Prospective Radiology-Pathology Correlation of DCE-MRI Derived Parameters as Quantitative Biomarker of Vascularity and Fibrosis in Pancreatic Cancer

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PURPOSE: To assess the agreement between quantitative imaging parameters derived from dynamic contrast enhanced (DCE) MRI and mean vascular density and percent fibrosis in participants with pancreatic ductal adenocarcinoma.

METHODS: 23 participants with suspected surgically resectable pancreatic adenocarcinoma were prospectively enrolled in this ongoing study. All patients underwent DCE-MRI of the abdomen at 1.5 T using a novel 3D stack of spirals T1 weighted GRE sequence with a sliding window reconstruction to achieve 3 second temporal resolution. A bolus of (0.1 mmol/kg) Gadopentetate dimeglumine was injected via IV at 2mL/s. One patient was imaged a second time before surgery with identical parameters and 0.03 mmol/kg Gadofosveset trisodium 72 hours later as part of ongoing trial. DCE-MRI was acquired continuously in the axial plane from 0-90 seconds with multiple breath-holds. Subsequent breath-hold acquisitions were performed at 2, 3, 4, 5 and 10 minutes. Firevoxel image analysis software (NYU Medical Center, New York, NY) was used to draw ROIS and process the DCE data from 0-90 sec. The arterial input function was measured from an ROI over the aorta at the level of the pancreas in the axial images. No significant inflow effects were observed. ROIs were drawn by a radiologist (12 years experience) over the tumor and adjacent downstream normal pancreatic tissue if present. Time points with significant respiratory motion were discarded from the data. Signal intensity was converted to [Gd] before fitting the data to the extended Tofts model. Extracted perfusion parameters were compared to histopathology (mean vascular density (MVD), % fibrosis, tumor cell density) using Pearson correlation, where a p value of 0.05 was considered to be statistically significant.

RESULTS: 15 (7M: 8F; mean 68 y) patients proceeded to surgery including one with known metastatic disease where a focus of omental metastasis was resected. 8/23 patients were excluded because they did not proceed to surgical resection. 12 patients had pancreatic ductal adenocarcinoma, 1-mixed pancreatic/intestinal adenocarcinoma, 1-cholangiocarcinoma and 1- metastatic renal cell carcinoma from a remote primary tumor resected 20 years prior. Mean primary tumor size at surgery was 3.1 cm (1.7-4.5 cm). Tumor grade of the 10 pancreatic adenocarcinomas included in the final analysis ranged from G2 moderate (n=6), G2 moderate to poorly (n=2) to G3 poorly differentiated (n=2). 13/15 tumors were included in final analysis (a mucinous tumor was excluded due to non-cellularity and minimal mean vascular density and the omental implant was excluded because of its small size ($<1cm^3$). Mean K_{trans} for the 10 pancreatic adenocarcinomas included in the final cohort was 0.72 min^{-1} (+/-0.27) in keeping with previous results from Bali et al 2011. K_{trans} of the RCC metastases was 3.7 min^{-1}. Including RCC in the analysis, V_e had a negative correlation (r=-0.60) with percent fibrosis of tumor (p=0.03). Excluding RCC, V_e demonstrates a positive correlation (r=0.68) with tumor MVD (p=0.02).Mean K_{trans} for the 10 pancreatic adenocarcinomas included in the final cohort was 0.72 min^{-1} (+/-0.27) in keeping with previous results from Bali et al 2011.

Table 1: Comparison on DCE-MRI derived parameters using Gd-dimeglumine versus Gadofosveset trisodium

	Tumor K_{trans}	Tumor V_e	Normal Pancreas K_{trans}	Normal Pancreas V_e
Gadopentetate dimeglumine	0.526976	0.240553	3.534483	0.187549
Gadofosveset trisodium	0.685289	0.081467	1.294756	0.061116

CONCLUSION: 3D stack of spirals T1 weighted GRE was used quantitatively in DCE-MRI permitting whole liver/pancreas coverage with sub 3 second temporal resolution. V_e and k_{ep} may serve as biomarkers of fibrosis and MVD while K_{trans} does not. This may be due to the characteristic high desmoplasia and relatively low perfusion of pancreatic adenocarcinomas. Higher temporal resolution can be extracted from this data and in addition to the inclusion of later dynamic time points alternative kinetic modeling may further bring out the unique features of pancreatic adenocarcinoma. Preliminary results in humans comparing DCE metrics with Gadofosveset trisodium to extracellular agents are presented.

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