Fundamentals of MRI measurements for gel dosimetry

Y De Deene
MR department (-1K12), Ghent University Hospital, De Pintelaan 185, 9000 Gent, Belgium

E-mail: yves.dedeene@ugent.be

Abstract. In radiotherapy gel dosimetry a humanoid phantom is irradiated according to the planned treatment of a patient. This results in a three-dimensional dose distribution. In order to read-out the gel dosimeter phantom, magnetic resonance imaging (MRI) is often used. Due to specific disturbances both the spatial and the dose reliability can be compromised. It is essential that the measurement sequence is optimized and that possible imaging artifacts are compensated in such a way that the proposed spatial and dose accuracy are met. In this review, several sources of disturbances are treated and compensation strategies are proposed. A code of good practice for the read-out technique is proposed. Finally, a tool for quality control of the imaging sequence is presented.

1. Introduction

In the early days of gel dosimetry, magnetic resonance imaging (MRI) was suggested as the method to read-out the gel dosimeters. The use of magnetic resonance imaging as a non-destructive measurement of a dosimeter gel was first proposed in 1984 by Gore et al [1]. The proposed method uses the Fricke ferrous sulfate chemical dosimeter solution [2]. It was found that the conversion of ferrous (Fe^{2+}) to ferric (Fe^{3+}) ions by ionizing radiation alters the magnetic moment of the metal ion [1]. As a result, the spin relaxation times (T1 and T2) of the hydrogen nuclei in the aqueous gel are reduced. Different models have been described that explain the mechanism of how the relaxation rates are affected by the paramagnetic substances [1,3–5]. Several experimental studies were performed on Fricke gels investigating the effect of the gelling substances [6], the relation between dose sensitivity and the ferrous sulfate concentration [7] and the relaxation mechanisms at different field strengths [3,4].

In monomer/polymer gel dosimetry, the conversion of co-monomers to polymer aggregates upon irradiation alters the mobility of surrounding water molecules. This also results in a change in the spin-lattice relaxation rate R1 (= 1/T1) and spin-spin relaxation rate R2 (= 1/T2) [8]. The dose-response of R2 is more pronounced than of R1. To explain the effect that the radiation-induced polymerization has on the R2 relaxation rate, a model of fast exchange [9] is adopted [10–12]. It is shown in later studies that not only the relaxation rate can be used as an imaging parameter but also other MR contrasts such as magnetization transfer [13–15] and chemical shift [16].

The target figure of accuracy that is aimed in gel dosimetry for high-precision radiotherapy is about 2–3% of the maximum dose in regions of homogeneous dose and a spatial error of less than about 2 mm in regions of high-dose gradients. However, in a conventional MR scanner, several imaging artifacts may cause errors in the final dose map. These errors may be classified in dose inaccuracies or in deformations of the dose maps. Studies of these different artifacts have resulted in different compensation strategies.
The problem in evaluating the final accuracy of the dose maps obtained with gel dosimetry is that there is no such thing as a “golden standard” to compare with. The most reasonable strategy is to compare doses obtained with gel dosimetry with doses obtained by the “most reliable” dosimetry techniques that apply to a certain spatial dimension. As such, dose profiles of a single field (photons and electrons) can be compared with dose profiles obtained with an ionization chamber or diamond detector [17–18]. In two dimensions, gel dosimetry can be compared with film dosimetry [17,19–20]. Dose distributions obtained with gel dosimetry have been compared with the outcome of treatment plans [19,21–27]. The verification of the treatment plan can be seen as the major purpose of gel dosimetry in radiotherapy quality assurance.

Besides the possibility of systematic errors, the dose maps will also contain stochastic noise. To minimize the stochastic noise in the images, the imaging sequence parameters should be optimized. At this moment, other imaging techniques apart from MRI are investigated to read out gel dosimeters, amongst which optical scanning [28], CT scanning [29], ultrasound [30] and others.

2. MR contrast and imaging sequence

Whatever imaging technique is applied to map a dose-effective contrast (R1, R2, MT, optical absorbance, X-ray absorbance, ultrasound attenuation, dielectric constant, etc.) there are two essential criteria that should be accomplished in the imaging technique: First of all, the images should not contain systematic errors and secondly, the stochastic deviations on each voxel should be as low as possible within a reasonable measurement time and for a certain image resolution. An interesting parameter to evaluate the stochastic deviations is the minimum detectable dose difference, defined as the dose resolution [31].

It is regrettable that only in a few studies presented in the scientific literature, the imaging sequence is optimized with respect to signal-to-noise ratio and that almost no publication mentions a homogeneity study of the R2 maps. However, in applying gel dosimetry in three dimensions, the homogeneity of the field is highly determining the reliability of the dosimetry technique [32,33]. It should be noted, however, that in practice the optimal scanning technique depends on the application. For example, for most IMRT applications, it is important that the dose distribution can be obtained in three dimensions in a time span of one overnight with a resolution of about 1 mm and stochastic deviations in the order of 1% of the maximum dose. While investigating the dose distribution around a brachytherapy-source, a higher spatial resolution can be required but only a few 2D images may be sufficient instead. For these applications, the dynamic range of the gel system may be more important than the dose resolution issue. The same applies to dose verification of high-LET irradiations.

