Quantitative Biomarkers in Renal MRI: From Morphology to Physiology

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Highlights

- Kidneys are unique in that the regional tissue oxygenation is not flow limited and hence there is an inherent need to independently evaluate renal oxygenation.
- BOLD MRI is the only known non-invasive method that allows for evaluation of intra-renal oxygenation in humans.
- T2* or R2* can be used as a quantitative parameter but their direct relationship to oxygenation is not simple. A recent study has attempted to validate that relationship.
- Clinical applications to date include reno-vascular hypertension, renal transplants, ureteral obstruction, and diabetic nephropathy/chronic kidney disease. Pre-clinical data applied to iodinated contrast induced acute kidney injury are promising.

Title: ***Blood Oxygenation Level Dependent (BOLD) MRI***

TARGET AUDIENCE: – Radiologists, nephrologists, physicists, MR scientists, and MR technologists who are interested in clinical and/or research studies of the kidney.

OUTCOME/OBJECTIVES: – Attendees will gain an appreciation for the significance of renal oxygenation in addition to renal blood flow. They will learn how to evaluate relative oxygenation status of the kidney using MRI and see examples of both pre-clinical and clinical applications being pursued. Advantages, perspectives and limitations of BOLD MRI in the evaluation of intra-renal oxygenation will also be discussed.

PURPOSE: – In most organs oxygenation is tightly linked to blood flow and perfusion imaging may be sufficient to understanding regional oxygenation. In the kidneys, especially in the medulla, oxygen consumption could change independent of flow. So there is a need to evaluate renal oxygenation in addition to perfusion. Kidneys have the least pO2 difference between the renal artery and vein [1], suggesting that they may be well oxygenated. However, kidneys actually have regions that can be characterized to be hypoxic [2]. Only when spatially resolved measurements are used do the gradients in tissue oxygenation become apparent. Early measurements were made using microelectrodes inserted into rat kidneys [3]. With the availability of non-invasive imaging, translation of these invasive studies to humans became possible [4].

METHODS: – BOLD MRI is inherently sensitive to the oxygenation status of blood. If one assumes that blood oxygenation is in a dynamic equilibrium with the surrounding tissue oxygenation, BOLD MRI can be used to evaluate changes in tissue oxygenation. Early studies with BOLD MRI in humans [4] duplicated results using microelectrodes in rat kidneys. Even though the early studies were performed using EPI [4], multiple gradient echo (mGRE) sequence is now commonly used which allows for R2*/T2* mapping with higher image quality [5]. Combined with breath-holding, a single slice acquisition can be performed in about 10 to 15 s.

APPLICATIONS: - mGRE sequence is now a standard on all major vendor platforms and all of them offer inline mapping options. This offers availability of BOLD MRI for renal oxygenation studies on a widespread basis. This in turn has afforded an opportunity to duplicate the initial findings independently by several investigators throughout the world. To-date, BOLD MRI has been applied in the clinic to evaluate renal vascular hypertension [6], renal transplants [7, 8], ureteral obstruction [9] and diabetic nephropathy/chronic kidney disease [10]. Renal medullary hypoxia has an inherent relevance to acute kidney injury. However, clinical translation is lacking primarily due to logistical issues rather than technical feasibility. Pre-clinical data lend a strong support [11, 12].

DISCUSSION & CONCLUSION: – Renal BOLD MRI is feasible and independently verified in healthy human subjects and in pre-clinical models. However, applications to the clinic are not without certain practical limitations. We may need consensus on the preparation of subjects prior to the study. Consensus is also needed regarding analytical methods. Traditional regions of interest (ROI) analysis is inherently subjective and whole kidney methods are being pursued [13]. While R2*/T2* can be used as a quantitative marker, translation to absolute pO2 has remained elusive. A recent study has shown feasibility that R2' (= R2*-R2) can be calibrated to blood pO2 and, with further modeling, can be related to tissue pO2 [14].

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