI values (typically about 2000 ms) are used.

- With such long inversion times, there is nearly complete suppression of the signal from fluids (e.g.: cerebrospinal fluid) while there is excellent detection of signals from brain tissue, tumors, edema, and fat.

- FLAIR sequences are very useful for detecting lesions with a poor contrast to surrounding brain tissue.
Multiple echo sequences

- **Several echoes** can be generated in a single cycle with both SE and GRE sequences:
  - SE: additional spin echoes are produced by applying extra 180° refocusing RF pulses.
  - GRE: multiple gradient echoes are generated by repeated reversal of the frequency-encoding gradient.
Multi echo techniques are employed for two reasons:

- The generation of multiple echoes enables acquisition of a sequence of images that differ in their echo times and $T_2/T_2^\ast$ weightings.

  - e.g: with a TR of 2000 ms, a PD*w image (TE = 20 ms) and a T*w image (TE = 80 ms) could be obtained with a single measurement (double echo sequence).
• e.g: $T_2$ (SE) and $T_2^*$ (GRE) maps can be obtained by collecting a series of images with variable TE and fitting them pixel-by-pixel against the $T_2/T_2^*$ recovery equation.

➢ The multiecho technique accelerates data acquisition and can be used for ultrafast imaging.
There are several reasons why it is desirable to speed up scanning.

- A fast sequence allows one to perform dynamic studies, e.g. to track a contrast medium bolus.

- Shorter acquisition is less prone to motion artifacts. A sequence that is fast enough can be acquired during breath-hold and thus yields images without respiratory artifacts.

Various techniques are available to shorten scan time:

- Use of state-of-the-art gradient and RF systems to full capacity and more effective timing of conventional sequences (fast GRE).

- Sampling of multiple echoes with different phase encodings (FSE, EPI).

- Incomplete filling of k-space (fractional echo imaging, partial Fourier imaging, rectangular field of view).
K-Space

- Data collected from the signals is stored in a mathematical area known as k-space.

- K-space has two axes with the horizontal axis \((k_f)\) representing the frequency information and the vertical axis \((k_\phi)\) the phase information. It is a graphic matrix of digitized MR data that represents the MR image before Fourier transformation is performed.
Each line in k-space corresponds to one measurement and a line is acquired for each phase-encoding step. The center line (0) is filled with the data that is unaffected by the phase-encoding gradient (gradient isocenter) and is the most important line for the overall image intensity after FT.
The lines in k-space do not correspond one to one with the lines in the resulting MR image. Rather, data in the center of k-space (central lines: application of shallow phase-encoding gradient slopes) primarily determines contrast in the image while the periphery (outer lines: application of steep phase-encoding gradient slopes) primarily contains spatial information.

In routine 2D MR imaging, k-space is filled sequentially one line at a time from one extreme of k-space to the other (linear k-space ordering).

Alternatively, k-space can be filled starting from the center toward the periphery (centric k-space ordering).
Fast or Turbo Spin Echo Sequences

- Fast Spin Echo (FSE) sequences (also called Turbo Spin Echo (TSE) or Rapid Acquisition by Relaxation Enhancement (RARE) sequences by some manufacturers) are modified SE sequences with considerably shorter scan times.

- This can be accomplished by delivering several 180° refocusing RF pulses during each TR interval and briefly switching on the phase-encoding gradient between echoes. In this way, optimal use is made of the TR interval by sampling several echoes \textit{with different phase encodings} after each excitation pulse.

- During each TR interval an echo train is acquired and the number of echoes acquired is called the \textit{turbo factor} (or RARE factor or acceleration factor).

\[
\text{Scan time} = \frac{TR \times (n^\circ \text{ of phase-encoding steps}) \times NEX}{\text{turbo factor}}
\]
FSE sequences have a longer TR with respect to SE in order to deliver as many 180° refocusing RF pulses as possible (FSE : TR 4000+ ms; SE : 2000–2500 ms).

FSE are well suited for $T_2^*$ images since the effective TE of FSE sequences is normally longer.
Fast Gradient Echo (GRE) Sequences

- Fast gradient echo (GRE) sequences (also known as turbo gradient echo or ultrafast gradient echo sequences) used in conjunction with state-of-the-art gradient systems (active shielding) achieve echo times below 1 ms with repetition times of 5 ms or less.

- Fast GRE is basically a conventional GRE sequence that is run faster.

- It could make use of incomplete filling of k-space.

- Fast GRE sequences yield an excellent image quality although a slice can be acquired in only a few seconds (typically 2–3 sec).

- Fast GRE highly suitable for dynamic imaging, for example, to track the inflow of a contrast medium bolus.
Partial k-space acquisition

The k-space is symmetric with respect to the central line (the negative half is the mirror image of the positive half) and with respect to the center of the frequency axis.