While comparing imaging methods the mentioned criteria should be kept in mind. A fair comparison between different imaging techniques should include an evaluation of image uniformity, spatial resolution, point spread, total measurement time, the maximum phantom volume that can be scanned and dose resolution. It is highly appreciated that in publications on gel dosimetry where MRI is used, the sequence parameters (field-of-view (FOV), matrix size (MS), slice thickness (d), repetition time (TR), echo time (TE), inter echo time spacing (TEI), number of slices, number of echoes, number of acquisitions (NEX) and total measurement time), the scanner parameters (scanner type, coil used, field strength) and the signal-to-noise ratio in the parametric images (SNR) would be provided as this enables comparisons of different imaging sequences and scanners.

3. MR imaging artifacts and compensation strategies

In treating imaging artefacts, we will mainly focus on T1 and T2 measurements but many of the artifacts that occur in these measurements may also appear in images obtained with other MR sequences.
The spatial accuracy of the dose maps is affected by geometrical distortions. Eddy currents, main magnetic field inhomogeneities and gradient inhomogeneities cause machine related geometrical distortions, while susceptibility variations and chemical shift variations in the imaging volume cause object related geometrical distortions. Also dose inaccuracies can be machine related such as those caused by eddy currents, stimulated echoes, inhomogeneities in the B1-field and standing radiofrequency (B1) waves or they can be object related such as temperature drift and molecular self-diffusion. Table 1 gives an overview of the most important MRI artifacts that may compromise the reliability of gel dosimetry.

Table 1. Overview of important artifacts that may occur in MRI gel dosimetry classified by two criteria.

| Geometrical distortions | Dose inaccuracies |
|-------------------------|-------------------|
| Machine related         | Object related    |
| Field inhomogeneity     | Susceptibility differences |
| $B_0(x,y,z)$            | $\Delta \chi(x,y,z)$ |
| Gradient non-linearity  | Chemical shifts   |
| $g(x,y,z)$              | $\sigma(x,y,z)$   |
| Eddy currents           | Stimulated echoes |
| $\Delta B_0(t), \Delta g_{x,y,z} (t)$ | $M_{xy}(TE)$ |
| Temperature Drift       | Molecular self-diffusion |
| $T(t)$                  | $D(x,y,z)$        |

3.1. Image non-uniformities

3.1.1. Appearance. A parametric MR image of a uniform sample may demonstrate areas of non-uniform signal intensity. For gel dosimetry purposes, non-uniformities result in areas of over- and under-dosages if not corrected for.

3.1.2. Occurrence. Image non-uniformities will mainly occur in images recorded with a surface coil acting as a transmitter. Some imaging sequences are more sensitive to B1-field inhomogeneities than others, the main reason of image non-uniformities.

In T1 imaging for Fricke gel dosimetry, severe non-uniformities were found when a spin-echo sequence was used with different repetition times (TR) [33]. These non-uniformities are attributed to a non-uniform B1 field in combination with inherent differences in T1 relaxation for different relaxation times. These non-uniformities were found to be considerably less pronounced when an inversion recovery sequence was used with different inversion times (TI).
In T2 imaging for monomer/polymer gel dosimetry using a multi-echo sequence in combination with a circularly polarized (CP) head coil, the R2 map was found to be uniform over an area of 120 cm in the centre of the coil, while the R2 values (apparent dose values) decreased considerably near the edges of the coil (figure 1).

![Figure 1](image1.png)

**Figure 1.** R2 maps of a homogeneous cylindrical gel phantom scanned with the head coil (a) and with the body coil (b)

This was not the case when a body coil was used instead. However, measuring R2 using the body coil both as transmitter and receiver is at the cost of signal-to-noise. With high-field strengths (as for example in micro-imaging systems) a sample dependent non-uniformity can be seen. When using a multi-echo sequence with non-equal echo time intervals, non-uniformities in the R2-image are very likely to occur. Only a shift in one of the inter-echo time intervals may cause severe non-uniformities (figure 2).

![Figure 2](image2.png)

**Figure 2.** R2-images of a QA gel phantom recorded with a multi-echo sequence with different echo intervals. The upper left image was obtained with equal echo time intervals (TE = 20, 40, 60, ...). The lower image was obtained with non-equidistant echo time intervals (TE = 20, 40, 60, 90, 110, ...). The graph on the right is a profile through the images on the left.
3.1.3. Reasons. There are several mechanisms that are responsible for non-uniformities in normal spin-echo images. These include RF field inhomogeneity, RF standing waves, skin effect at high field strengths, crosstalk between multiple slices, mistuning of the head coil, eddy currents and static field inhomogeneities [34]. Most of these non-uniformities have an effect on the images that is proportional with the image intensity. As a result, the artifacts are cancelled out after fitting the quantitative parameter (T1 or T2). However, some of these artifacts may not vanish completely in the parametric images if some other sequence specific mechanisms interfere. In clinical MR-scanners, the non-uniformities in the T1 and T2 images are mainly caused by B1 field inhomogeneities. It is well known that the B1 field generated by a radio-frequency coil is not completely homogeneous. B1 field inhomogeneities are attributed to RF amplifier distortions [35], digitization of the RF pulse [36], RF coil geometry [37–39] and penetration in the scanned object [40,41].

In the quantitative T1 spin-echo experiment, the incomplete excitation in some parts of the phantom due to B1-field inhomogeneity makes that the restoration of the longitudinal component of the magnetization is different for different repetition times. It is clearly seen that the inhomogeneous signal intensity pattern varies over the different T1 weighted base images [33]. Also in our T2 studies, the non-uniformities are mainly caused by an inhomogeneous B1-field in combination with stimulated echoes. As a result of the inhomogeneous B1 field, the flip angle of the nuclear magnetic moments after an excitation or a refocusing pulse will not be the same throughout the scanned volume. Thus the history of spin magnetization during a multi spin echo sequence will depend on the position of the nuclear moments in the slice and therefore the deviation in the R2 value will depend on the position [42]. Computer simulations solving the Bloch equations for the multi-echo sequence predict the correlation of the measured R2 with the local B1 field. The simulations are completely in accordance with the experimental findings. By mapping the B1 field it is now possible to predict how the R2 deviations will vary with slice position [42].

