

Correlation of histological and IVIM-derived measures of vascularity in hypo- and hypervasculatized pancreatic lesions

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Target audience: radiologists with an interest in oncology, oncologists, and physicists with an interest in advanced diffusion imaging

Purpose:

Non-invasive intra-voxel incoherent motion (IVIM) MRI aids diagnosing benign and malignant pancreatic lesions¹⁻³. However, there is no data available on the correlation between histologically determined vascularization and IVIM parameters in pancreatic cancers. The aim of this study was to investigate the correlation between IVIM-derived parameters and histologically determined vascular density in hypo- and hypervasculatized solid pancreatic carcinomas.

Methods:

We included 36 patients with typically hypovascular pancreatic ductal adenocarcinoma (PACA) and 6 patients with typically hypervasculatized pancreatic neuroendocrine tumor (NET). Patients underwent DWI MR using the following parameters: EPI-DWI, TR/TE 2200/58ms, FOV 350 x 248mm, matrix = 130x92, 14 slices, 8 b-values (50-800 s/mm²). IVIM-parameters were extracted from manually drawn VOIs using MITK Diffusion (www.mitk.org/DiffusionImaging). The resected tissue was evaluated histologically using microvessel density⁴ (MVD). Pearson-correlation-coefficients reflecting the correlation of IVIM derived- and histological parameters were calculated.

Results:

Fig.1 shows a typical example of the IVIM and histological evaluation. The mean IVIM-derived parameters in PACA vs NETs were: $9.4\% \pm 5.4\%$ vs $15.5\% \pm 5.2\%$ (f) $1.2 \pm 0.2 \times 10^{-3}$ vs. $1.03 \pm 0.15 \times 10^{-3}$ mm²/sec (D) and $41.3 \pm 54.8 \times 10^{-3}$ vs. $53.8 \pm 51.1 \times 10^{-3}$ mm²/sec (D*). Fig. 2 shows a significantly lower f in PACA compared to NET (p<0.0001). Mean MVD was $36.8 \pm 25.9/\text{mm}^2$ in PACA and $80.0 \pm 26.1/\text{mm}^2$ in NETs. As can be taken from Fig. 3, f and MVD showed excellent correlation ($r=0.85$), D and D* did not correlate with the MVD ($r=-0.18/-0.10$).

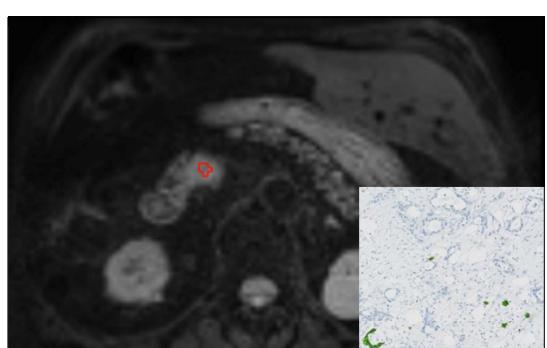


Fig.1: Diffusion-weighted image ($b=200$) of a hypovascular PACA in the pancreatic head. IVIM-derived f -value from the VOI: 1.4%. Inlay: corresponding histological specimen, the derived

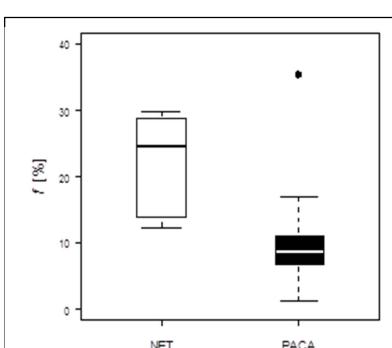


Fig. 2: Comparison of f -values for NETs and PACAs. Shown are median, upper and lower quartiles, whiskers and outliers.

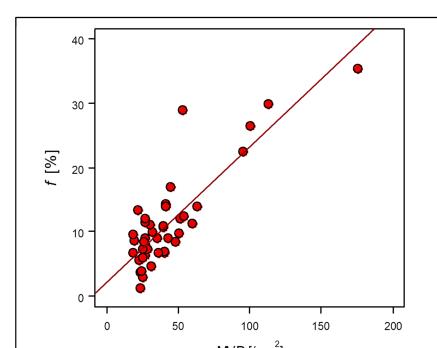


Fig. 3: Correlation of f and MVD. There is a clear spread in both parameters and a good correlation between them ($r=0.85$).

Discussion and Conclusion:

The IVIM-parameter f is supposed to reflect the vascular volume fraction. Additionally, angiogenesis is reflected by an increase in MVD and high MVD has been associated with poor prognosis in few reports dealing with pancreatic cancer⁵⁻⁷. In this first study investigating the histological correlation between f and MVD we could show a strong correlation between the IVIM-derived perfusion fraction f and the MVD in hypo- and hypervasculatized solid pancreatic tumors. Therefore, IVIM DWI imaging reflects MVD and may serve as noninvasive marker of tumor vascularity in pancreatic cancer.

Literature:

1. Concia M, Sprinkart AM, Penner AH, et al. Diffusion-weighted magnetic resonance imaging of the pancreas: diagnostic benefit from an intravoxel incoherent motion model-based 3 b-value analysis. *Investigative radiology* 2014;49:93-100.
2. Kang KM, Lee JM, Yoon JH, et al. Intravoxel incoherent motion diffusion-weighted MR imaging for characterization of focal pancreatic lesions. *Radiology* 2014;270:444-53.
3. Klauss M, Lemke A, Grunberg K, et al. Intravoxel incoherent motion MRI for the differentiation between mass forming chronic pancreatitis and pancreatic carcinoma. *Investigative radiology* 2011;46:57-63.
4. Fujioka S, Yoshida K, Yanagisawa S, et al. Angiogenesis in pancreatic carcinoma: thymidine phosphorylase expression in stromal cells and intratumoral microvessel density as independent predictors of overall and relapse-free survival. *Cancer* 2001;92:1788-97.
5. Ikeda N, Adachi M, Taki T, et al. Prognostic significance of angiogenesis in human pancreatic cancer. *British journal of cancer* 1999;79:1553-63.
6. Karademir S, Sokmen S, Terzi C, et al. Tumor angiogenesis as a prognostic predictor in pancreatic cancer. *Journal of hepato-biliary-pancreatic surgery* 2000;7:489-95.
7. Ueda T, Oda T, Kinoshita T, et al. Neovascularization in pancreatic ductal adenocarcinoma: Microvessel count analysis, comparison with non-cancerous regions and other types of carcinomas. *Oncology reports* 2002;9:239-45.