Transcapillary transport of Gd-DTPA in the human heart increases in proportion to myocardial blood flow.

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Introduction: For MRI myocardial perfusion studies, the exchange of water across the capillary wall and transcytolemal barriers leads to additional complexity in describing the pharmacokinetics of an extracellular contrast reagent (CR) , indirectly detected by its relaxation effects on the ^1H_2O signal. A better understanding of transendothelial CR transport may be important for the determination of capillary recruitment in the heart during vasodilation. A description of transendothelial transport during the first-pass of an extracellular CR, requires combining a comprehensive, multi-site ^1H_2O magnetization exchange model with a tracer kinetic model. In this study we sought to elucidate the relationship between transendothelial CR transport and myocardial blood flow (MBF).

Methods: 20 volunteers, of ages 48-80 years underwent first-pass Dynamic Contrast Enhanced (DCE) MRI studies in a 1.5 Tesla clinical MR scanner, using a flexible 4-element phased array RF coil. DCE MR images during the CR (Magnevist, Berlex; dose: 0.04 mmol per kg of body weight) bolus first-pass were acquired with a T_1-weighted gradient echo pulse sequence, with saturation recovery magnetization preparation (TR/TE/TI/ flip = 2.2/1.2/90 ms/ 18˚, 256 x 152 matrix, receiver bandwidth of 31 kHz, FOV: 280-340 mm by 300 mm), both at baseline and during maximal vasodilation (iv adenosine 0.14 mg/kg/min for > 3 minutes). Region-of-interest signal intensity curves were generated for eight myocardial sectors in each short axis slice by manual image segmentation. A linear three-site-exchange formalism was combined with the Kety-Schmidt model to estimate transendothelial CR transport [1], in addition to flow [2]. The capillary CR pseudo first-order extravasation rate constant (K^{trans}) , and the blood volume fraction, were determined with a non-linear least squares optimization, while the capillary uni-directional water extravasation rate constant was fixed at 2.5 s^{-1}, the average intracellular water lifetime was set to 0.7 s, and the percentage extracellular/extravascular space (ESS) volume was set to 20%. Absolute MBF was independently determined by model-independent deconvolution [2], a method validated using measurements with radio-isotope labeled microspheres.

Results: An initial sensitivity analysis showed that the best-fitted values of K^{trans} were rather insensitive to that of the unidirectional water extravasation rate constant, because of the short duration of the first pass. The latter parameter was therefore kept constant for all subsequent analyses. K^{trans} increased with flow (linear regression model $K^{trans} \sim MBF$; *MBF* coefficient (±S.E.) = 0.23 (±0.03); $p < 0.0001$) (Figure 1). Calculation of the permeability surface area product (PS) from K^{trans}, using the independently determined *MBF*, showed that *PS* is proportional to, and essentially equal to K^{trans}, indicating that CR extravasation is barrier limited in the heart. The blood volume fraction (*BV*) in the Kety model was more accurately described by a $BV \sim a \cdot MBF + b \cdot MBF^{1/2}$ [3] than a simple linear function of *MBF* ($p < 0.001$ for chi-square test) (Figure 2).

Discussion: The increase of K^{trans} with *MBF* demonstrates capillary recruitment and /or enhanced PS with induction of vasodilation. The non-linear increase the blood volume fraction with flow is consistent with previously described models and experimental data for intravascular tracers [3]. To the best of our knowledge this is the first study demonstrating both changes of capillary wall CR permeability and myocardial blood volume, using an extracellular CR in first-pass DCE MRI studies.

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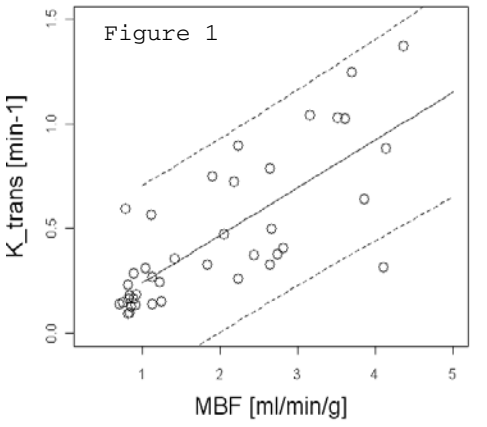

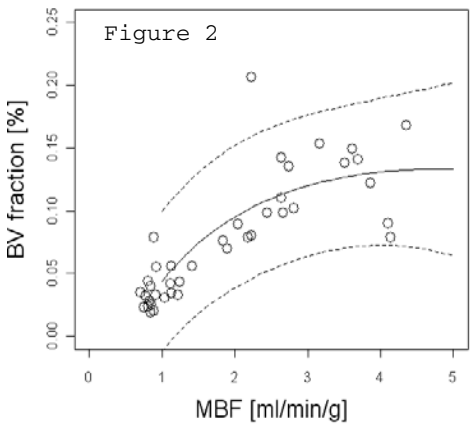

References:

[1] Li, Rooney, Springer, (a) *Proc. Int. Soc. Mgn. Reson. Med.* 12:145 (2004). (b) *Magn. Reson. Med.* 54: 1351-1359 (2005).

[2] Jerosch-Herold, Swingen, Seethamraju. *Med Phys*. 2002; 29(5):886-97

[3] Mohlenkamp S et al, Ann N Y Acad Sci. 2002; 972:307-16.