![Temperature images recorded with the proton resonance frequency method at several time points during a multi-echo sequence. The interval between two successive maps is approx. 4 hours. The sequence was stopped after the recording of image IV. The scale is in degrees Celsius.](image)

Figure 3. Temperature images recorded with the proton resonance frequency method at several time points during a multi-echo sequence. The interval between two successive maps is approx. 4 hours. The sequence was stopped after the recording of image IV. The scale is in degrees Celsius.

Another source of non-uniformities is an inhomogeneous temperature drift of the gel phantom during scanning. Due to RF power absorbed by the gel, a temperature rise in the order of 1–3 °C is not uncommon. As the outer boundaries of the phantom are surrounded by air (mostly in flow), temperature differences in the phantom will build up [43]. As the T2 of the dosimeter gel is...
temperature dependent, dose errors in the order of 3% to 10% (relative to the maximum dose) can be expected.

3.1.4. Compensation strategies. It has already been mentioned that T1 images can be obtained by an alternative spin inversion recovery sequence [33] if the uniformity in the T1 images exceeds 2-3% with the spin-echo sequence. It is the authors' opinion, (although not experimentally tested yet), that strong spoiling gradients at the end of the phase loop may give some improvement.

The B1 field can be measured by several ways and can be used to correct the R2 images. However, in that case, also the influence of the B1 field upon the R2 image has to be known. An analytical expression cannot be derived easily. Computer simulations solving the Bloch equations may help in deriving this correlation. A more practical, but theoretically less founded method is to measure the R2 distribution in a homogenous phantom (for example, the gel phantom before irradiation) and using this image-set as a template to correct the resulting R2 images. It is obvious that these post-processing corrections are founded on the fact that the position of the phantom can be determined accurately. In applying this strategy, quality control of the reproducibility of the non-uniformities and the dependency of the non-uniformities on phantom shape should be performed on a regular basis. A more direct way of minimizing B1-field related non-uniformities is by using the body coil as a transmitter. This way, a more homogeneous B1-field will be applied over the phantom. However, if the body coil serves as both receiver as transmitter, the signal-to-noise ratio will be significantly lower than in the case of a head or surface coil. Some scanners are equipped with receive-only coils that can be used in combination with the body coil acting as transmitter. This results in a more homogeneous B1-field while still preserving a good signal-to-noise ratio.

The temperature drift related non-uniformities can be disposed of by centric k-space filling [43]. This issue will be discussed further (in paragraph 3).

As non-uniformities may lead to severe dose errors and are very likely to occur to some extend in three dimensional scanning of the gel phantom, it is of ultimate importance that the uniformity of the parametric images is measured in advance and that scanning is performed subsequently to keep the non-uniformity level below acceptable levels.

3.2. Image distortions

3.2.1. Appearance. The geometrical shape of the phantom is deformed in the dose maps (parametric images). These deformations may have an effect on the global image or may occur only locally in part of an image, especially around inclusions of other structures in the phantom. Some structures of the phantom may be displaced with respect to others. Important to note is that displacements and scaling of the whole phantom may also occur both in plane as out of plane.

3.2.2. Occurrence. Low magnetic field scanners may suffer more from machine related image distortions than cryogenic magnets. The inclusion of other structures such as air cavities and low-density materials may result in object related distortions in the vicinity of these structures. Slice displacements may occur in scanners with non-active shielded gradients.

3.2.3. Reasons. Spatial encoding of the recorded MR-signal is based upon the correlation of magnetic field strength and the frequency of the rf pulses, described by the Larmor equation: $\Omega_f = \gamma B(r)$. By switching linear magnetic field gradients in three orthogonal directions during the MR-sequence, an encoding in three orthogonal directions is obtained. These gradients, invoked by use of gradient coils, may deviate from there linearity to some extend. Furthermore, the main magnetic field, $B_0$, is not completely homogeneous.
Figure 4. Frequency encoding in the ideal situation of a linear gradient and in the case of non-linear gradients in the frequency encoding direction.

This results in a deformation of the recorded image. Figure 4 illustrates how the frequency encoding is perturbed in the presence of a non-linear magnetic field gradient. Similar encoding errors occur during phase encoding and slice selection.

To measure the magnitude of deformations from non-linear gradients and main magnetic field inhomogeneities several phantoms have been proposed [44–46]. In observing in-plane distortions a pin-cushion phantom is often used. To account for errors in the construction of the phantom, the phantom is first scanned by use of CT. By overlaying the images indicating the positions of the tubes of the MR images on the CT images a distortion map can be derived. Apart from these static deviations in the magnetic field and gradients, the magnetic field may also deviate from the theoretical expected shape due to time-varying magnetic field components. These time-dependent magnetic field deviations are caused by “eddy currents”. The eddy currents are induced through switching of the imaging gradients giving way to an electromotive force that acts on the cryostat and metal casings. Several techniques to measure and analyze eddy currents in clinical scanners have been described [47–55]. The eddy current induced magnetic field is mostly described by a first order approximation composed of a global offset of the main magnetic field, $\Delta B_0(t)$ and a change in the magnetic field gradients, $\Delta g_i(t)$ ($i = x,y,z$) [47].