From this observation two possibilities arise for speeding up acquisition:

- **Partial Fourier Imaging**: only half the lines (or slightly more) in the phase-encoding direction are filled.

- **Fractional or Partial Echo Imaging**: refers to a technique with incomplete filling of the frequency-encoding lines by sampling only part of each echo.
Contrast Agents

- **Image contrast** in MR imaging results from differences in signal intensity (SI) between two tissues and is determined by intrinsic and extrinsic factors. These are respectively properties of the different tissues and properties of the MR scanner, especially of the pulse sequence used.

- **MR contrast media** are pharmaceutical preparations that are administered in MR imaging to further enhance the natural contrast and to obtain dynamic (pharmacokinetic) information.

- Contrast agents used for MRI must have specific physicochemical properties and suitable pharmacokinetic profile.
Most MR contrast agents contain unpaired electron spins. The magnetic moments of electrons are 657 times greater than those of protons.

Unlike radiographic contrast media, which are directly seen on an X-ray absorption image, a MR contrast medium, such as a gadolinium complex, acts indirectly by altering the relaxation properties of surrounding hydrogen protons mainly by:

- Shortening $T_1$ and $T_2$ relaxation times
- Faster dephasing of magnetization through local field inhomogeneities (susceptibility effects)
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The interactions occurring between contrast medium electrons and tissue protons comprise “inner-sphere relaxation” (through interaction with bound water) and “outer-sphere relaxation” (e.g. arising from the diffusion of water nearby). Both processes contribute substantially to the overall effect of MR contrast media.
CONTRAST AGENTS

Magnetism

- **Diamagnetic substances**: all the electrons are paired. No magnetic moments: this substances show mild negative effects on local magnetic fields. By far the majority of all substances are diamagnetic.

- **Paramagnetic substances**: they have a magnetic moment (resulting from individual unpaired electrons spins). When no external magnetic field is present, the magnetic moments occur in random pattern and there is no net magnetization. Because of their powerful magnetic moment, substances with unpaired electrons are preferred as MR contrast media. Most of the clinically available MR contrast media are paramagnetic metal ion compounds (gadolinium chelates, manganese, iron).

- **Superparamagnetic substances**: Very strong magnetic moment (10- to 1000-fold) resulting from the arrangement of the paramagnetic ions in a rigid crystal lattice. Superparamagnetic contrast agents are solid substances that not only have $T_1$ and $T_2$ effects but also markedly distort the local magnetic field (magnetic susceptibility).

- **Ferromagnetic substances**: similar to the previous category. These substances retain their magnetization even after the external magnetic field has been removed and subsequently become permanent magnets. The best known example is iron (Fe).
Two main categories of contrast agents exist:

- **Positive agents**: they increase the signal in $T_{1w}$ images (Gd-chelates, Mn$^{2+}$)
- **Negative agents**: they diminish the signal in $T_{2w}$ images (Iron Oxide Particles).
Gd chelates

- Gd$^{3+}$ is a very paramagnetic ion (7 unpaired electrons) but, as most of the metal ions is highly toxic (its diameter is virtually identical to that of calcium ions). It may not be introduced into the body as a free ion but only after chelation to a ligand.

- The ligands used for complexing should have a strong and specific affinity for the metal ion (DTPA, DOTA, DTPA-BMA, HP-DO3A, BT-DO3A, BOPTA). However, as complex binding is a reversible process (equilibrium reaction between free and bound forms), a small portion of the central ion may be released.

- The amount of release is so small that no appreciable toxic effects occur. As an additional safeguard, most commercially available contrast medium preparations contain excess amounts of free complexes (typically Ca/Na complexes) to immediately intercept any gadolinium ions which are released.

- Besides greatly reducing the toxicity of gadolinium, the ligands determine the biodistribution of the compound.
Most MR contrast media used today belong to this group and behave as extracellular contrast media that distribute in the vascular and interstitial spaces following intravenous administration.
Super Paramagnetic Iron Oxide nanoparticles (SPIO : AMI-227, ferumoxtran, SineremR/CombidexR) can be administered indirectly (subcutaneously), directly (endolymphatically), or intravenously.

Other names are Ultrasmall Super Paramagnetic Iron Oxide particles (USPIO) or Monocrystalline Iron Oxide Nanoparticles (MION). Following intravenous infusion, these agents remain in the blood for 24–36 hours before they accumulate in the lymphnodes and lymphatic vessels. As they are phagocytosed by macrophages and hence reach high local concentrations.

They have a pronounced $T_2$ shortening effect which decreases the signal (negative contrast).

Iron oxide nanoparticle preparations are also being developed as vascular contrast media (blood pool agents).
Joseph P. Hornak website: http://www.cis.rit.edu/htbooks/mri/

«How Does MRI Work ?»
Dominik Weishaupt, Victor D. Köchli, Borut Marincek

«MRI In Practice»
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