Assessment of reproducibility of IVIM based perfusion fraction and diffusion coefficient in the pancreas

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Target audience: Clinical physicists.

Purpose: Intravoxel incoherent motion (IVIM) is a model for diffusion weighted imaging (DWI) which, in addition to diffusion, takes into account the effects of perfusion. The perfusion fraction f obtained by IVIM can potentially be used as a biomarker to differentiate between carcinoma and healthy tissue in the pancreas[1]. However, IVIM is very sensitive to noise and requires DWI to be performed with many b-values and multiple averages. In addition, respiratory and cardiac motion and bowel peristalsis can cause signal voids and misalignments between different DWI images. For this purpose, we have optimized an imaging sequence for DWI, and developed an in-house post-processing toolkit for IVIM modeling. The aim of this study was to investigate the reproducibility of f and the diffusion coefficient D in the pancreas as a function of the number of averages.

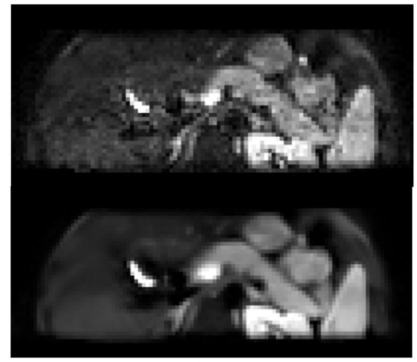

Figure 1: b=10 s/mm^2 raw image (top) and after denoising and averaging (bottom).

Methods: Eight healthy male volunteers (mean age 30 years) were scanned twice (3T Philips Ingenia) using a single-shot echo-planar sequence: voxel size 3x3x3.7 mm^3, 0.3 mm slice gap, FOV=432x108x72 mm^3 (FxPxS), TE/TR=44/2300 ms, BW=62.5 Hz/voxel. Fourteen b-values (0, 10, 20, 30, 40, 50, 65, 80, 100, 125, 175, 275, 375 and 500 s/mm^2) were measured three times in three orthogonal directions. The acquisition of the entire volume for a single b-value in one diffusion weighting direction was triggered using a navigator at expiration during each respiratory cycle. The volunteers were instructed to hold their breath during each trigger (2.3 s). Typically the acquisition time varied between 15-20 minutes. In one male patient (age 56) with histologically proven pancreatic adenocarcinoma (3.5x2.3 cm) the same protocol was scanned and IVIM parameters between tumorous and healthy pancreatic tissue were compared.

All images were denoised using a Rician adaptive non-local means filter[2]. Slices with signal drop-out due to cardiac motion during signal encoding were removed by the post processing algorithm. Subsequently, we used elastix[3] to perform a mutual information based non-rigid registration. As a reference image we selected a volume from the b=10 s/mm^2 set. This approach dealt with errors due to potentially limited performance of respiratory triggering, peristaltic motion between triggers and eddy-currents. The reference scan was then registered to a high resolution anatomical T1w image in which the pancreas was manually delineated.

The IVIM model[4] used takes into account the different signal contributions due to differences in T1 and T2 of blood (T1/T2=725/43 ms [5]) and pancreatic tissue (T1/T2=1932/275 ms [6]). For all fits the S_0 was constrained to the average value of all b=0 s/mm^2 ±2SDs. By fitting IVIM to all pancreatic data from all volunteers we found a pseudodiffusion coefficient D^* of 0.0871 mm^2/s. D^* was fixed to this value for all subsequent analyses.

The reproducibility of f and D was determined by Bland Altman analysis. Repeatability index (RI) was defined as the 1.96xSD of the paired differences divided by the mean of all values times 100%. The RI was studied as function of the number of averages.

Results: Figure 1 shows a normal, and an averaged, denoised b=10 s/mm^2 image. Figure 2 shows a delineation and IVIM fit in a typical healthy volunteer. Averaging all fit parameters, fitted separately for each volunteer, we found D=1.40±0.07x10^{-3} mm^2/s and f=9.4±1.8 %. The Bland Altman plot (Figure 3), gives RI_f=17 % and RI_D=13 %, for f and D separately. Figure 4 shows that the RI of f and D both decrease with an increasing number of averages. RI_D does not further decrease above 5 averages, suggesting that the remaining variability in D has a physiological source. In the patient, we found f_C<1 % (fit bound), D_C=2.3x10^{-2} mm^2/s, f_H=8.3 % and D_H=1.8x10^{-3} mm^2/s for carcinoma and healthy tissue respectively (Figure 5).