The eddy current related spatial encoding errors are mainly due to eddy current fields that are present during frequency encoding and slice selection. The different encoding errors are listed in figure 5.

To measure slice displacements, a pyramidal phantom can be used [55]. A special designed quality control phantom consisting of a perspex plate with holes drilled in special directions and filled with gel can also visualize slice warping (see further).
Figure 5. Different slice displacements caused by eddy currents invoked by switching of slice selection and frequency encoding gradient. An offset in the main magnetic field during slice selection causes a slice shift in the direction of the slice selective gradient (a) while a main magnetic field offset during frequency encoding causes a shift in the direction of the frequency encoding gradient (b). A gradient offset induced by eddy currents of the frequency encoding gradient will cause a slice rotation in the direction of the freq encoding gradient (c) while a gradient offset induced by the slice selective gradient will cause a change in viewing direction (d).

To extend gel dosimetry to phantoms that include air cavities (for example to investigate effects of electronic disequilibrium), materials with different electron densities are inserted in the gel phantom. These materials possess most often a different magnetic susceptibility. This will result in susceptibility related distortions in the base images and in the final parametric images. The distortion is inversely proportional to the receiver bandwidth. Also the inclusion of materials with a different chemical composition (organic liquids, fats) in the gel may result in a (chemical) shift of these objects in the frequency encoding direction.

Figure 6. Two cylindrical gel phantoms scanned in different directions illustrate susceptibility related deformations at the interface between both recipients. The circular lines are drawn on the image to show the actual boundary of the phantoms.

In figure 6 an example of a susceptibility related artifact is shown. This example was obtained by coincidence: In order to save some measurement time, two gel phantoms were placed in the scanner at the same time. The magnetic field and the frequency encoding direction are oriented upward in the images. It can be clearly seen that the phantoms are distorted near the interface between the phantoms. When the phantoms are oriented perpendicular to the magnetic field, the artifact disappears. Also
changing the frequency and phase encoding direction will make the distortion disappear. Another example of susceptibility artifacts caused by the guiding catheter of a brachy source can be found in another abstract in these proceedings [56]. In this example the magnetic field distortion is shown as imaged and calculated numerically.

3.2.4. Compensation strategies. External (fiducial) markers on the phantom are often used to allow image fusion with computer planning or other dosimetry techniques. These external markers may also serve as an indicator (solely!) of deformations or slice displacements. A scaling error of the phantom can also be detected by use of image fusion/matching software.

To measure machine related distortions, use can be made of a dedicated quality control phantom (as discussed further). A distortion map can be derived and used as a correction matrix for the dose map as has been done for MR-guided stereotactic neurosurgery [46].

Object related geometrical distortions may be compensated by first measuring or simulating the local magnetic field distortions caused by susceptibility differences and chemical shift artifacts. These magnetic field maps can then be used to construct a correction template that can be used to correct the parametric images [57]. Another method to correct for local magnetic field distortions is by view-angle-tilting [58]. This method has the advantage that no post-processing is needed but has the disadvantage that the point-spread function is broadened. Important to emphasize is that the artifacts act on a pixel-related scale instead of a geometrical scale. Increasing the resolution will decrease the artifact on a geometrical scale. Another important parameter is the receiver bandwidth. The distortions are inversely proportional to the receiver bandwidth. However increasing the bandwidth will decrease the signal-to-noise ratio.

3.3. Dose errors

3.3.1. Appearance. Dose errors cannot be observed directly by inspection of the parametric images or dose maps but may be discovered by comparison against another dosimetry technique or sometimes, if the causing effect is time-dependent, by repeating the experiment. In some cases, the dose response was dependent on the scanning orientation and other sequence parameters such as field-of-view. The whole dose response can be higher or lower with a constant offset or the dose sensitivity can be altered.

3.3.2. Occurrence. With the use of a multi-echo sequence the dose-response curve can be dependent upon scanning orientation and image parameters (field-of-view). These effects may be more pronounced in scanners with non-active shielded gradients and in applications where high gradient strengths and short echo times are used. It is well known that the R2 values of the gel are temperature dependent [8,17]. A temperature increase during scanning may result in a dose-underestimation. If the gels are not thermally equilibrated before scanning, temperature changes may cause severe dose errors. The chance for dose errors to occur is higher if scanning of the calibration tubes is performed in different circumstances and imaging parameters than the gel phantom.

3.3.3. Reasons and compensation strategies. The creation of eddy currents has already been discussed in paragraph 2. The magnetic fields induced by eddy currents experience a certain decay time. The succession of many imaging gradients in a multi-echo sequence may lead to a continuous increase of magnetic field during the start of the sequence. From measurements of the eddy currents created by gradient trains containing different numbers of gradients it is proven that a saturation in the eddy current induced magnetic field offset is obtained after 10 gradients [55]. Through computer simulations (solving the Bloch equation numerically) it is proven that the continuous change in the eddy current induced magnetic field offset during the first 10 echoes leads to a deterioration of the
slice profiles. This is believed to be linked with the change in excitation history of stimulated echo-components. The result is a change in the measured T2-decay curve. As the eddy currents (and especially the magnetic field offset) are dependent on the imaging direction, the disturbance of the excitation history of stimulated echoes is different and therefore also the measured T2 values.

![Diagram](image)

**Figure 7.** Multi-echo sequence with compensation for eddy current induced dose errors. A gradient train of 10 gradient units is added before each phase loop to bring eddy currents in steady state before the start of echo recording.

