Description of quality assurance measurements for quantitative MRI in the IQ-EMBRACE trial

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Version: Feb 21, 2018

Introduction

In the IQ-EMBRACE study ‘Quantitative MR Imaging in Locally Advanced Cervical Cancer; Sub-study under the EMBRACE II protocol’, participating centers will include quantitative imaging in the MRI exam that is conducted prior to treatment of patients with cervical cancer. As an option, such quantitative sequences can also be added to the MRI scans performed for brachytherapy treatment planning. To ensure that the quantitative imaging data collected in this trial is of high quality and consistent between participating centers, a quality assurance procedure is required before starting patient inclusion.

Within the group of participating centers a wide variety in scanners exists, from different manufactures, field strengths, and ages. As a result, novel sequences may be available in one institute but not in another. One approach to achieve consistency between centers would be to specify the trial sequences in great detail. The drawback however is that this inevitably would force us to design sequences for the oldest platforms, resulting in relatively old, slow and possibly imprecise sequences. We have therefore chosen a strategy where each participating center can optimize quantitative sequences, making optimal use of the possibilities of their scanner.

The quality assurance procedure consists of a series of measurements on phantoms, aimed to validate the accuracy and precision of the quantitative sequences proposed by each center for use in the clinical trial. The measurements are compared to ground-truth values available for the applicable phantoms.

As potential deviations from ground-truth values may arise from the specifics of the trial sequence, but also from specific calibration issues of the scanner itself, we also will scan so called benchmark sequences. These sequences are well established sequences, but typically too slow to allow use in a clinical setting. The calibration sequences are specified in more detail, so that intrinsic consistency between platforms may be expected.

This document describes the requirements for trial sequences, benchmark sequences, the phantom and the measurements required for four quantitative MRI techniques: T2 mapping, T1 mapping, diffusion-weighted imaging (DWI) and dynamic contrast-enhanced (DCE) imaging. In the descriptions of the sequences we followed the terminology of the quantitative imaging biomarker alliance (QIBA) by using the terms ideal, target, and acceptable. In this way there is some room to keep the acquisition time acceptable.

Experiments will be carried out in each participating center. Before starting the phantom measurements for quality assurance, the sequences should be tested on volunteers to verify image quality and absence of image artifacts. These images will be evaluated by the trial coordinators. The trial coordinators will be
available to advise on sequences and the details of the scanning procedure. If required, a visit to the center to participate in the QA measurements can be considered. Analysis of the data will be done at the Netherlands Cancer Institute and results will be reported back to the institutes.

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T2 mapping

Description of trial sequence

- accelerated multi-echo spin echo sequence or any alternative available
- Imaging plane: transversal
- Field of view (FOV) in APxRL > 260x260 mm
- Frequency encoding direction = RL to reduce breathing artifacts
- The pixel size is not specified, but should be sufficient to provide good SNR. Reconstruction pixels should be no less than half the size of acquisition pixels.
- coverage in FH direction: ideal = 120 mm, target/acceptable: 100 mm
- slice thickness: ideal = 3 mm, target/acceptable < 5 mm
- Minimum number of echoes: ideal ≥ 10, target/acceptable: 8
- Dynamic range (=range of echo times (TE) that must be covered): up to 200 ms
- Repetition time (TR): between 2000 and 5000 ms
- Echo spacing: determined by number of echoes and dynamic range
  - For Philips scanners: use dTE that results in perfect (i.e. nontruncated) pulses. Rule of thumb = minTE + 3ms, but check pulse design.

Description of benchmark sequence

- Non-accelerated multi-echo spin-echo: no parallel imaging, no partial fourier imaging
- Imaging plane: transversal
- Dynamic range: up to 200ms
  - echo spacing: use dTE that results in perfect (i.e. nontruncated) pulses. Rule of thumb for Philips scanners = minTE + 3ms, but check pulse design.
- TR: 2000 ms
- The FoV should encompass the phantom (250x250 mm², voxel size 2 x 2 x 4 mm³)
- Only a single slice needs to be scanned.

