Flow compensated IVIM as a tool to probe microvasculature
Andreas Wetscherek¹, Bram Stieljes², Wolfram Semmler³, and Frederik Bernd Laun¹
¹Dept. of Medical Physics in Radiology, German Cancer Research Center, Heidelberg, Germany, ²Quantitative imaging based disease characterization, German Cancer Research Center, Heidelberg, Germany

Introduction
The intravoxel incoherent motion (IVIM) model introduced in 1988 [1] has proven valuable for differentiation of lesions in pancreas [2] and liver [3]. As the fast decaying IVIM component could be identified as blood [4], the work at hand aims to understand the model’s diagnostic capabilities by investigating tissue microvasculature using flow compensated (FC) diffusion weighted (DW) MRI.

Materials and Methods
Sequence: A fully flow compensated single-shot single-refocusing EPI sequence with bipolar (BP) and FC DW gradient schemes (Fig.1) was implemented. By symmetric positioning of the DW gradients with respect to the 180° pulse as proposed in [5] it was possible to reduce the influence of concomitant fields enabling FC DWI with b-values up to 500 s/mm² and diffusion times T up to 100 ms. At 1.5 T abdominal DW MRI data of 5 healthy volunteers (age 19-31) was measured such that during each expiratory breath hold 2 b-values in 6 DW directions and 3 b0 images were acquired (TR=2.1 s, TE=120 ms, BW=2000 Hz/px, matrix 100 x 78, resolution 3.5 mm, 7 slices with 5/1 mm thickness/distance, GRAPPA 2, Siemens Magnetom Avanto).

Simulation model: Starting from the IVIM equation [1]: \( S/S_0 = \exp(-bD)\left[1-f+D^*\right] \), which assumes one tissue and one blood compartment, we further propose to describe the latter, which contributes the perfusion fraction f to the unweighted signal, by the following model: Blood travels with velocity v and changes its direction after a time \( \tau \) randomly by an angle \( \alpha \). Due to the DW gradients, this motion results in a certain distribution \( \rho(b,T,\alpha,\tau,v) \) of the particle phases. The signal attenuation of the blood compartment is then \( F(b,T,\alpha,\tau,v) = |<e^{\sqrt{-1}\alpha}>|^2 \). For numerical evaluation the distribution \( \rho(b,T,\alpha,\tau,v) \) was calculated from the normalized \( (bTv^2=1) \) distribution \( \phi(\alpha,\tau/T) \), which we determined for the DW schemes shown in Fig.1 by simulating 25x10⁶ particle paths for each combination of angles \( \alpha \) between 0° and 180° and \( \tau/T \) ranging from 2x10⁻⁴ to 20. It was assumed that the starting directions of the moving particles are isotropically distributed and that the first directional change occurs randomly between 0 and \( \tau \).

Results
Fig.2 shows the signal attenuation measured in a region of interest in the pancreas (markers) averaged over directions with standard error from inter-individual variations and simulated attenuation curves (lines) using the displayed parameters. Those were optimized with respect to the squared sum of differences to all acquired data points. While \( f \) and \( D^* \) can be well determined, it was found that a lot of different sets of microscopic parameters can reproduce the experimentally obtained signal attenuation curves. Values for \( \tau \), \( \alpha \) and \( v \) in Fig.2 should only be considered valid with respect to the order of magnitude. For all suitable configurations we found \( \tau >100 \) ms and \( v \) between 0.6 and 1.2 cm/s, while exact numerical values strongly depended on the choice of \( \alpha \). The model data could predict the large signal decay at low b-values using BP gradients and the trend of increasing signal attenuation with \( T \) using FC gradients. We define the apparent diffusion coefficient (ADC) to be the negative slope of the logarithmic signal decay at small b-values (b<100 s/mm²). It was determined from a linear fit and its dependence on \( T \) compared to model derived ADCs for the FC data is shown in Fig.3. A measure \( D^*\) similar to the pseudo-diffusion coefficient in the IVIM model was defined by \( D^* = (ADC-D)/f \) and shows strong T-dependence in Fig.3.

Discussion
Two results presented in this abstract are particularly novel: The measurement of the time-dependence of a pseudo-diffusion coefficient \( D^* \) (Fig.3) and of the IVIM signal decay curves (Fig.2) using varying DW gradient profiles. Information about the microvasculature was obtained by relying on a particular model of blood motion. Despite the simplifying assumptions of the used model its universal behavior (data not shown) indicates that some inferred results should hold for real blood flow with high certainty: We found \( \tau >100 \) ms which implies that a large fraction of the blood volume did not change its flow direction during the experiment and thus can explain separation of the FC curves from the BP curves in Fig.2. The dependence of the FC signal attenuation on the diffusion time \( T \) is reproduced by the proposed IVIM model. Regarding the large range of suitable microscopic parameter sets one could conclude that blood flow in the investigated region is diverse in terms of velocities, times and angles between directional changes. We consider flow compensated IVIM experiments to be promising for assessing changes in vasculature and suggest FC DW MRI with dense sampling at low b-values as a promising tool in oncologic imaging.