The addition of a gradient train consisting of a 10 fold repetition of the imaging gradients of one echo time interval brings the eddy currents in a steady state regime (figure 7). It is shown by computer simulations that with this preparation gradient train, the slice profiles are shifted in the slice-encoding direction but the shape of the slice profiles is not altered.

![Diagram](image)

**Figure 8.** R2 versus dose curve measured in the three different main directions of the scanner. The open symbols (and dashed lines) are for a measurement using an uncompensated standard multi spin echo sequence while the solid symbols (and solid lines) are for measurements using the same sequence preceded with a gradient train.
From figure 8 it is seen that with the gradient train compensation, the dose-response curve remains the same when scanning is performed in the three main imaging directions. It should be mentioned that the results shown in figure 8 were obtained with a PHAPS sequence on a Siemens SP1.5T Magnetom scanner that does not have active shielded gradient coils. For other scanners, the situation might be different. Therefore, it is advisable to measure the eddy current field for different numbers of gradients in order to determine the actual number of gradients required to bring eddy currents in a steady state regime.

Another source of dose errors is related to a temperature drift in the phantom during scanning. Although precautions are made in letting the gel phantom equilibrate at the room temperature of the scanner, a temperature increase may still occur during scanning by absorption of the RF energy of the excitation and refocusing pulses. In figure 9, the temperature in the gel phantom during a long scanning experiment is shown.

![Figure 9. Temperature course during a long-term scanning experiment of a cylindrical gel phantom. The temperature is recorded by use of a fluoroptic thermometry system with 6 operating channels (probes). The measurement history is also provided in a corresponding timetable.](image)

Note that a temperature increase is present during T2 scanning but not during temperature mapping (FLASH-sequence) illustrating the high-energy transmittance during the multi-echo sequence. The sequence can be made far less sensitive to temperature drift by using a centric k-space ordering scheme instead of a standard linear ordering scheme [43].

It should also be noted that partial volume effects may also lead to a misinterpretation of the dose in a pixel. It has been shown that partial volume effects can cause severe dose discrepancies in pixels adjacent to a point source as occurring in a brachytherapy experiment [59]. Also outer volume effects may result in dose errors. In-plane outer volume effects are related to the point spread function while in the slice selective direction outer volume effects may be expected from imperfect slice profiles. In multi-slice imaging care has to be taken in excitation of the slices. Even if excitation of the different slices is performed interleaved, cross-talk between slices may lead to inter-slice variations. These problems can be solved by using special designed slice-selective RF pulses and by increasing the time between excitation of adjacent slices.

Some websites that provide lists of other imaging artefacts that may occur in clinical imaging applications are provided in the references [60–62].
4. How to optimize a quantitative T2 imaging sequence?

As the time available at the MR scanner is often limited in many institutes, the parametric imaging sequence should be optimized with respect to signal-to-noise. For quantitative T1 imaging, different optimization strategies have been proposed in the scientific literature [63,64]. Also, the statistical approach given for signal-to-noise optimization of the inter-echo-time interval in T2 imaging [65], can be easily extended to T1 imaging. For quantitative T2 imaging, the optimal inter-echo-time interval has been determined mathematically and experimentally verified for different sequences and computational algorithms [65,66]. It has been shown that the optimal echo-time recording period – this is the total time interval in which multiple spin-echoes are acquired (product of inter-echo-time spacing and number of echoes) – is independent of the inter-echo-time spacing.

Up to now, R2 maps are obtained in different slices resulting in a limited spatial resolution in the direction perpendicular to the dose maps. It can be expected that with the development of faster MR imaging techniques, gels will be scanned in three dimensions in a reasonable time period. It can be proven that in multi-slice imaging, it is better to optimize the number of echoes than to optimize the inter-echo-time spacing only. The reasoning behind this is based on the fact that within an optimal echo time recording period it is preferable to acquire as many echoes as possible. This is limited by the minimal inter-echo-time-spacing which is determined by machine related characteristics such as maximum gradient strength, sampling rate and SAR considerations. In practice, it is also advisable to check for imaging artefacts (uniformity, dose errors and geometrical distortions) while decreasing the inter-echo-time-spacing.

Then, if more than one slice is acquired, the time interval between the end of the echo-time recording period and the repetition time can be used to scan another slice (figure 10).

Figure 10. Multi-slice multi-echo sequence showing the optimal sequence parameters. The number of spin-echoes acquired for each slice is optimized.

As from a certain number of slices, not all slices can be recorded within one repetition time. In that case, the repetition time can be extended to cover exactly the time needed to acquire all slices. The algorithm to determine the optimal echo time looks as provided in figure 11.
Figure 11. Flow-chart of the algorithm to determine the optimal number of spin-echoes in a multi-slice multi-echo sequence. The minimum inter-echo-time spacing and the minimum repetition time are imposed by scanner related limitations. The range of R2-values is gel specific (i.e. determined by the dynamic dose range and dose sensitivity of the gel). For the total R2-range, an optimal inter-echo-time can be derived mathematically along the equations provided in reference 65. If the total calculated echo-time recording period for all slices is smaller than the repetition time the echo-time recording period is artificially extended to cover the total repetition time. If the total calculated echo-time recording period for all slices extends the minimum repetition time, it is the repetition time that is increased to the total calculated echo-time recording period.

