Tumour Response Assessment Using Diffusion-weighted MRI
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Introduction
The ability to detect tumour response at an early stage of treatment is desirable. Accurate assessment of response at an early stage may allow modification of treatment by intensifying therapy in non-responders with the aim of improving clinical outcome; or early termination of ineffective treatment to avoid unnecessary drug toxicity. In drug development, detection of drug effects on tumours in early phase clinical trials aids understanding of the mechanistic actions of drugs, and can help in determining a biological active drug dose for subsequent application.

Why use diffusion-weighted MRI?
Diffusion-weighted MR imaging is unique among imaging techniques as the image contrast and tissue quantification is based on differences in the mobility of water protons between tissues, which indirectly reflects cellular density and the integrity of cell membranes. No other current imaging technique provides insight into this aspect of the tissue microenvironment. The technique allows qualitative (visual signal intensity) and quantitative (apparent diffusion coefficient and diffusion volumes) evaluation of tumours before and after treatment.

When tumours are treated by a range of anticancer therapies (e.g. chemotherapy, radiotherapy, radiofrequency ablation, cryoablation, embolization and targeted novel therapies), treatment induced cell death by apoptosis, necrosis and cell lysis will lead to an increase in the mobility of water in the tissue microenvironment. This increase in water diffusion translates to an increase in the measured tissue ADC, which can be measured. Studies in animals and humans in a variety of tumour types have shown that successful anticancer therapy results in an increase in the measured tumour ADC.

How to measure treatment response by diffusion-weighted MRI?
To record tumour ADC values, a region of interest (ROI) is usually drawn to encompass the tumour of interest and the mean or median ADC value within the ROI recorded. ROIs can be manually drawn or by applying statistical region growing techniques available on some software. Increasingly, with the availability of more sophisticated software, it may be possible to segment a volume of interest (VOI) across the entire tumour region and make such comparison before and after treatment.

As tumours are often inherently heterogeneous, more sophisticated analysis of the imaging data could be considered. For example, using histogram analysis, it is possible to analyse the proportion of imaging voxels above or below set ADC threshold values before and after treatment. The use of the minimum ADC (ADC_{minimum}) within a ROI has also been advocated. However, it is important to note that when considering the ADC_{minimum}, this should not be taken from an area with significant artefacts, as spuriously low values may be encountered. One method of visualising tumour heterogeneity is by evaluating the distribution of ADC values within a tumour using frequency histograms, as well as by describing the kurtosis and skewness of the distribution. More recently, functional diffusion maps, also known as parametric response maps, have been applied to detect early and heterogeneous tumour response to anticancer treatment.

The significance of ADC change in relation to treatment should be considered by the level of statistical significance, measurement reproducibility, as well as biological relevance.