Pulsatile Microvascular Perfusion Demonstrated in the Human Brain with Intravoxel Incoherent Motion (IVIM) MRI

Christian Federau¹, Kieran O’Brien², Markus Müller¹, Matthias Stuber¹,³, Reto Meuli¹, Philippe Maeder¹, and Patric Hagmann¹
¹Radiology, CHUV, Lausanne, VD, Switzerland, ²CIBM, Université de Genève, Lausanne, VD, Switzerland, ³The Abdus Salam International Center for Theoretical Physics, Trieste, Trieste, Italy, ⁴CIBM, Lausanne, VD, Switzerland

Purpose
Microvascular perfusion can be measured in the brain with Intravoxel Incoherent Motion (IVIM) MRI [1], as first proposed by Le Bihan et al [2]. By fitting a double exponential model to the diffusion sequence signal amplitude as function of b (for b < 1000 mm²/s), one obtains 3 IVIM microvascular perfusion parameters, f, the perfusion fraction, D*, the pseudo-diffusion coefficient, and fD*, which is related to blood flow [3], as well as one non-vascular parameter D, the (thermal) diffusion coefficient. To better understand those parameters, we studied here their dependence on the cardiac cycle.

Materials and Methods
Imaging was performed on 20 healthy subjects, using a standard EPI spin echo sequence with embedded Stejskal-Tanner pulsed gradients sequence, at 3 Tesla using a 32-channel receiver head-coil, with prospective cardiac triggering. Repeat measurements were acquired with evenly spaced time delays across the whole cardiac cycle for 13 patients to compare the IVIM parameters between systole and diastole. In a further 7 subjects, the repeat measurements were evenly spaced over systole. A single axial brain slice was acquired at the level of the basal ganglia. Due to the Cardiac triggering TR was variable, but set to a minimum of 5s. Other image parameters were TE 88-92ms, 1.2x1.2mm in plane resolution, BW 1134 Hz/pixel and b-values of (0, 10, 20, 40, 80, 110, 140, 170, 200, 300, 400, 500, 600, 700, 800, 900 s/mm²), in 3 orthogonal directions. A region of interest was then drawn around the total brain parenchyma of the axial slice, and the pixel containing cerebro-spinal fluid were excluded by thresholding the b0 image. The signal obtained was then averaged for each b-value, and fitting a double exponential model to the diffusion sequence signal amplitude as function of b (for b < 1000 mm²/s), one obtains 3 IVIM perfusion parameters f, D*, and fD*, which is related to blood flow [3], as well as one non-vascular parameter D, the (thermal) diffusion coefficient. To better understand those parameters, we studied here their dependence on the cardiac cycle.

Results
A clear dependence on the cardiac cycle was observed for all 3 IVIM perfusion parameters f, D*, and fD*, while D, as expected, remained stable (Fig 1). During systole (defined from 0-250ms after the R-wave), D* and fD* were increased significantly compared to diastole (D* systole = 12.07 ± 9.40 ·10⁻³ mm²/s⁻¹; D* diastole = 5.06 ± 1.91 ·10⁻³ mm²/s⁻¹; p = 1·10⁻⁴; fD* systole = 0.92 ± 0.69 ·10⁻³ mm²/s⁻¹; fD* diastole = 0.69 ± 0.20 ·10⁻³ mm²/s⁻¹; p = 5·10⁻⁵), while f (related to the microvascular volume) was not statistically different. The global aspect of the time dependence of the flow in the ACA and the IVIM flow related parameter fD* (Fig 2) were similar. Mean time to peak (TTP) of fD* occurred 133 ± 15 ms after the R-peak, slightly delayed in comparison to the mean TTP flow in the ACA measured at 127 ± 18 ms (p = 0.17).

Discussion
Our findings represent direct experimental evidence of pulsatile flow in the human brain microvasculature. These results correlate well with recently reported measurement of pulsatile blood flow in the microvasculature of the cortex of the mice brain by Santisakultarm et al [5] using two-photon microscopy. In conclusion, the present results further validate IVIM as a method to measure human brain perfusion.

References
4. Federau, C., et al., Pulsatile Microvascular Perfusion Demonstrated in the Human Brain with Intravoxel Incoherent Motion (IVIM) MRI, to be published.