5. A quality control phantom for gel dosimetry

In order to perform a fast check-up of the most important characteristics of the quantitative sequence, a multi-purpose quality control phantom can be used. The cylindrical phantom as drawn schematically in figure 12 is filled with a gelatine gel and contains different structures constructed in polymethyl methacrylate (PMMA). If the phantom is scanned in eight different equidistant slices, information is obtained on different characteristics that enable to evaluate the performance of sequence and scanner with respect to quantitative imaging (figure 12). When performed at different sites, this enables to make an inter-comparison between different sequences and scanners.
Figure 12. The multi-purpose quality control phantom of which eight image slices through the phantom provide a check of respectively (from left to right and top to bottom) image resolution, slice profile, signal-to-noise ratio, slice warp, ghost artifacts, pincushion distortion, quadrature errors and susceptibility and chemical shift artifacts. With the drawing of the different sections, some images as obtained at the Expert 1T Siemens scanner (Ghent University hospital) are provided. The different sections are discussed in detail in the text.
The structures in the phantom are very similar to other quality control phantoms as from the concerted research project of the European Community [67,68] and from the American Association of Medical Physicists (AAPM) [69].

5.1. High contrast spatial resolution (section A)

This section consists of two blocks of PMMA. For the purpose of measuring the spatial resolution in the frequency- and phase-encoding direction, they have been arranged diagonally and rotated by 90 degrees to each other. Each block contains seven arrays of square pins. Each of the smaller pin arrays contains five to nine square pins of the same size. The centre-to-centre spacing of the pins is equal to twice the size of the pin. The sizes of the pins are $s = 0.4, 0.5, 0.7, 1.0, 1.5, 2.0$ and $2.5$ mm.

![Figure 13. Spatial resolution section with holes of different sizes.](image)

In order to obtain an objective measure of the resolving power, the use of the modulation transfer function (MTF) is highly recommended. The MTF is defined in terms of how an imaging system demodulates the amplitude of a sinusoidal input.

![Figure 14. Schematic black box scheme illustrating the action of MR imaging on two different signal input functions](image)

The MTF can be defined as the ratio of the output and input modulation function. If $S_i_1$ and $S_i_2$ are the minimum and maximum amplitude in the sinusoidal input respectively, the input modulation function is defined as

$$ M_i = \frac{S_i_2 - S_i_1}{S_i_2 + S_i_1} \quad (1) $$

and similarly the output function is

$$ M_o = \frac{S_o_2 - S_o_1}{S_o_2 + S_o_1} \quad (2) $$
The modulation transfer function is then defined as

\[ MTF = \frac{M_o}{M_i} \]  

(3)

The MTF is a function of the spatial frequency in alternations between high-signal and low-signal regions and can thus be written as MTF(k). The input function in the case of the square holes in section A of the PMMA phantom is a symmetric square wave. Note that the square wave contains different spectral components. The square wave can be written as a combination of different spectral components according to a Fourier series expansion. In order to predict the output of the square wave after MR imaging, each sinusoidal component should be multiplied with the modulation transfer function applying for that specific frequency.

The MTF(k) can also be obtained from the response on a step function. In section A, this step function is realized by use of a square Perspex block with sharp edges (figure 15a-b).

![Figure 15](image)

**Figure 15.** Procedure to extract the MTF(k) from an edge response function (ERF(x)). The procedure is further explained in the text.

The ERF(x) is obtained by taking a profile through a phantom containing a structure with an abrupt change in proton density like a gel phantom containing a massive block of PMMA. Apart from the PMMA blocks containing the holes, section 1 of the MPGP also contains a square massive PMMA block. Intensity profiles are taken through the square (see figure 15b-c). The ERF(x) is then spatially differentiated to obtain the line spread function (LSF(x)) (see figure 15d). The modulation transfer function (MTF(k)) is obtained by taking the Fourier transform of the LSF(x) (figure 15e). To obtain the optimum pixelsize, the MTF(k) can be multiplied by the spatial frequency k (figure 15f).
MTF(k) is a function of the imaging resolution (FOV/MS). A higher imaging resolution (finer pixel size) will result in a broader MTF (see figure 16c).

Figure 16. MTF(k) for different imaging resolutions: The edge response function, ERF, for different resolutions (a) is differentiated along the x-direction to obtain the line spread function, LSF (b). The LSF is then Fourier transformed to obtain the modulation transfer function, MTF as a function of spatial frequency (c). Upon multiplication with the spatial frequency the optimum pixel-size can be derived (d).

5.2. Uniformity and signal-to-noise ratio (section B)

Besides the position indicators this section is without any structures. In accordance to the NEMA-standard, the signal-to-noise ratio (SNR) can be obtained by scanning the same section two times and calculating the difference image [70]. The signal-to-noise ratio is then defined as:

\[
SNR = \sqrt{2} \cdot \frac{\bar{S}}{\sigma_{\text{diff}}}
\]  

with \( \bar{S} \) the average pixel intensity in the original images and \( \sigma_{\text{diff}} \) the average standard deviation in the difference image. By this method, non-repetitive noise is investigated. For gel dosimetry (no moving structures), the non-repetitive (stochastic) noise is unstructured.

An alternative method to obtain the SNR is to subdivide the scanned image in square regions (e.g. 7-by-7 pixels) and calculating both the mean value and the standard deviation in all regions. The structural SNR is defined as the ratio of the mean pixel intensity and the standard deviation of all mean pixel intensities in the different regions or mathematically:
The stochastic SNR is defined as the ratio of the mean pixel intensity and the mean value of the standard deviations in all regions or mathematically:

\[
SNR_{stoch} = \frac{\bar{S}}{\sqrt{\frac{1}{n} \sum_{l=1}^{n} \sum_{i,l} (S_{i,l} - \bar{S})^2}}
\]

In these equations, \(\bar{S}\) is the average pixel intensity in the area covered by the phantom, \(n\) is the number of square regions covered by the phantom, \(N_{reg}\) is the number of regions, \(S_{i,l}\) is the pixel intensity in pixel \(i\) of square region \(l\) and \(\bar{S}_l\) is the average pixel intensity in square region \(l\).

