Predictive value of MRI - perfusion parameters in patients with liver metastases

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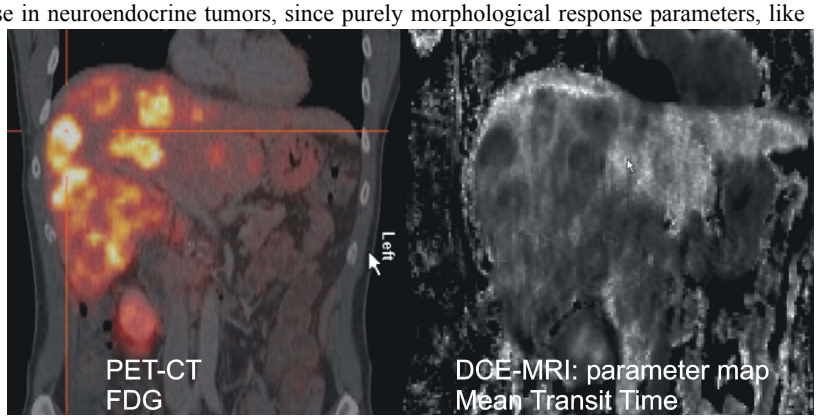
Introduction:

New imaging modalities are needed to monitor treatment response in neuroendocrine tumors, since purely morphological response parameters, like RECIST criteria, do not appropriately reflect therapy response (1). In these patients, functional parameters like specific uptake values from PET-CT have been proven to better reflect therapy response. The aim of the current study was to determine the value of dynamic contrast enhanced MRI (DCE-MRI) of neuroendocrine liver metastases for assessment of therapy response. Different perfusion-parameters from DCE-MRI should therefore be correlated with specific uptake values (SUV) derived from PET-CT imaging and other clinical parameters.



Material and methods:

Dynamic contrast enhanced-MRI data were acquired at 3T (Siemens Verio) in 56 patients with proven metastases of NET using the 3D gradient-echo sequence TWIST (57 coronal slices, 4mm thickness, 192x192 matrix, 2.1sec temporal resolution, 5min acquisition). A standard dose of Gd-EOB-DTPA (flow: 2ml/min; 25 µmol/kg BW; Primovist, Bayer) was used. 48 of these patients also underwent PET-CT with the somatostatin-receptor specific PET-tracer Ga-DOTATATE or with ^{18}F-Fluordesoxyglucose. By visual coregistration region of interests were placed in maximal three corresponding hepatic metastases (>2cm) which were visible both on PET-CT and MRI images. Additionally one ROI was placed in non-metastatic normal appearing liver tissue (NALT) both in DCE-MRI and PET-CT datasets. DCE-MRI datasets were analyzed using a dual-inlet two-compartment uptake model for liver specific MRI contrast agent (Gd-EOB-DTPA; Primovist, Bayer) and perfusion parameters (arterial and venous plasma flow, extracellular mean transit time, extracellular volume, intracellular uptake rate and uptake fraction of Gd-EOB-DTPA) as well as SUVmax and SUVmean values from PET-CT datasets were computed for all ROIs using an inhouse costumized software. For every tumor ROI, the parameters were normalized to the background liver tissue both in PET-CT and DCE-MRI parameters, using a quotient of metastasis-value and NALT-value. The hepatic tumorload of all patients was estimated from visual registration on a coronal T1 vibe-3d sequence. Ki-67-indexes were collected from patient charts. Different tumor-markers (NSE, Chromogranin A) and other blood-parameters (Bilirubin, CRP, GOT, GPT, y-GT, Cholinesterase, alpha-Amylase, Lipase) were measured at the same day as DCE-MRI-examination. Patients sub-datasets were excluded of corresponding correlations due to date-difference between PET-CT and DCE-MRI (> 30 days), small metastases (< 2cm), breathing related MRI-artifacts, non-acquisition of histopathologic- or blood-parameters. Correlations were calculated by spearman correlation, using SAS 9.3.

DCE-MRI Perfusion-Parameters	Correlation-Parameters	Correlation coefficient r; p-value; 95%CI; no of metastases
Arterial Plasma Flow	Normalized mean SUV **PET-CT (FDG)**	R = 0.73; p=0.0022; 95CI: 0.30 to 0.90; n=14
Extracellular MTT		R = -0.75; p=0.0014; 95CI: -0.91 to -0.33; n=14
Extracellular MTT	Ki-67 Index Histopathology	r = -0.45; p=0.0002; 95CI: -0,63 to -0.22; n=60
Extracellular Volume		r = -0.44; p=0.0003; 95CI: -0,62 to -0.21; n=60
Arterial Plasma Flow	NSE (Tumormarker)	r = 0.35; p=0.005; 95CI: 0.11 to 0.55; n=62
Uptake Rate	Chromogranin A (Tumormarker)	r = -0.32; p=0.0122; 95CI: -0.53 to -0.07; n=59
Arterial Plasma Flow	Cholinesterase (blood parameter)	r = -0.41; p=<.0001; 95CI: 0.25 to 0.62; n=75
Extracellular MTT		r = 0.31; p=0.059; 95CI: 0.09 to 0.50; n=75

Results:

Arterial plasma flow was highly correlated with metasbolism of the metastasis, as defined as the FDG uptake from the PET-CT (see table). It also showed correlations with tumormarkers, such as NSE. The extracellular MTT and Volume correlated with the mitosis index from histopathology. See table for further correlations between DCE-MRI Parameters and clinical parameters.

Conclusion: MRI-perfusion parameters from the dual-inlet two-compartment uptake model provide functional information for liver metastases of neuroendocrine tumors and correlate to other functional imaging methods and clinical parameters. Especially the correlation between ^{18}F-Fluordesoxyglucose-PET SUV-values and the arterial plasma flow in metastases shows that the metabolism can indirectly be monitored by DCE-MRI parameters.

References:

1. Frilling A, Sotiropoulos GC, Li J, Kornasiewicz O, Plöckinger U. Multimodal managment of neuroendocrine liver metastases. *HPB 2010;12(6):361-379.*