Relation between dynamic Gadolinium uptake rate and response to chemotherapy in colorectal liver metastases: preliminary results

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Introduction: Colorectal cancer is one of the most common cancers in the western world and approximately half of the patients will develop distant metastases. Despite advances in surgery and chemotherapy, prognosis of metastasized colorectal carcinoma is still poor. Chemotherapy is effective only in a subgroup of patients. Therefore, early selection of patients who could benefit from chemotherapy is desirable. Since delivery of chemotherapy is dependent on tumor vasculature, dynamic contrast enhanced MRI (DCE-MRI) may provide a useful non-invasive measure for the prediction of treatment outcome and the follow up of therapy. We investigated the relation between dynamic Gadolinium uptake rate measured by DCE-MRI with response to chemotherapy in patients with liver metastases of colorectal cancer.

Patients and methods: DCE-MRI was performed on a 1.5 T Siemens Vision MR system in 19 patients with colorectal liver metastases before start of first, second or third line chemotherapy (5-fluorouracil, Irinotecan and/or Oxaliplatin containing regimens). Patients gave written informed consent and the study was approved by the local ethical committee. 15 ml 0.5M Gadolinium-DTPA (Gd-DTPA, Magnevist®, Schering, Berlin, Germany) was administered intravenously in 6 seconds by a Spectris^{TM} MR injection system (Medrad, Inc.). Using a T1-weighted fast low-angle shot (FLASH) sequence with a time resolution of 2 seconds Gd-DTPA uptake in the tumor and the bolus passage in vessels in the spleen was monitored (TR 50 ms, TE 4.4 ms, flip angle 90°, slice thickness 7 mm, 4 slices, matrix 160x256, FoV 263x350, acquisition time 90 s). Analysis of DCE-MRI data has been described previously (1). In brief, we obtained a vascular normalization function from pixels in the spleen using an automated algorithm based on the concentration of Gd-DTPA (high in blood vessels) and time to bolus passage (short in arteries). Using a physiological pharmacokinetic model (2) the Gd-DTPA uptake rate k_{ep} was calculated per slice. The spatial distribution of k_{ep} was represented in a map. A region of interest (ROI) was applied to the map of Gd-DTPA uptake rate in order to obtain single values of k_{ep} for all tumor pixels. The geometric mean of the Gd-DTPA uptake rate of these pixels was calculated after log transformation and averaged over all slices containing tumor tissue, resulting in an average k_{ep} value (s^{-1}) for the whole tumor. In case multiple liver metastases were present a maximum of three metastases was selected and the mean k_{ep} value of these metastases was used to correlate with response to treatment. Response was determined on conventional T1 weighted axial images using the RECIST criteria. Conventional MRI was performed before start of chemotherapy and after 2 months of chemotherapy. Complete response was defined as a complete disappearance of all lesions; partial response as a decrease in longest tumor diameter of ≥ 30%; progression as an increase of ≥ 20%; stable disease is reserved for the remaining patients.

Results & Discussion: On the T1-weighted MR image recorded just before Gd-DTPA administration the metastases could easily be detected in all patients. In figure 1A a T1-weighted MR image is shown for one patient. On this image a region of interest was drawn to delineate the tumor, which was then applied to the k_{ep}-map of Gd-DTPA uptake (figure 1B) to select the single values of k_{ep} for all tumor pixels. Mean values of k_{ep} for all lesions ranged from $0.009 – 0.067\ s^{-1}$ (mean $0.034 \pm 0.018\ s^{-1}$). Response data were available for all 19 patients. 1 patient showed a complete response, 3 patients a partial response, 12 patients stable disease and 3 patients progressive disease. As yet no relation between the Gadolinium-DTPA uptake rate k_{ep} and response was observed (fig. 2). In previous studies a correlation between DCE-MRI parameters and outcome has been reported, e.g. in rectal cancer (3,4), but also a lack of correlation, e.g. in Ewing sarcoma (5). According to Larsson's model of k_{ep} depends on tumor blood flow and the PS product (*p*ermeability of perfused capillaries and the total surface area of perfused capillaries) (2). The lack of correlation between k_{ep} and outcome suggests that tumor blood flow and the PS product are not limiting factors for response to chemotherapy in colorectal liver metastases. Although in our study the number of patients with partial or complete response and progressive disease is still small and we are currently expanding our data set, from these preliminary results the Gadolinium-DTPA uptake rate k_{ep} does not seem to be a valuable parameter for prediction of therapy outcome in individual patients with colorectal liver metastases.

Conclusion: As yet no relation between pre-treatment values of Gadolinium-DTPA uptake rate k_{ep} and response to chemotherapy was observed in patients with liver metastases of colorectal cancer.

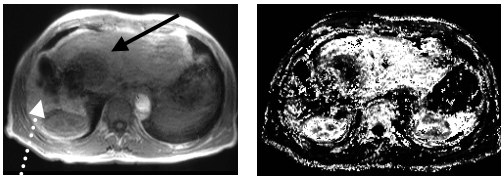

Fig. 1 T1 weighted image of the upper abdomen (A) and the corresponding map of Gd-DTPA uptake rate k_{ep} (B). The liver metastasis is indicated with the solid black arrow; radiation necrosis due to previous radiofrequency treatment with the dotted white arrow)

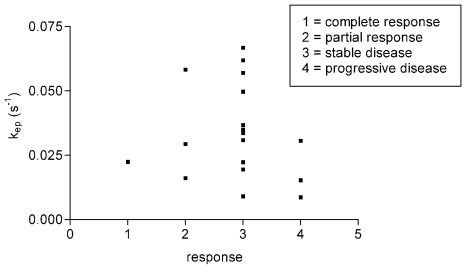

Fig. 2 Gadolium-DTPA uptake rate k_{ep} and response to chemotherapy.

References:
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