Phantom

- Eurospin II TOS (Diagnostic Sonar LTD, Livingston, Scotland)
- at room temperature (put the phantom in MR room a few hours before scanning to adjust to room temperature)
- Use coils that will be used for patients in the trial
- Measure temperature by putting a tube filled with water next to phantom. This tube should also be in MR room a few hours before scanning. Measure temperature before and after exam.
- The phantom is positioned in the center of the bore, tubes in cranial-caudal direction. See Fig. 1 for the selection and position of tubes in the phantom.
Fig. 1 Eurospin phantom with selected tubes for T2 mapping (left) and coronal view to show slice positioning (in yellow) for benchmark sequence

**Measurements**

- Measure temperature before scanning
- Plan the slice of the benchmark sequence through the tubes in the middle of the Perspex holder (see Fig. 1).
- Scan benchmark sequence
- Scan trial sequence
- Repeat benchmark sequence 3 times for short-term repeatability
- Repeat trial sequence 3 times for short-term repeatability
- Measure temperature after scanning

**Data transfer**

- Dicom files of the individual echoes
- Dicom files of the T2 map, if calculated by the scanner
- Temperature measurements
- Protocol parameters description of trial and benchmark sequence (e.g. txt file, pdf, examcard in case of Philips)
**T1 mapping**

**Description of trial sequence**

- Any sequence to measure the T1, for example: variable flip angle (VFA), inversion recovery, look-locker
- Imaging plane: transversal
- Field of view (FOV) in APxRL > 260x260 mm
- Frequency encoding direction = RL to reduce breathing artifacts
- The pixel size is not specified, but should be sufficient to provide good SNR. Reconstruction pixels should be no less than half the size of acquisition pixels.
- coverage in FH direction: ideal = 120 mm, target/acceptable: 100 mm
- slice thickness: ideal = 3 mm, target/acceptable < 5 mm
- Scanning of a B1 map with the same FOV is required for 3T systems, optional for 1.5T systems in case a variable flip angle approach is used.

**Description of benchmark sequence**

- series of inversion recovery (IR) sequences
- Imaging plane: transversal
- TR = 8000 ms
- Separate sequences with the following IR delays are to be scanned: 30, 50, 75, 100, 150, 200, 250, 300, 400, 500, 750, 1000, 1250, 1500, 2000, 4000 ms
- The FOV should encompass the phantom: 250 x 250 mm²
- voxel size: 2 x 2 x 4 mm³;
- Only a single slice needs to be scanned
- acceleration (e.g. parallel imaging, partial fourier) not allowed

**Phantom**

- Eurospin II TOS (Diagnostic Sonar LTD, Livingston, Scotland)
- at room temperature
- Measure temperature by putting a tube filled with water next to phantom.
- The phantom is positioned in the center of the bore, tubes in cranial-caudal direction
- Use coils that will be used for patients in the trial
- See Fig. 2 for the selection and position of the tubes.
Fig. 2 Eurospin phantom with selected tubes for T1 mapping

Measurements

- Measure temperature before scanning
- Plan the slice of the benchmark sequence through the tubes in the middle of the Perspex holder (as for T2 mapping see Fig. 1).
- Scan benchmark sequence. Note: please see page 11 for a modification of this measurement where tube #9 is replaced by tube #0 of the concentration series for DCE measurements. This saves an additional IR series measurement
- Scan trial sequence
- Optional: scan B1 map for 3T in case VFA approach is used
- Repeat trial sequence 3 times for short-term repeatability
- Measure temperature after scanning

Data transfer

- Dicom files of the series
- Dicom files of the T1 map, if calculated by the scanner
- Dicom files of the B1 map
- Temperature
- Protocol parameters description of trial and benchmark sequence (e.g. txt file, pdf, examcard in case of Philips)
Diffusion-weighted MRI

To assess the performance of the DWI sequence at each center, we follow the technical performance assessment of the QIBA DWI profile (1).