Figure 17. Subdivision of the image in square regions for statistic measurements

To obtain a measure of the uniformity in a larger scan area, a larger phantom can be used. A liquid filled phantom can be used, but care should be taken with convection currents of the liquid that may occur in the phantom. These currents may lead to additional motion artifacts that may be interpreted as non-uniformities. In our measurements we use two cylindrical phantoms filled with a gelatin gel: one phantom measures 30 cm by 10 cm diameter and provides uniformity characteristics in the longitudinal direction while the other one measures 12 cm by 30 cm diameter and provides uniformity characteristics in the axial plane.

5.3. Slice profile (section C)

This section contains two 11.3 ° opposed wedges in PMMA. The dimension of each wedge is 50 mm \(\times\) 100 mm. To obtain the slice profile, the “edge response function” is extracted first by averaging over several horizontal lines. The edge response function is then differentiated and the x-coordinates are scaled by a factor equal to 0.2 \(\times\) FOV \(\times\) MS. The y-coordinates are scaled by a factor to convert to percentages of maximum intensity. The slice profiles are obtained for all base images. This way, one can verify if the slice profiles change in shape for the different echoes (for example due to eddy currents or stimulated echoes).
Figure 18. Phantom section for measuring slice profiles consists of two opposite oriented wedges with an opening angle of 11.3 ° (a). The image shows a gradually change in pixel intensity due to partial volume effects (b). The slice profiles are obtained (c) for the different base images by spatially differentiating the intensity profiles. The slice thickness in this example was 5 mm.

From figure 18c it can be seen that apart from the slice profiles through the first and second base image, all slice profiles have a similar shape but different amplitude. The differences in the shape of the first two profiles are attributed to a non-equilibrium in the contribution of stimulated echoes to the signal [32]. This also causes deviations in the measured mono-exponential T2 signal decay. As a result, it is better to leave out the first two base images in the R2 fitting.

The slice profiles also give a measure of outer slice contributions to the measured dose in each voxel. In figure 18c the dose outside the region indicated by the dashed lines also contributes to the measured dose as the dose weighted by the relative signal intensity.

5.4. Quadrature ghosts, spatial linearity (section D)

This section contains a 10 mm thick plate of PMMA, with a signal-producing hole of 30 mm diameter located at an eccentric location. Additionally, a pattern of four arrays of holes is arranged on a square. The holes are 1.5 mm diameter and the centre-to-centre spacing is 5 mm.

Figure 19. Schematic drawing from phantom section D for investigating point mirrored ghost artifacts. The different regions used for calculating the magnitude of the ghost artifacts (G, N and T) are indicated (a). A typical MR base image is shown in figure (b).
Receive quadrature errors can be evaluated using the image passing through section D. When the object is in the lower right corner, the ghost will appear in the upper left corner. Regions-of-interest (ROI) values are taken from both the true image and the ghost image (figure 19a). The magnitude of the ghost error ($E_{rqe}$) is quantified by expressing the ghost ROI value ($G$) minus the background ($N$) as a percent of the true ROI value ($T$) of the objects image.

$$E_{rqe} = \frac{(G - N)}{T} \times 100\%$$

(7)

Spatial linearity can be measured by evaluating the image of the holes arranged on a square. The deformation of the square can be expressed as a percentage by taking the ratio of the maximum deviation and the real dimensions of the square (i.e. 110 mm).

![Figure 20. Schematic view of a pin-cushion distortion indicating the characteristic lengths $l$, $l_{ph}$ and $l_{ro}$ used for the calculation of the relative maximum distortion](image)

The spatial distortion in the read out direction ($ro$) is then given by the value $SD$ as

$$SD_{ro} = \frac{(l - l_{ro})}{l} \times 100\%$$

(8)

and in the phase encoding direction

$$SD_{ph} = \frac{(l - l_{ph})}{l} \times 100\%$$

(9)

5.5. Phase encoding errors (section E)

Besides the position indicators this section is without any structures. For multi-slice measurements the center slice should be positioned at the centre of section E.

![Figure 21. Schematic drawing of section E indicating the different regions of interest G, N and T that are used in equation 10 to calculate the phase encoding error.](image)
Phase-encoding errors will appear as multiple images displayed along the phase-encoding axis of the image. Regions-of-interest (ROI) values are taken from the true image, the brightest ghost region and the background. The magnitude of the ghost error ($E_{\text{phe}}$) is quantified by expressing the ghost ROI value ($G$) minus the background ($N$) as a percentage of the true ROI value ($T$) of the image.

$$E_{\text{phe}} = \frac{(G - N)}{T} \times 100\%$$  \hspace{1cm} (10)

5.6. Transmit quadrature errors (section F)

Besides the position indicators this section is without any structures. For multi-slice measurements the central slice should be positioned at the centre of section E. Transmit quadrature ghosts are evaluating using the image passing through section F acquired in multi-slice mode with the image passing through section E. The ghost will be located at the same relative position in section F as the object in section D. ROI's are taken over the ghost ($G$) and some active area ($T$) of the object section F, to determine the percentage error ($E_{\text{tqe}}$).

$$E_{\text{tqe}} = \frac{(G - N)}{T} \times 100\%$$  \hspace{1cm} (11)

No error should appear on systems with digital transmit modulators.

