Comparison between ADC and QSI-derived parameters mapping and early effect of radiation therapy in a rodent tumour model

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Introduction

Q-space imaging (QSI) (1) is a MR diffusion imaging technique that does not rely on the assumption of a Gaussian probability density function (PDF) for the diffusion of water molecules within biological tissues. Because of restriction and hindrance of water diffusion in the complex micro structural architecture of tissues, QSI-derived diffusion parameters could be more powerful in probing micro-architectural disruption than the standard mean Apparent Diffusion Coefficient (ADC) which assumes a Gaussian PDF. Up to now QSI has been clinically applied to cerebral tissue with high 'native' anisotropy (2,3) and usefulness of QSI has not been investigated outside the brain. In a preliminary experimental setting, we compared changes in ADC versus QSI-related parameters before and 3 days after external radiation therapy in a rodent tumor model.

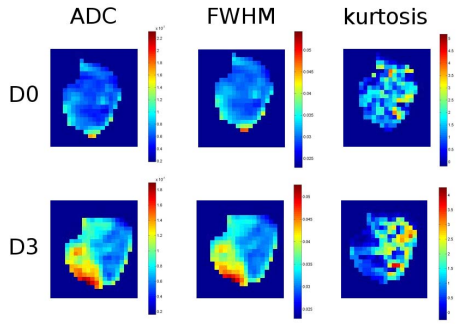
Materials and methods

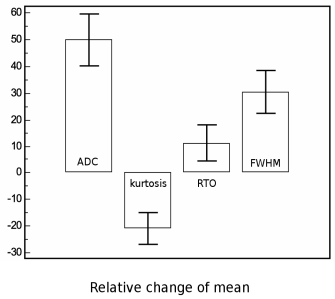
Micro-fragments of a syngenic rhabdomyosarcoma were subcutaneously grafted in both thighs of 10 male WAG/RijHsd rats resulting in 19 analyzable tumors. After reaching a sufficient size for efficient MR imaging (ranging from 1 to 3cm in diameter), rats were anesthetized and embedded within a homemade and individually-tailored alginate mould fitting the inner volume of a 4-channel wrist coil (Sense Wrist Coil, In Vivo Corp, Gainesville, Florida). Acquisitions were performed on a clinical 3T system equipped with 80mT/m gradients (Achieva 3T, Philips Health care, Best, The Netherlands). The SE-EPI QSI sequence had diffusion weighting for 16 b-values in the range 0 – 22 000 s/mm^2 (or equivalently: 16 equidistant q-values in the range 0 – 110 mm^{-1}) and for 6 diffusion gradient directions. Five axial slices of 5mm thickness covering the central area of the tumors were obtained. The in plane resolution was 1.5mm, 2 signal averages and a SENSE-factor of 2 were used. The acquisition time was about 10 minutes. Two acquisitions were performed: one with diffusion time Δ=54 ms (TE=110ms) and one with Δ=113 ms (TE=150ms). Immediately after the completion of the MR procedure, 14 Gy in a single dose were delivered to each tumor. An similar MR diffusion protocol was repeated 72 h after radiation therapy (RT) with re-use of the same mould as for the pre-RT session. Rats were thereafter euthanatized by a lethal injection of ketamine. Eight out of the 19 tumors were removed and fixed in formaldehyde for further pathological analysis. Data was processed using a homemade software developed with Matlab (The Mathworks Inc). Data for b=1000 s/mm^2 was used to reconstruct the standard mean ADC image. Q-space analysis yielded PDFs for all six directions. The PDFs were characterized by three quantities: the height (RTO: return to origin probability), the width (FWHM: full width at half maximum) and the kurtosis (k). A tensor analysis of the different quantities enabled the generation of mean value (trace/3) and fractional anisotropy (FA) maps for each parameter. Spatial averaged values (m) and standard deviations (sd) were calculated over all tumor voxels of the slice passing through the center of each tumor. Relative changes in m and sd when comparing pre- and post-RT data were calculated. Bar plots were generated for ADC, RTO, FWHM, and kurtosis using Medcalc® statistical software (Medcalc®, Mariakerke, Belgium).

Results and discussion

Figure 1 shows reconstructed maps of the mean ADC, FWHM and kurtosis before (D0) and three days after (D3) external RT in one of the 19 tumors. The area of increased ADC/FWHM in the lower left quadrant of the tumor at D3 corresponded to necrosis, as assessed by pathological analysis (not shown). The same area in the kurtosis map (right column) showed a decreased k-value which is consistent with less restricted (more Gaussian) diffusion within necrosis. The RTO-maps had more or less the inverse contrast of the FWHM-maps since the area of the PDF was normalized to 1 (not shown). Relative changes in m (mean with standard error to the mean (SEM)) for all 19 tumors are displayed in Figure 2 for ADC, k, RTO and FWHM. ADC seemed to be the most sensitive parameter with a mean increase of 50%. Dispersion is overall comparable for all parameters. Similar observations were made for the sequence with 113 ms diffusion time showing that full effect of micro-structural barriers on diffusing spins was already obtained at Δ=54 ms. For the FA of the different parameters, smaller changes were observed (not shown). Mean changes in sd are displayed in Figure 3, the sd being a measure for the average contrast. Much more dispersion is present, except for kurtosis. The values significantly varied with diffusion time Δ, demonstrating that Δ was crucial for optimizing the contrast.

In conclusion, ADC seems best suited for studying early tumor changes after radiation therapy. QSI provides additional information of which relevance needs further investigation.





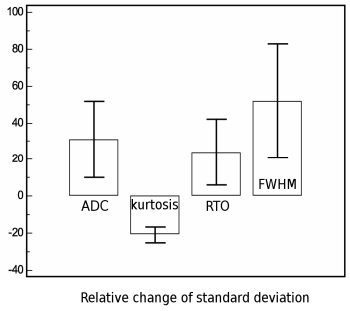


Fig. 1: tumoral parametric maps of the mean ADC, FWHM and kurtosis before (D0, upper row) and three days after (D3, lower row) external RT.	**Fig. 2:** Bar plot representation of the relative change of the mean for ADC, kurtosis, RTO and FWHM (Δ=54 ms) before and after RT. Error bars correspond to the SEM.	**Fig. 3:** Bar plot representation of the relative change of the standard deviation for ADC, kurtosis, RTO and FWHM (Δ=54 ms) before and after RT. Error bars correspond to the SEM.

References :

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