Discussion: The data shows a clear reproducible bi-exponential decay in the healthy volunteers, indicating that IVIM is a robust method in the pancreas. Depending on the desired reproducibility, the DWI measurement can be shortened by decreasing the number of averages. RI_f benefits from increasing the number of averages up to at least 9. RI_D does not improve after 5 averages.

Conclusion: Using our acquisition and post-processing toolkit, we found reproducible values for f and D in the pancreas. In addition, we showed the feasibility of using an IVIM model to describe changes in the pancreas carcinoma compared to healthy tissue in the same patient, which was in agreement with the literature[1].

References:[1] A. Lemke et al., Invest. Radiol. **44**, 769 (2009). [2] J. V Manjón et al., JMRI **31**, 192 (2010). [3] S. Klein et al., IEEE Trans. Med. Imaging **29**, 196 (2010). [4] A. Lemkeet al., MRM. **64**, 1580 (2010). [5] A.M. Standeven et al., Carcinogenesis **13**, 1319 (1992). [6] G.J. Stanisz et al., MRM **512**, 507 (2005).

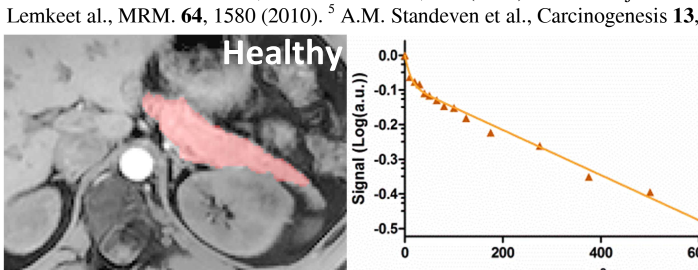

Figure 2 (above): A pancreas segmentation and IVIM fit in a healthy volunteer.

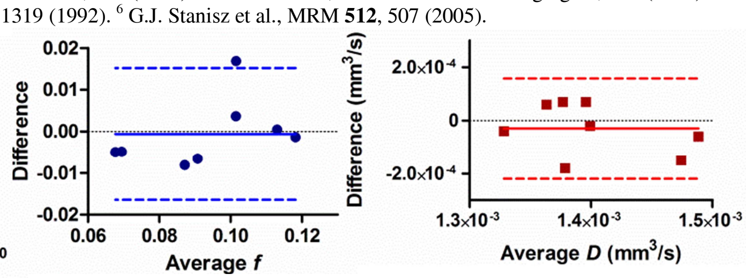

Figure 3 (above): Bland Altman plots of f and D. Solid line indicates the average. Dotted lines show the 95% confidence interval for the difference between repeated.

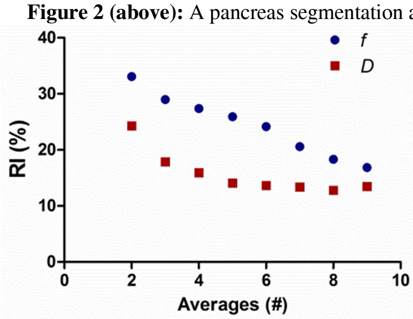

Figure 4 (left): Reproducibility as function of number of averages.

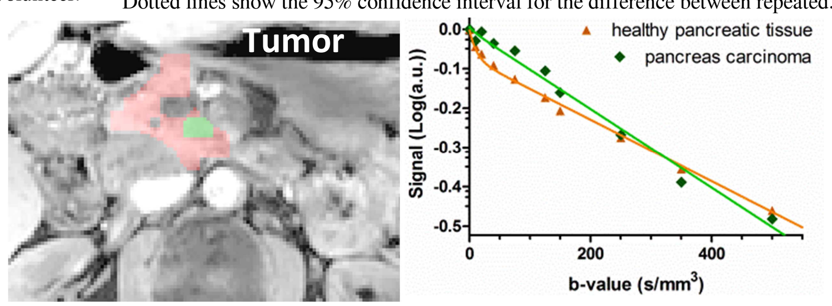

Figure 5 (right): Tumour segmentation (left) and IVIM model (right) in pancreas carcinoma (orange) and in healthy pancreatic.