**Description of trial sequence**

- any sequence to measure DWI is allowed: single-shot Spin-Echo EPI, but may be alternative such as non-EPI
- Imaging plane: transversal
- b-values: at least 0, 200 and 1000 s/mm²;
- other b-values are allowed
- TE: ideal < 70 ms, target = minimum TE, acceptable < 90 ms
- TR > 2000 ms
- Maximize bandwidth by parallel imaging and partial fourier; use maximum gradients and slew rate available
- Fat suppression: yes
- Field of view (FOV) in APxRL > 260x260 mm²
- Frequency encoding direction = RL to reduce breathing artifacts
- The pixel size is not specified, but should be sufficient to provide good SNR. Reconstruction pixels should be no less than half the size of acquisition pixels.
- coverage in FH direction: ideal = 120 mm, target/acceptable = 100 mm
- slice thickness: ideal = 3 mm, target/acceptable < 5 mm
- Optional: B0 map.

**Description of benchmark sequence**

Use the sequence as recommended by the QIBA/RSNA committee. The protocol includes 4 b-values (0, 500, 900, 2000). Slice thickness is 4.0 mm with 25 slices being acquired, and 5 slices (typically slices 11 through 15) being used for analysis. TR is 10 seconds and TE is 101 ms. The phase-encoding direction is AP. Further details are provided in the manual for Philips (1.5T and 3.0T), Siemens 3T and GE 3T scanners. Please contact the trial coordinators if this manual is not available for measurements.

**Phantom**

- Diffusion Phantom Model 128 (High Precision Device, Inc, Boulder, Colorado, USA)
- Phantom preparation according to the phantom manual. Please be aware that this should be done already a day before!
- Allow for time to stabilize temperature at 0°C.
- Make sure tubes are entirely immersed in ice water; add some Gd to the water to reduce T1 and T2.
- Use coils that will be used for patients in the trial
**Measurements**

- Measure temperature
- Set-up according to the phantom manual: position central tube at center of bore to avoid distortions of b-values by gradient nonlinearities. For these set of measurements we only perform those related to the axial positioning of the phantom as described in the manual (see figure 7 in the manual).
- Perform trial sequence 4 times
- Perform clinical sequence 4 times
- Acquire a B0 map (if possible)
- Optional: Spatial measurements
- Measure temperature

**Data transfer**

- Dicom files of the individual b-value images
- Dicom files of the ADC map, if calculated by the scanner using b-values between 200 and 1000 s/mm²
- B0 field map if available of the same field of view
- Temperature
- Protocol parameters description of trial and benchmark sequence (e.g. txt file, pdf, examcard in case of Philips)
Dynamic Contrast-Enhanced MRI
To validate the performance of DCE-MRI sequences QIBA suggests to validate the following aspects (2):

- Accuracy and repeatability of T1 mapping sequence
- Signal stability over time
- Accuracy of measuring the concentration of the contrast agent

The accuracy of T1 mapping will be tested with the Eurospin T05 phantom. The latter two aspects will be investigated with a phantom consisting of different concentration values. We don’t use a benchmark sequence in this case

Description of trial sequence

- Spoiled gradient echo sequence or equivalent, mDixon is allowed
- Imaging plane: transversal
- Field of view (FOV) in APxRL > 260x260 mm\(^2\) such that also the femoral arteries are included in FOV.
- Frequency encoding direction = RL to reduce breathing artifacts
- The pixel size is not specified, but should be sufficient to provide good SNR. Reconstruction pixels should be no less than half the size of acquisition pixels.
- Coverage in FH direction: ideal = 120 mm, target/acceptable: 100 mm
- Slice thickness: ideal = 3 mm, target/acceptable < 5 mm
- The TR is defined by the number of slices and the size of the acquisition grid. Ideal: 5 ms, acceptable < 7ms
- TE as long as possible within the specified TR (to get good SNR for phase images). Acceptable: if phase data cannot be acquired, shortest TE can be used.
- Flip angle: Ideal = as large as possible, target/acceptable: > 20 degrees.
- Dynamic interval: < 5 s
- Number of dynamics sufficient to cover a total scanning time of 5 minutes
- Add at least two dummy scans
- Acquire both magnitude and phase of the signal. Acceptable: for 1.5T magnitude signal is allowed
- A power injector is required

Phantom
The phantom consists of ten tubes filled with gadolinium (Gd) concentration in an aqueous solution of manganese(II) chloride. The Gd concentrations (Dotarem) vary between 0 – 10 mM. 0.03% sodium azide has been added to prevent bacterial growth. This makes the solution toxic, so careful handling is required when opening the tubes.

