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**What do BOLD MR imaging changes in donors' remaining kidneys tell us?**

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malizing T2-weighted signal intensity to the bladder urine signal intensity may improve image-repeat image reproducibility.

We demonstrated this by retrospectively analyzing 14 patients who underwent repeat multiparametric MR imaging studies with two different machines (3.0-T Achieva [Philips, Best, the Netherlands] and 1.5-T Ingenia [Siemens, Erlangen, Germany] between February 2009 and March 2015, with a maximum of 3 months between imaging examinations (E.J., S.P., unpublished data, March 2015). A board-certified radiologist contoured the normal transition zone and peripheral zone on a single section at the mid-gland level for each acquisition and normalized the T2-weighted signal intensity to largest possible ellipsoidal regions of interest positioned within the bladder and on OI muscle.

We found that reproducibility coefficients (5) decreased from 55% to 37% for the transition zone and from 64% to 34% for the peripheral zone when normalized to the bladder (vs OI muscle), which could be explained by the higher signal-to-noise ratio of this region. In addition, we found that reproducibility coefficients for skewness and kurtosis were very poor (>100%) for both apparent diffusion coefficient maps and T2-weighted images, which could explain why these parameters did not contribute to their best performing models.

Multiple imager, multicenter studies provide the most robust evidence of efficacy of quantitative imaging parameters as tools for clinical decision making (6). However, there is an equally important parallel need for prospective studies to determine and improve the reproducibility of quantitative MR imaging-derived metrics.

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## Response

From

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We thank Drs Johnston and Punwani for their interest in and comments on our article, and we agree that every effort should be taken to assess the accuracy and the reproducibility of quantitative MR imaging metrics.

It is also our experience that the signal-to-noise ratio is higher in the urine-filled bladder than in the obturator muscles. Hence, our choice of normalization by muscle yields suboptimal precision.

MR images typically show a loss of signal intensity with depth, even in a homogeneous material. This phenom-

enon is called the intensity nonuniformity artifact (1). The rate at which the signal decays with depth depends on coil configuration, coil size, and radio-frequency pulse and is usually not predictable. We chose normalization by the obturator muscle because obturator muscle and prostate are located at approximately the same depth within the body. When a surface coil is being used, the bladder is near the anterior coil, whereas the prostate is located deeper, approximately halfway between the anterior coil and the posterior coil. Hence, normalization by the bladder is likely to be affected by intensity nonuniformity and can introduce a machine-dependent bias in the measurements. By normalizing with the obturator muscle, it was always possible to choose the region of interest, within the prostate, and the region used for normalization, within the muscle, at the same depth. This is what we did in our study.

The choice of the region for normalization is therefore a trade-off between bias and precision. As of today, there is no clear consensus which is best, and future studies are needed.

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## What Do BOLD MR Imaging Changes in Donors' Remaining Kidneys Tell Us?

From

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#### Editor:

In the June 2016 issue of *Radiology*, Dr Seif and colleagues reported on renal blood oxygenation level–dependent (BOLD) magnetic resonance (MR) imaging of donors and recipients of kidney transplantations (1).

The authors state that the study was aimed to “determine renal oxygenation changes” by monitoring the effective transverse relaxation rates ( $R2^* = 1/T2^*$ ), which are presented to be “inversely related to tissue partial pressure of oxygen” (tissue  $P_{O_2}$ ). Dr Seif and colleagues observed a 10% decrease in medullary and cortical  $R2^*$  in the remaining kidneys of donors. The authors assert that this suggests “increased oxygen content” and conclude that BOLD MR imaging “may be used to monitor longitudinal changes in renal tissue oxygen levels....”

These claims are not backed up by the authors’ data or the literature. Simultaneous  $P_{O_2}$  and  $T2^*$  measurements demonstrated considerable discrepancies in the quantitative relationship between changes in renal  $T2^*$  and in renal tissue  $P_{O_2}$  (2). This relationship is not exclusively governed by renal blood oxygenation but heavily influenced by confounders (3). These include changes in the blood volume fraction (BVF) and in the kidney-specific tubular volume fraction (3,4).

In this light, we encourage Dr Seif and colleagues to consider a different cause for the observed reduction in  $R2^*$ . As  $R2^*$  reflects the amount of deoxygenated hemoglobin per tissue volume, changes in the BVF influence BOLD MR images. The impact of renal BVF changes on BOLD MR images exceeds that of other organs, since the tubular volume fraction is quite large and is dependent on the glomerular filtra-

tion rate (GFR). Estimated GFR of the donor’s kidneys increased by 20% (1). As the renal capsule is rather tough, the ensuing increase in tubular volume probably compresses intrarenal vessels (3,4). This will reduce the BVF so that the reported decrease in  $R2^*$  in the remaining kidney could simply result from increased GFR, rather than from “...increased oxygen content.”

Dr Seif and colleagues ascribe the decrease in  $R2^*$  to “...increased glomerular volume...a result of increased metabolic demand for reabsorption of solutes...that requires a large amount of oxygen” (1). Yet, increased oxygen utilization for reabsorption favors reduced, not increased, renal oxygenation.

To summarize, the notion that renal tissue  $P_{O_2}$  and  $R2^*$  are closely correlated per se for all renal layers and in various pathophysiologic and physiologic scenarios is premature.

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#### Response

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Concerning our article (1), Dr Niendorf and colleagues suggest that we “consider a different cause for the observed reduction in  $R2^*$ ” rather than changes in renal tissue oxygen levels. We are pleased that Dr Niendorf and colleagues agree with us about the validity of the results of our study, that is, the potential of BOLD MR imaging to monitor renal functional changes in remaining and transplanted kidneys, but rather comment on the interpretation.

Dr Niendorf and colleagues are correct that BVF and tubular volume fraction contribute to  $R2^*$  changes and may be confounding factors and that we should have been more careful in discussing these additional potential sources. In fact, we already noted in a *Radiology* article from 2006 that “...the BOLD signal intensity is influenced by blood flow, volume, and oxygen concentration...” (3). Similarly, in our current article (1) we mention the influence of renal blood flow (“Thus, in-



creased levels of tissue oxygen in transplanted kidneys may be attributed to increased blood flow..."). Dr Niendorf and colleagues suggest that our findings of changed  $R2^*$  are due to the strong effect of renal BVF on the BOLD signal in combination with reduced BVF due to compressed intrarenal vessels. While this interpretation of our results is interesting, it ignores the strong renal volume changes. We therefore prefer our previous interpretation.

As already stated previously (4), Dr Niendorf and colleagues claim that "the notion that renal tissue  $PO_2$  and  $R2^*$  are closely correlated per se for all renal layers and in various pathophysiologic and physiologic scenarios is premature." While, as explained above, this is of course correct, first we analyzed  $R2^*$  for five section positions

"covering a large part of the kidney." Second, Dr Niendorf and colleagues point out in the same article (4) "the close medullary tissue  $PO_2/T2^*$  correlation during the hypoxic challenge..." (despite potential confounders). Therefore, while it is correct that confounding factors may play an important role, we still consider changes in renal tissue oxygenation as the most likely cause for our findings.

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