Quantitative Renal Perfusion in Human Subjects using an Iron Oxide Blood Pool Agent

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Introduction: Renal perfusion status is an important clinical parameter which is not readily assessable using conventional gadolinium based MR contrast agents due to contrast agent extraction and glomerular filtration In the current study, kidney perfusion was measured using an intravascular iron oxide based contrast agent. Since this contrast agent is not renally excreted, studies have suggested that quantitative perfusion can be measured based on the first-pass response of the contrast agent through the kidney parenchyma (1). The purpose of this study was to evaluate quantitative renal perfusion based on first-pass imaging in human subjects following bolus injection of the iron oxide based contrast agent. A further objective was to compare different deconvolution methods and address possible limitations and sources of error using this method.

Methods: First-pass imaging was performed in 11 subjects in three centres as part of a phase II clinical trial.
Contrast agent: The iron oxide based contrast agent Clariscan (NC100150 Injection, Amersham Health, Oslo, Norway) was injected as a rapid bolus at a dose of 1.25 mg Fe/kg b.w.
MR imaging: A single slice double–echo gradient echo sequence with a temporal resolution of 1 second was used. The first-pass images were angulated so that both kidneys and a section of the abdominal aorta were included in the slice. The following image parameters were used: TR/TE1/TE2/flip/voxel size = 11.7 ms / 4.5 ms /9.0 ms /12 deg / 2.75 x 2.72 x 6.0 mm^3 (centre 1 and 2) and 11.8 ms / 3.4 ms /9.0 ms /12 deg / 1.37 x 1.37 x 6.0 mm^3 (centre 3). The first-pass images were acquired with breath-hold during the first passage of the bolus through the kidneys.
Data analysis: The arterial input function (AIF) was measured from the visible section of the aorta in the short-echo images. The temporal signal change was converted to ΔR2* values using previously described methods (2). Due to the large difference in R2* effects in the aorta and renal cortex, the first echo was used to calculate ΔR2* for the AIF. The R2* change in the renal parenchyma was similarly determined from either the first echo, the second echo or both echoes by quantitative determination of R2* on a pixel-by-pixel basis. The tissue response was deconvolved with the AIF using two different deconvolution methods: singular value decomposition (SVD) (3) or a Fourier based method (FFT) (4). Additionally, the FFT deconvolution was performed both on the raw unprocessed first-pass data as well as on gamma-variate fitted data. The AIF was visually inspected for signal saturation, and quantitative perfusion estimation was only performed in those patients were the AIF was not saturated. The perfusion parameters were measured in kidneys with no significant stenosis as determined by X-ray angiography.
Blood flow (BF) and blood volume (BV) maps were generated on a pixel-by-pixel basis and the global value for each parameter was estimated by segmentation of the cortical tissue in each kidney. All image processing was performed in nICE (NordicNeuroLab AS, Bergen, Norway).

Results and Discussion: Renal perfusion and blood volume could be determined in 7 out of 11 patients. In the remaining patients, the AIF was severely saturated due to excessive T2* effects. The measured perfusion values depended strongly on the echo time used to calculate ΔR2*. Shorter TE gave lower perfusion values. This is likely to be due to confounding T1-effects which tend to oppose the T2* effect at short TE values when iron oxide agents with a large r1 relaxivity is used, as previously described (2). The largest perfusion values were generally obtained when R2* was measured quantitatively from both echoes, thereby eliminating T1 effects. Blood flow values were on average 24% higher using double echo compared to single echo (TE2). The measured perfusion values were relatively insensitive to deconvolution method when the signal-noise was high in the raw data. For noisy datasets, there was a much larger dependence of obtained perfusion values on the deconvolution method used. The method most sensitive to low SNR was gamma-variate fitted FFT. Figure 1 shows mean cortical blood flow calculated with SVD and FFT deconvolution techniques using double echo data in the patients were the AIF was not saturated. The bars represent, from left to right per patient; SVD with gamma variate-fitted AIF (SVD g), SVD with raw AIF (SVD raw), non-parametric FFT with gamma-variate fitted AIF (nFFT g) and finally FFT with gamma-variate fitted data and AIF (pFFT g). The relationship between the first three methods are relatively stable for most of the patients while the pFFT g method was more sensitive to low SNR. Figure 2 shows example of quantitative blood flow map obtained in one patient. Note that the requirement of including both kidneys and part of the abdominal aorta in a single slice makes it difficult to select optimal slice orientation in both kidneys.

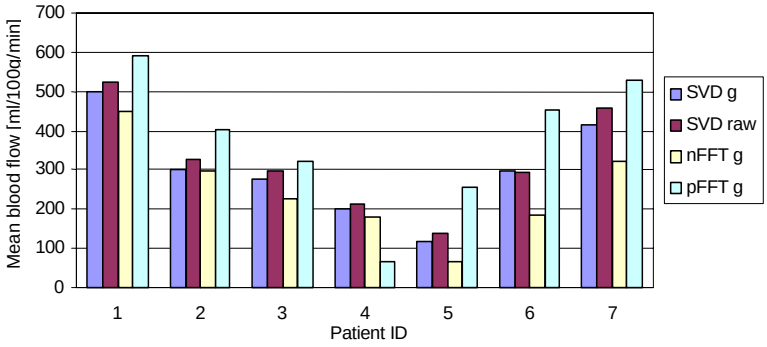

Figure 1

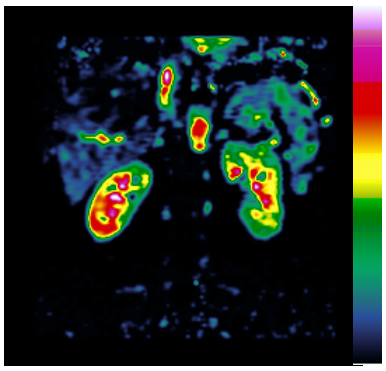

Figure 2

Conclusions: Quantitative renal perfusion can be measured using a rapid double echo sequence in combination with a bolus injection the iron oxide contrast agent Clariscan. Due to large differences in T2* effects in blood and tissue, different echo times must be used to assess the AIF and the renal response. Ideally ΔR2* should be estimated from two echoes, thereby eliminating T1 effects. The robustness of the method is strongly dependent on good signal-noise in the dynamic data. A significant centre effect was observed, making it challenging to compare perfusion values obtained from different sites, or on different MR systems.

References:

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