The phantom should be used in combination with the Perspex holder of the Eurospin II T05 object.
To fill up the remaining gaps in the phantom, we provided eleven empty tubes. These should be filled at the institute with doped water: use 500 mL of water doped with about 0.5 mL contrast agent to fill the tubes. The exact amount of contrast agent is not important for this purpose.

![Image: Phantom set-up: front view (left) and side view (right): numbers represent numbers of tubes, whereas f refers to the filling tubes.](image)

**Fig. 4** Phantom set-up: front view (left) and side view (right): numbers represent numbers of tubes, whereas f refers to the filling tubes.

Without the Eurospin phantom holder, the phase signal cannot be validated well. Please contact us to discuss alternatives. For validation of the magnitude signal only, the tubes can be taped together.

**Measurements**

**Stability of the DCE-MRI sequence**

- Put the tubes in the scanner according to the set-up shown in Fig. 4.
- Place the holder in such a way that the tubes are aligned with the B0 field (see side view in Fig. 4)
- Run the full trial sequence (5 min) with all tubes in the FOV.
- Scan a B1 map in case of 3T

**Accuracy of concentration measurements**

This experiment consists of two parts

1. Estimate the T1 of the tubes with an inversion recovery series
   - TR = 8000 ms
   - Sequences with the following IR delays are scanned: 50, 75, 100, 150, 200, 300, 400, 500, 750, 1000, 1250, 1500, 2000, 4000
   - Only a single slice needs to be scanned. The FOV should encompass the phantom (250x250 mm, voxel size 2x2x4); the slice thickness and pixel size need to be sufficient to provide good SNR
   - acceleration (e.g. parallel imaging, half scan) not allowed
   - the same set-up can be used as with the previous experiment.
   - Measure temperature from one of the filling tubes before and after the IR series using an electronic thermometer.
• Optional: it is possible to perform these measurements together with the inversion recovery series for T1 mapping. For this replace tube #9 in Fig. 2 by tube #0 of the concentration series. In this case the above measurements can be omitted.

2. For evaluation of the phase signal it is important that the position of the different concentrations is the same. Therefore this experiment will be a little different:
• To set-up the phantom fill eleven gaps with the filling tubes, leaving one spot in the center for the actual concentration series
• Start with tube #0
• Acquire a survey followed by a short DCE sequence of 5 dynamics
• Replace tube #0 with tube#1, run short DCE sequence again, etc
• Make sure that no new pre-scans are made between the separate DCE scans. If this is not possible, one can also make a longer DCE series of 50 dynamics (5 dyns per tube) and have a pause after the fifth dynamic to change the tubes.

Data transfer
• Dicom files of all images acquired with the dynamic sequences
• Dicom files of the images with the inversion recovery series
• Description of dicom file content (tube numbers corresponding to the filenumbers)
• Temperature measurements
• Series number of DCE phantom (see label on phantom)
• Protocol parameters description of trial and benchmark sequence (e.g. txt file, pdf, examcard in case of Philips)
References


List of Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AP</td>
<td>Anterior-posterior</td>
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<td>DCE</td>
<td>Dynamic-contrast enhanced</td>
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<td>DWI</td>
<td>Diffusion weighted imaging</td>
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<td>EPI</td>
<td>Echo planar imaging</td>
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<td>FH</td>
<td>Feet-head</td>
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<td>FOV</td>
<td>Field of view</td>
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<tr>
<td>IR</td>
<td>Inversion recovery</td>
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<td>ME-SE</td>
<td>Multi-echo spin echo</td>
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<td>QIBA</td>
<td>Quantitative imaging biomarker alliance</td>
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<td>RL</td>
<td>Right-left</td>
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<td>TR</td>
<td>Repetition time</td>
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<td>TE</td>
<td>Echo Time</td>
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<td>VFA</td>
<td>Variable flip angle series</td>
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