Quantification of Perfusion Changes in Childhood Tumors in Response to Therapy Using DCE MRI

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Introduction

Dynamic contrast-enhanced (DCE) MRI in combination with a two-compartment model allows the estimation of tissue perfusion, which is considered to be a capable tool to monitor diagnostic changes during oncologic therapy [3]. This technique was used to quantify changes in tumor perfusion, to test whether the novel application of this method to childhood tumors such as *Wilms' tumors*, *osteosarcomas*, and *lymphomas* is feasible for early detecting a response to therapy. Although it has been shown that changes in tumor perfusion occur before morphological changes [1,2], so far, these tumors are solely judged by their morphology, and therapy effects are determined predominantly based on changes of tumor size. Moreover, knowledge about the tumor perfusion (and oxygen supply) before therapy may aid in predicting the possible success of chemo-/radiotherapy. A pilot study was carried out and different methods to quantitatively describe the distribution of perfusion parameters within the tumor were used and assessed in their ability to allow for a comparison between follow-up studies as well as their ability to highlight changes.

Materials and Methods

All MRI examinations were performed on a 1.5 T scanner (Magnetom Sonata, Siemens, Erlangen). Routine T1-weighted and T2-weighted images were acquired in several slices covering the entire lesion, before as well as after contrast media injection (Magnevist, Schering, Berlin, 0.15ml/Kg, 40–60s). A T1-weighted rapid spoiled gradient echo sequence (SR-TurboFLASH: TR/TE/TI/FA = 7.0ms/3.86ms/120ms/12°) was used to acquire 2–3 slices (FOV/TH/matrix = 350mm/7mm/256x192) continuously over a period of 7–8 minutes with a temporal resolution of 1.5–5.8s and a pixel size of 1.37 x 1.37mm. When necessary, image registration was performed [6]. A pharmacokinetic analysis software was developed in MATLAB (The Mathworks, Inc., Natick), optimized in terms of robustness, and is being used successfully in large studies of adult tumors. Signal-time-curves (STC) were extracted on a pixel-by-pixel basis. A two-compartment model [5] with an additional time shift (t_0) was fitted to the STCs and the model parameters A, k_{21}, t_0 determined, as well as the descriptive parameters area-under-curve (AUC), max. signal enhancement (MSE), and time-to-peak (TTP). These were depicted in color-coded parameter maps.

To characterize the parameter distribution within the tumor section (heterogeneity) quantitatively the probability density function (PDF) was estimated for a ROI, based on an algorithm to calculate the optimal histogram bin size [4]. Furthermore, the cumulative distribution function (CDF), Shannon entropy ($H = \Sigma\, p_i \log(1/p_i)$), and percentiles (box plots) were calculated for the same ROI for comparison between follow-up studies.

Results and Discussion

Eleven children were studied with DCE-MRI of which five received a chemotherapy and were included in the follow-up study: two osteosarcomas of the femur, two lymphomas (Hodgkin, non-Hodgkin) and one Wilms' tumor. MRI of these patients was performed before and during chemotherapy.

Perfusion analysis was feasible in all cases and showed a marked change of the perfusion parameters in the follow-ups. The most valuabe parameters were the model amplitude A (correlated with extra-cellular/-vascular space) and exchange rate k_{21} (correlated with vascular permeability/surface), which both tended to decrease under therapy, although in some cases A initially (first few days) increased but decreased clearly later. Examples of k_{21} parameter maps for an osteasarcoma and Wilms' tumor are shown in *Fig.1*. The AUC and MSE correlated strongly with A, but appeared to be more robust measures in areas with low signal enhancement and SNR. t_0 did not vary significantly within the an image slice, but served as a reference point for the TTP, which allowed easy discrimination of slow and fast enhancing regions.

The heterogeneity of perfusion within the tumor and its change in the follow-ups was well described by the CDF and box plots (10, 25, 50, 75, 90% percentiles), as shown in *Fig.2* for the osteosarcoma. Compared to the PDF (histogram), the CDF contains more detailed information (no bins) and was much clearer when several curves were combined in one graph for comparison. Interquartil ranges proved to be a more sensitive measure than the entropy (high for inhomogeneous regions), which showed a too low sensitivity unless the distribution becomes very narrow.

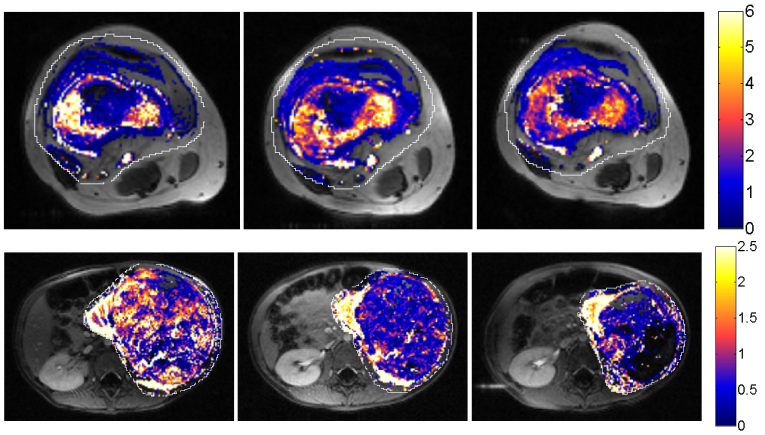

***Fig.1**:* Color-code maps of parameter k_{21} in 1/min for an osteosarcoma (top: day 0, 13, 17) and Wilms' tumor (bottom: day 0, 4, 11) under therapy.

Conclusions

DCE-MRI perfusion estimation for the studied childhood tumor is feasible and appears capable of showing perfusion changes early during therapy. Marked changes of perfusion parameters were observed in all cases, and were well depicted in color-coded maps of the model parameters A and k_{21} as well as TTP. Follow-up results could be compared best using the CDF and box plots. As an simple numerical measure interquartil ranges were better suited than the entropy. The promising results of this pilot work should motivate further studies with larger numbers of patients to achive a correlation with histology.

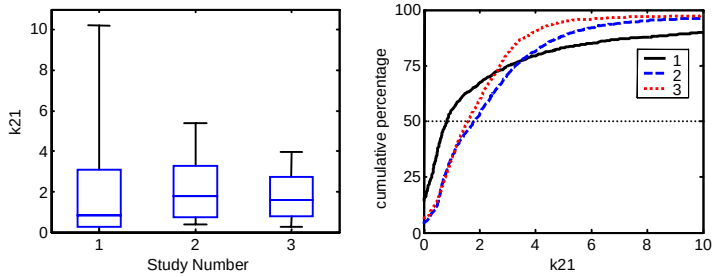

***Fig.2**:* Box plot and CDF of parameter k_{21} in 1/min for the osteosarcoma of *Fig.1* before therapy (1) and 13 days (2) and 17 days (3) later during therapy.

References and Acknowledgement

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