Automatic Tumor Delineation by Multiparametric MR Analysis based on Endogenous Contrast

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Introduction Planning of tumor treatment with MRI-guided High Intensity Focused Ultrasound (HIFU) is generally based on contrast-enhanced T_1-weighted imaging. A waiting time between planning and HIFU treatment is required, because it is considered a toxicity hazard to start HIFU treatment with residual Gd-chelate still present in the tumor, as heating by HIFU may cause Gd entrapment in the tumor or accelerated transmetallation.[1] Treatment planning based on endogenous contrast would alleviate the need for a contrast agent, and thus reduce the toxicity hazard and shorten the total examination time. Furthermore, automated tumor delineation would allow for fast and objective target definition. However, previously described methods of (semi-)automatic tumor segmentation generally include contrast-enhanced MRI.[2,3] The aim of this study was therefore to investigate, whether accurate tumor delineation is also possible by multiparametric MR analysis based on endogenous MRI parameters.

Figure 1 Flow chart of the automatic tumor delineation method for feature vector $\{T_2, ADC\}$ with k=6.

Methods 10-12 weeks-old Balb/c mice were inoculated subcutaneously in the right hind limb with 2×10^6 CT26 colon carcinoma cells. MRI was performed approximately 10 days after inoculation. The multi-slice imaging protocol consisted of T_2-weighted imaging, Look-Locker-based T_1 mapping, MLEV-prepared T_2 mapping and double-spin-echo prepared Apparent Diffusion Coefficient (ADC) mapping (b-values 0-400 s/mm^2). For all sequences signal read-out was performed with echo planar imaging (EPI) to allow for fast acquisition. T_1, T_2 and ADC maps were determined from fittings with the appropriate signal models. Regions of interest (ROIs) were manually drawn by an expert reader to delineate the tumor in each slice of the T_2-weighted images. k-means clustering was applied on a large rectangular region containing the tumor and surrounding muscle, tumor edema and bone. Clustering was performed for each mouse separately. Optimization of the k-means method was performed by clustering with all possible feature vectors and various numbers of clusters k (k=2,3,4,5,6,7). Sensitivity and specificity values were derived by comparison between the k–means-defined tumor ROI and the user-defined tumor ROI. The sensitivity was calculated as the number of pixels that was correctly assigned by the k-means algorithm to tumor tissue divided by the number of pixels in the user-defined tumor ROI. The specificity was calculated as the number of pixels that was correctly assigned by k-means as not belonging to the tumor divided by the corresponding number of pixels not belonging to the tumor from the user-defined delineation. A flow chart of the automatic tumor delineation method is shown in Figure 1.
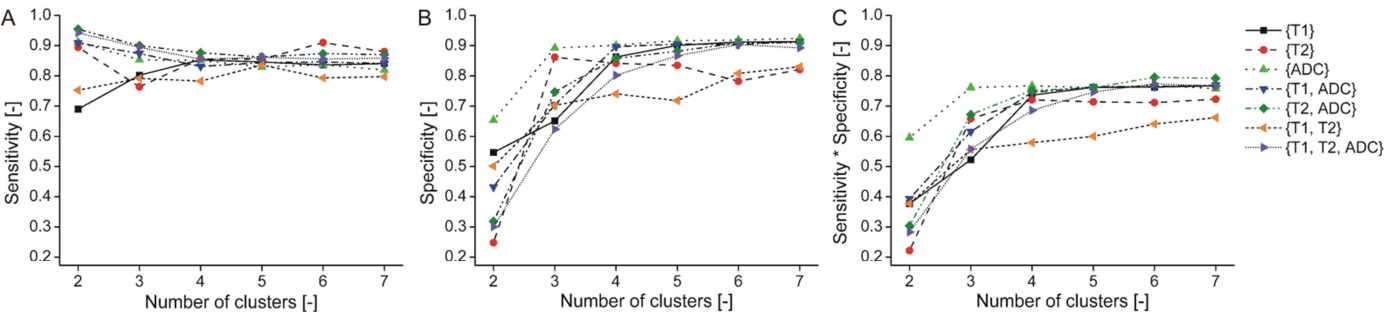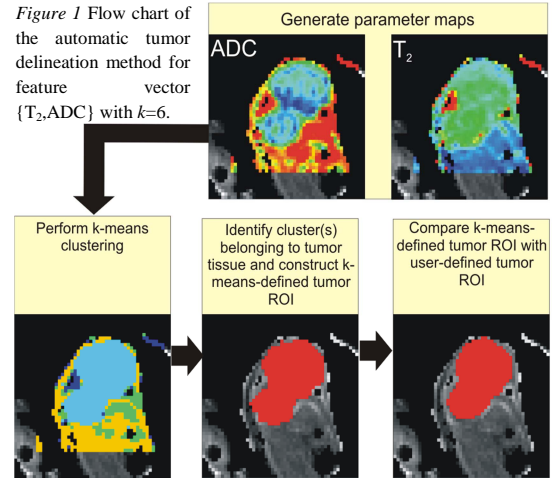

Figure 2 Sensitivity (A), specificity (B) and sensitivity*specificity (C) values for the different feature vectors (see upper right) as function of the number of clusters.

Results Sensitivity and specificity values for the different feature vectors as function of the number of clusters are displayed in Figure 2A and B, respectively. Selection of the optimum k-means method was based on the product of sensitivity and specificity (Figure 2C). The maximum value of this product was found for feature vector $\{T_2, ADC\}$ with the number of clusters k=6. For this k-means method the sensitivity and specificity were 0.87 and 0.90, respectively. A strong one-to-one correspondence was observed between tumor volumes derived from the user-defined delineation and those derived from the delineation resulting from k-means clustering with feature vector $\{T_2, ADC\}$ and k=6 (slope 1.02, R^2=0.99, Figure 3).

Discussion and Conclusion These results show that accurate tumor delineation can be performed with multiparametric MR analysis based on endogenous MR contrast. High sensitivity (0.87) and specificity (0.90) values were observed for k-means clustering with feature vector $\{T_2, ADC\}$ and k=6. Furthermore, a strong correlation between k-means-defined tumor volumes and user-defined tumor volumes was observed. In the near future, clinical translatability of this method will be investigated by application of the method on MRI data of patients with breast tumors. Ultimately, clinical introduction of this automatic tumor delineation method might allow for fast, objective and accurate tumor demarcation without the requirement of contrast agent injection.

[1]Hijnen et al, *Focused Ultrasound 2012*, ID:P-116-EA [2]Kannan et al, *J Med Sys* 2012;36-321-33
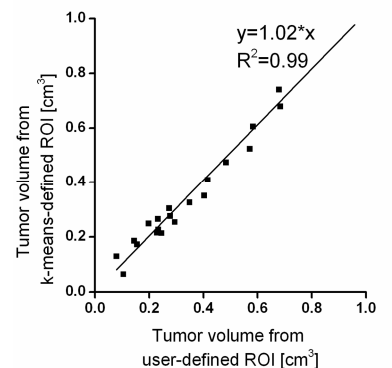[3]Alderliesten et al, *Invest Radiol* 2007;42:42-9

$y=1.02*x$
R^2=0.99

Figure 3 Tumor volumes derived from user-defined ROIs vs. tumor volumes derived from k-means with feature vector $\{T_2, ADC\}$ and k=6.