5.7. Slice position, slice warp (section G)

This section contains a 10 mm thick plate of PMMA with two arrays of angled holes, each measuring 1.5 mm in diameter. The holes are crossing each other at the centre of the plate and are arranged such that the holes of one array are at 90 degrees to the holes of the other. The holes are also inclined at a 45° angle to the main axis of the plate. To evaluate a possible slice shift one can use the projection of the holes as seen in the image. A slice shift can be measured by the indicated distance, D (figure 22b).

![Figure 22. Section G illustrating an ideal slice through the center of the section (a) and a slice that is shifted with respect to the center (b).](image)

The slice is shifted by a distance $S = D / \sqrt{2}$, whereby D is the distance of the centre of the two orthogonal parts of the array element.
Figure 23. Plot of slice warp. The original image of section G (a) is filtered in order to remove the background noise and the circular border of the phantom and is then subdivided in several square regions (b). The shift in the z-direction (c) is calculated from the crosses as indicated in figure 22b.

The average slice shift over all regions is a measure of how much the slice is shifted from the aimed slice position. Note that a mispositioning of the phantom will also result in an average slice shift different from zero.

The inter-slice variation can be comprised in a standard deviation with respect to the average slice shift. In the case of figure 23, the average slice shift amounted to 0.38 mm and the inter-slice variation to 0.31 mm.

5.8. T1/T2 contrast and relaxation times (section H)

This section contains five cylindrical vials that are filled with gel doped with Gd-DTPA. The measured R1 and R2 values may depend on many sequence parameters (such as field strength, used RF-coil, slice position, etc.). The five samples span a wide range of R2 values which enables to get a measure of the ability of the imaging sequence to measure R2. The five vials as indicated in figure 24 contain gels with Gd-DTPA concentrations as listed in table 2.
Figure 24. Schematic drawing from phantom section H indicating the five samples containing different concentrations of Gd-DTPA (a) and a corresponding spin echo image (TE = 20 ms; TR = 3 s)

Table 2. The concentrations of Gd-DTPA in the different samples.

| Vial | [Gd-DTPA] |
|------|-----------|
| I    | 0 mM      |
| II   | 1 mM      |
| III  | 2 mM      |
| IV   | 5 mM      |
| V    | 10 mM     |

Figure 25 shows typical R1-concentration plots for the five samples. A linear regression to the R1 values in figure 25a gives

\[
R1 = 0.739 + 3985.3985739.0\text{[Gd – DTPA]}^{-1}
\]  \hspace{1cm} (12)

and for R2 measured with the multi-spin echo sequence (figure 25b)

\[
R2 = 1.411 + 5222.5222411.1\text{[Gd – DTPA]}^{-1}
\]  \hspace{1cm} (13)

with [Gd-DTPA] the concentration of Gd-DTPA in molar and R1 and R2 in s\(^{-1}\).

Figure 25. R1 (a) and R2 (b) in the different vials as a function of the concentration of Gd-DTPA. The upper curve in b is measured with a single spin echo sequence using two different echo times while the lower curve in b is obtained using a multiple spin-echo sequence.

The five samples are chosen to cover a large range of R2 values. It should be noted that these 5 solutions may not be optimal for quality assurance of specific gel dosimeters. It is advisable to use irradiated monomer/polymer gel samples for a fair multi-center comparison of dose-R2 curves.
6. In conclusion

The different research groups applying gel dosimetry use different imaging sequences and different MR scanners (with different field strengths). The sequence parameters have not always been completely provided in the papers that report on their results. This can be misleading as the outcome is difficult to compare. The signal-to-noise ratio in MR images cannot be considered apart from the measurement time, the inter-echo time, receiver bandwidth and image resolution. Also it is seldom mentioned how sensitive the sequence and scanner are to imaging artifacts such as eddy currents, B1-field in-homogeneity, temperature drift and susceptibility differences.

Different MR characteristics should be investigated before using MRI as a read-out technique for 3D gel dosimetry. It is highly recommended to scan the gel phantom filled with a blank gel (i.e. a non-irradiated or radiation insensitive gel) prior to the gel dosimetry experiment in order to determine the homogeneity of the R2 maps. The R2 deviations can be easily translated in terms of dose errors. The imaging sequence should then first be optimized in order to minimize the non-uniformities in the R2 maps. Therefore the source of imaging artifacts should be determined and adequate compensation strategies should be applied. Apart from imaging artifacts it is also important to be aware of the slice profile and the actual image resolution. Spatial image distortions should also be quantified. Special attention should also be paid to possible temperature drifts during scanning, especially when much RF power is used as in the case of 3D applications. When imaging artifacts are minimized so that non-uniformities are reduced to less than 2% of the maximum dose, the number of echoes and repetition time should be optimized with respect to the signal-to-noise ratio in the final R2 maps.

The use of a quality control phantom provided with an imaging control procedure may help in assuring the accuracy of a certain measurement sequence to obtain dose maps. It can help in detecting sources of error in the dose maps. Also, it may help in establishing a more rigorous comparison between different quantitative T2 sequences and scanners. The quantitative sequences used for gel dosimetry have to meet more stringent requirements than for any other MR application and than mostly provided by scanner manufacturers. A multi-centre inter-comparison of the performance of different sequences can help in formulating the properties that sequences have to meet for gel dosimetry and in distributing knowledge to compensate for different errors.
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