QUANTITATIVE BIOMARKERS IN RENAL MRI: FROM MORPHOLOGY TO PHYSIOLOGY

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Arterial Spin Labelling

- Renal ASL provides a non-invasive method to assess kidney perfusion. Examples will be shown.

- Renal ASL is technically challenging due to the need to: overcome motion artefacts arising from breathing, ensure good labelling, collect images with the optimal readout scheme, and remain within the SAR limits at 3 Tesla. Strategies to overcome these limitations are described.

TARGET AUDIENCE: Physicists, radiologists, imaging scientists and MR technologists.

OBJECTIVES: To outline the current status of renal Arterial Spin Labelling, the challenges involved, and the optimal schemes to employ for renal ASL.

METHODS AND RESULTS: Arterial spin labelling (ASL) [1] provides a non-invasive quantitative assessment of tissue perfusion and is an attractive alternative to dynamic contrast-enhanced MRI (DCE-MRI) [2]. Arterial spin labelling uses the magnetic spins of freely diffusible water in blood magnetization as an internal endogenous contrast agent. It does so by labelling the magnetization of blood water, typically by inverting the blood water spins before they enter the tissue of interest. The labelled water then exchanges with tissue water, with the magnetization then decaying at a rate limited by the longitudinal relaxation time of the tissue water. By subtracting the difference of a labelled image from a control image with unlabelled blood water, a perfusion-weighted image is obtained for which the signal intensity is proportional to perfusion. However, because the perfusion-weighted signal change is small, the signal-to-noise ratio (SNR) is low and ASL imaging relies on the acquisition of multiple label and control image pairs, and averaging of the resulting images.

Broadly, ASL can be divided into two variants, pulsed ASL (PASL) and continuous/pseudo-continuous ASL (CASL/PCASL). The majority of renal ASL studies have used the pulsed flow-sensitive alternating inversion recovery (FAIR) ASL scheme [3,4] in which a single radio frequency pulse is applied to invert a labelling slab (*Figure 1*). The ASL label is short-lived and decays with the T_1 relaxation time; this necessitates rapid image acquisition after labelling and it also ensures that the signal is not affected by venous outflow and that the kinetics are only related to arterial inflow. Recently, a number of studies have also been published using the PCASL technique [5, 6]. PCASL [7] utilizes a train of discrete RF pulses spaced as sort as possible, typically 1 ms, to mimic continuous tagging. However PCASL is highly sensitive to labelling efficiency and so its reproducibility can be limited for renal ASL.

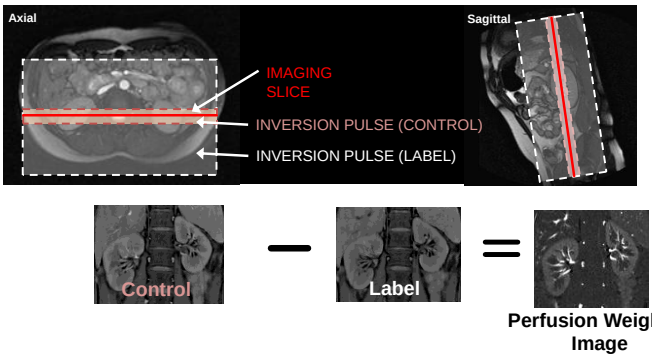

Figure 1: Perfusion weighted image formed using a FAIR scheme from the subtraction of a label image from a control image.

A number of different readout strategies have been used for renal ASL. Echo planar imaging (EPI) techniques [4] and non-EPI acquisitions, such as True fast imaging with steady state precision (True-FISP or bFFE) [3, 8] or turbo spin echo (TSE) acquisitions [6] have been shown to provide high

SNR for renal ASL readout schemes with minimal image distortions (illustrated in *Figure 2*). With recent advances in parallel imaging, exploiting multichannel coils to accelerate the time it takes to acquire an image, multi-slice readout schemes have been used allowing the imaging of the whole kidney with ASL [4]. However, there is a lack of large studies to validate or compare the variants in terms of sensitivity, specificity, reproducibility and change with disease.

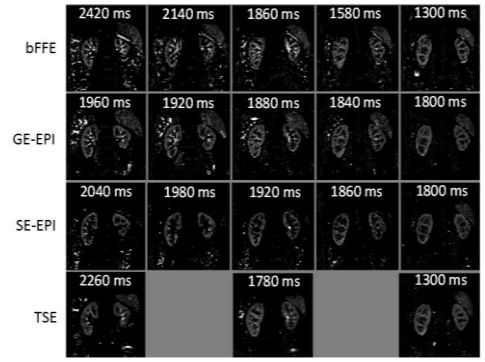

Figure 2: Use of differing readout strategies for renal ASL perfusion weighted images collected at 3 Tesla.

