Multiparametric imaging of tumor boundaries using linear discriminant analysis

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Introduction.

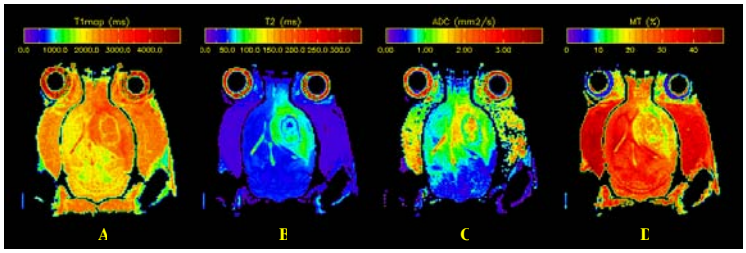
One of the main concerns in clinical tumor imaging is the correct delineation of tumor boundaries. In the case of high grade gliomas, tumor growth is associated with the appearance of necrotic areas, as well as surrounding edema. As possible markers for tumor delineation by MRI, previous studies have used different tissue parameters such as, the apparent diffusion coefficient (ADC) or the transversal relaxation time (T_2) of water. In this work, we report a novel approach based in the combined use of several MRI techniques and linear discriminant analysis (LDA) to discriminate between proliferative tumor, edema and healthy brain in rats bearing C6 gliomas. For this purpose, ADC, T_2, T_1 and magnetization transfer (MT) maps were obtained and LDA applied pixel by pixel to calculate the best combination of these parameters that would optimally discriminate the different regions. Our results reveal that the linear combination of the parameters provided significantly better discrimination within the different zones than the use of maps of independent parameters. LDA allowed the identification of tumor tissue in 98.9 % of the cases, edema in 93.5% of the cases, and healthy brain with a 91.9% success.

Materials and Methods.

Tumor model. C6 cells (10^5) cells were implanted stereotaxically in the brain of female Wistar rats (200-220 g). *In vivo MRI.* All the experiments were performed on a 7 T horizontal-bore magnet (16 cm bore) interfaced with a Bruker Pharmascan console, using a 3.8 cm commercial Alderman-Grant resonator. Anesthesia was initiated in an induction box with a mixture of isofluorane/oxygen (2%, 2.0 ml/h) and maintained (1.2 ml/h) throughout the MRI examination. T_2 weighted coronal images (6 slices 1 mm, TR: 4000 ms, TE: 65 ms) were acquired for tumor localization. Series of T_1, T_2, Diffusion weighted and magnetization transfer images were acquired in order to obtain parametric maps of each one. The same matrix size (128x128) was employed in all the acquisitions, so that direct pixel by pixel correlation could be investigated. T_1 weighted images were acquired with a spin-echo sequence (TR: 60-6000 ms, TE: 9.2 ms); T_2 images were obtained using a multi-echo sequence that collects one image per echo time (TR: 5000 ms, number of echoes: 45 and TE: 10-450 ms). Diffusion weighted images were acquired by a modified spin-echo sequence with diffusion gradients (TR: 2500 ms, TE: 25 ms, δ: 1.5 ms, Δ: 4 ms and b: 100-1000 s/mm^2). Finally, MT images were obtained using a spin echo sequence with or without a magnetization transfer module switched on (TR: 2500 ms, TE: 9.76 ms, MT module: 50 Gaussian pulses of 5 ms, interpulse delay: 300 µs, offset 1500 Hz, bandwidth 548 Hz). Data were transferred to a PC platform and analyzed with software written in-house in IDL (Iterative Data Language, Research Systems, Boulder, CO). Parametric maps of T_1, T_2, ADC and MT ratio were generated. Different regions of interest (ROIs) were selected in each slice and animal (edema, proliferative part of the tumor and healthy brain). Linear discriminant analysis was performed pixel by pixel in selected regions using the SPPS program as implemented in a PC platform.

Results and Discussion.

Figure 1 shows representative maps of T_1 (A), T_2 (B), ADC (C) and % MT (D). Average values obtained for each parameter in each region of interest are shown in Table. Both ADC and T_2 were much higher in the edema as compared to tumor or healthy tissue. ADC values were higher in the proliferative area of the tumor than in the contralateral healthy tissue, suggesting a lower cellular density in these tumors. The % MT values were significantly higher in the healthy brain than in the tumor indicating a higher content of immobilized water in the healthy brain. Interestingly, % MT values were not significantly different between tumor tissue and the surrounding edema. This suggests that the peritumoral edema region, as delineated in T_2 and ADC maps, may retain significant amounts of macromolecules, as in inflammatory responses or necrosis. Thus, the three imaginng methods used separately did not completely agree on the delineation of tumor boundaries. We investigated then the combined used of these methods using LDA. Step by step LDA showed that tumor tissue could be successfully identified by linear combinations of the A-C imaging methods in 98.9 % of the cases, edema was correctly predicted with a 93.5% of success, and healthy brain with a 91.9%.



	Region of Interest		
	Tumor	**Edema**	**Healthy tissue**
ADC (mm^2/s)	0.80 ± 0.12	1.37 ± 0.21	0.66 ± 0.16
T_2 (ms)	63.08 ± 5.38	80.54 ± 8.95	47.17 ± 2.89
% MT	21.23 ± 3.65	19.89 ± 3.68	34.26 ± 4.43

Figure 1: *Parametric maps for T_1, T_2, ADC and % MT*

Conclusions

Our results indicate that the delineation of tumor boundaries solely on the basis of single T_2, ADC or even MT maps is imprecise and that the combined use of these three imaging methods improves significantly tumor delineation.

Bibliography

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