Radiographic considerations of a multi-parameter MR research protocol for evaluating human tumour microvasculature.

J. J. Stirling[1], L. A. Culver[1], N. J. Taylor[1], A. R. Padhani[1]

[1]Paul Strickland Scanner Centre, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN, United Kingdom

Purpose: Proper design and execution of multicentre clinical trials involving the application of dynamic contrast enhanced MRI (DCE-MRI) requires close attention to a number of practical factors. These include imaging facility and equipment selection, patient (and lesion) choice, the need for flexible examination protocols and adequate quality assurance procedures. Having highly qualified and motivated technologists at the patient interface is key to success and here we describe the important practical radiographic aspects of this process.

Pre-examination preparations: The ability to undergo DCE-MRI studies may be an entry criterion for clinical trials and cancer patients are often highly motivated to undergo this. Informed consent with a full and clear explanation of the objectives and practical aspects of the study is needed initially. DCE-MRI studies are longer and require greater patient cooperation than routine studies, and with the need for repeat studies, patient compliance becomes a greater problem. To improve the success of examinations, the patient should view the imaging facility and meet the team involved in advance of their first scan. Arrival time has to allow for intravenous cannula insertion and time for patients to empty their bladder as a comfort factor and to evacuate the bowel in order to reduce internal organ motion and susceptibility artefacts. An accurate patient weight should be obtained for calculating contrast agent dose.

Positioning: Patient comfort for the duration of the study is important. Patient torso and coil repositioning has to be identical for each patient repeat study. The coil should be placed over the lesion under investigation and centred to the magnetic field for the measurement phase. Gd-doped water reference tube samples are also sited so that they can be seen on the measurement images (see quality assurance procedures). Constant patient contact and relaxing music gives patients a time frame that they can relate to. For further patient assurance and to reduce the sense of isolation, regular information - particularly when an injection is given - is needed.

Scan protocol: Advance preparations with phantoms and volunteer studies are often required to ensure that slice positioning, fields of view (FOV), phase encoding directions and slice distance factors are identical without incurring artefacts. Such images can be checked for the presence of artefacts, acceptable signal and contrast to noise measurements and sensitivity to the presence of contrast medium. Designing a protocol check list at this stage helps minimise accidental mismatching of scanning variables and acts as an *aide memoire*. As patients differ with regard to lesion location, the FOV, phase encoding and matrix may be adapted inline with accepted scan parameters. These modifications need to be noted and reproduced in the next imaging session. To choose the optimal imaging slice positions, T_1w/T_2w orthogonal anatomical images should be obtained and reviewed by a radiologist. The presence of an adequate lesion, representative of the tumour as a whole and confirmed to be in a region away from significant movement and source of artefact is usually needed.

Our T_1-weighted DCE-MRI protocol involves the acquisition of proton density (PD - TR=350ms, TE=4.7ms, FA=6^o, TA=162s,) and multiple T_1-weighted (T_1W) spoiled gradient-echo images (TR=11ms, TE=4.7ms, FA=35^o, TA=12s, 40 sets of images) with no change in gain or scaling factors. Contrast medium (0.1mmol/kg) is injected after four baseline images are acquired. The PD/T_1W image combination is used to quantify the changes in T_1-relaxation rates using a calibrated look-up table, which is converted into contrast agent concentration for each time point. The kinetic model of Tofts and Kermode[1] is used to derive values of K^{trans} (transfer constant) and v_e (extravascular extracellular leakage space).

Our T_2* DCE-MRI protocol uses a similar spoiled gradient-echo sequence (TR=30ms, TE=20ms, FA=10, TA<2s) which is run 60 times to measure the first passage of Gd DTPA (0.2mmol/kg). Time varying changes in signal intensity are converted into changes of R_2* and the application of a gamma variate function allows perfusion parameters rBV (relative blood volume), rBF (relative blood flow) and MTT (mean transit time) to be calculated.

Contrast medium injection: Injections are made using an automated power injector; this ensures the contrast injection rate (4 - 5ml/s), timing and normal saline flush volume/rate are consistent for the whole trial.

Follow-up studies: When imaging has to be duplicated on a number of occasions it is often not possible to ensure that the same technologist scans the patient. Operator errors can be reduced by having a team of at least 2 people, one an experienced radiographer-technologist and the other the physicist in charge of analysis or the clinician responsible for the study. Following initial anatomical imaging, the placement of imaging slices can be improved by constructive argument between machine operators. The protocol check sheet and a filmed record of slice positioning help ensure consistency. If lesions change in position, size or configuration with internal organ motion or as a result of a treatment effect, the new lesion location and corrected slice positions needs to be identified and recorded.

Calibration curves and quality assurance: T_1-relaxation rates are computed from a look-up table using the ratio of the matching T_1w dynamic and PD pixel intensities. The look-up table is created using a test phantom (Eurospin) with known T_1-relaxation rate gels using the same sequences and coils as in the main imaging study. The signal intensities of the gels are plotted against the known T_1-relaxation rates and a mono- or bi-exponential curve is fitted. Such calibration curves have to be produced for each coil, for each sequence in the study and when changes are made to the scanner (cryogen fills, service and software upgrades). An ongoing quality assurance program enables drifts in signal and contrast to noise ratios to be detected and corrected.

References

[1]Tofts, P.S. and Kermode, A.G. *Magn Reson Med.* 1991; **17**: 357