Because ASL is a subtraction technique, a major challenge to all abdominal ASL applications is movement arising from respiratory-related motion, leading to blurring or marked movement of the kidney between each image acquisition. Renal ASL acquisition schemes have therefore been examined to reduce blurring and shot-to-shot variability, such as breath hold, respiratory triggering, navigator-echo methods, and background-suppressed ASL data acquisition [4, 6]. Alternatively, post-processing approaches have been followed, including retrospective sorting and discarding of images, or the use of realignment algorithms to correct respiratory-induced motion [4, 6].

Arterial spin labelling measurements in the kidney are often performed using a single post-label delay time (termed TI), which is chosen to allow blood to traverse the vasculature and perfuse the kidney, and perfusion values have been estimated using a simple model fit. However, the use of single transit time can lead to inaccuracies in the estimation of perfusion and it is accepted that although transit time is short, it is not negligible. The accurate quantification of perfusion using ASL relies on determining the transit time as well as the tissue T_1 relaxation time and this is particularly important in patient groups. Often this is performed in separate scans by acquiring data at a range of label delay times and a separate T_1 map, and using these parameters to fit for perfusion, but this method is time consuming. Alternatively a multiphase (or Look Locker) TrueFISP (or bTFE: balanced turbo field echo) ASL technique can be used [9] which combines the advantage of high-resolution imaging with the rapid acquisition of image readouts at multiple TIs following a single labelling period (Figure 3). This allows the assessment of transit delay (which itself may be prolonged in CKD), thus improving perfusion quantification, as well as providing T_1 maps (themselves markers of fibrosis). Direct quantification of perfusion in mL/100 g per min can be calculated voxel wise in the kidney from a kinetic model if knowledge of the tissue T_1, blood–tissue partition coefficient and transit time of the blood water to tissue water is known or assumed.

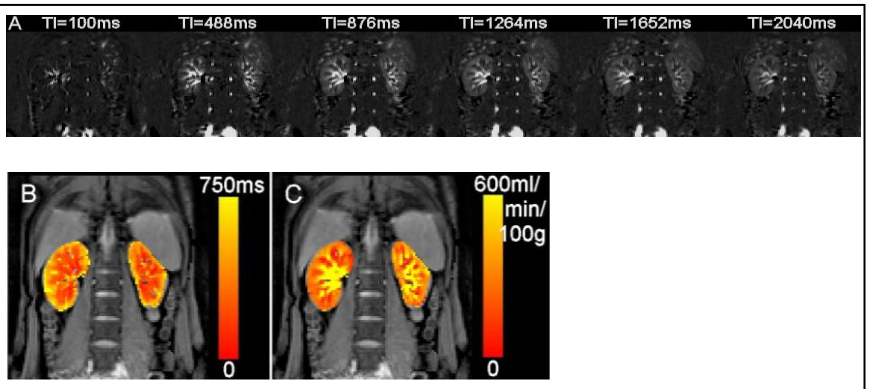

Figure 3: (A) Example perfusion weighted images collected at multiple TIs, and corresponding (B) transit time map and (C) perfusion map.

Kidney perfusion estimates measured with FAIR-ASL have been validated against radiolabelled microspheres in a swine model [10] and para-aminohippurate clearance in humans. It has been shown that ASL can differentiate between medullary and cortical perfusion and is capable of being competitive with contrast-enhanced magnetic resonance at 3 T [2], and shows good reproducibility [11]. ASL measures revealed that transplanted kidneys exhibited lower levels of perfusion compared with native kidneys at similar estimated GFR [12]. In addition, ASL has recently demonstrated

differential effects of 0.9% saline with balanced crystalloids and plasma-lyte on renal perfusion [13, 14]. ASL has also shown differentiation effects in cardiorenal syndrome, with accompanying changes in kidney T_1 cortex values [15].

CONCLUSION:

- The non-invasive and repeatable nature of renal ASL makes it suitable for the assessment or study of organ ischemia and an alternative to exogenous contrast media. It can be used to provide a quantitative measure under a physiological or pharmacological challenge.
- Commercial availability, technical developments and the incentive to avoid use of contrast media are likely to accelerate the translation of renal ASL into clinical practice.
- The clinical utility of renal ASL will be increased by automating the post-processing steps (including T1 measurement and kinetic modelling) to allow real-time ASL perfusion maps to guide clinical decisions.

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