# Change in Intra-Renal Oxygenation by BOLD MRI as Early Marker of Iodinated Contrast Induced AKI (CIAKI)

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## Abstract

Recent reports have questioned the causality of CIAKI [1]. This is related to the clinical definition of CIAKI based on delayed serum creatinine measurements 48-72 hours post-contrast media (CM). Novel markers such as neutrophil gelatinase-associated lipocalin (NGAL) can detect evidence of injury within hours post-contrast [2]. Previous reports using blood oxygenation level dependent (BOLD) MRI have shown near real-time responses to iodinated contrast in CIAKI susceptible rats [3]. However, it is not yet clear if these responses can be related to outcome measures that indicate AKI and if these responses can be mitigated by interventions to prevent AKI.

## Objectives

The purpose of this study was to evaluate whether the BOLD MRI response observed following the administration of CM in CIAKI susceptible animals leads to AKI as determined by urinary NGAL and if this can be reversed by targeted interventions.

## Methods

Male Sprague-Dawley rats (n=18) were anesthetized using inactin (100 mg/kg i.p.). All received nitric oxide synthase inhibitor, N-nitro-L-arginine methyl ester (L-NAME, 10mg/kg) and prostaglandin inhibitor, indomethacin (10 mg/kg) as pre-treatment. Rats were divided into 3 groups based on what intervention they received prior to iodixanol (1600 mg): Control: receiving saline (1ml/kg) ), FUR: receiving furosemide (10mg/ kg); NAC group: receiving n-acetylcysteine (60mg/kg). Group assignments were made in a random order and blinded fashion. Urine samples obtained at baseline and 4 hours post-CM were used to measure NGAL levels as a marker for acute renal injury. To account for the variable dilution of urine, NGAL concentrations were normalized to urine creatinine (uCr) measurements.

## Results

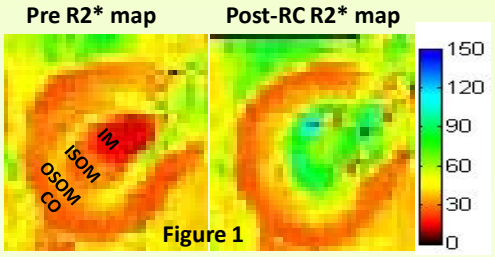


Figure 1 shows representative R2* maps from one rat. Different renal regions where ROIs were defined is indicated on the pre R2* map: inner medulla (IM), inner and outer stripe of outer medulla (IOSM and OSOM) and cortex (CO). Also shown is post R2* map displayed with the same window settings. Note the increasing R2* values following CM suggesting increasing levels of hypoxia, especially in ISOM.

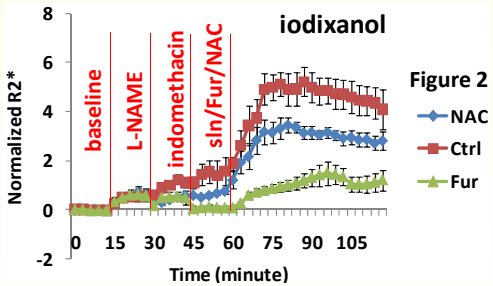


Figure 2 is the summary of BOLD R2* readings from the inner stripe of outer medulla (ISOM) in the three groups of rats. The ISOM is the most sensitive region to changes observed in response to pre-treatment and contrast agents. Each point is the mean±SE over the 6 rats in each group. Note the progressively increasing R2* after each pre-treatment and following contrast in the control group. Furosemide minimized the increase in R2* post-CM compared to control or NAC groups.

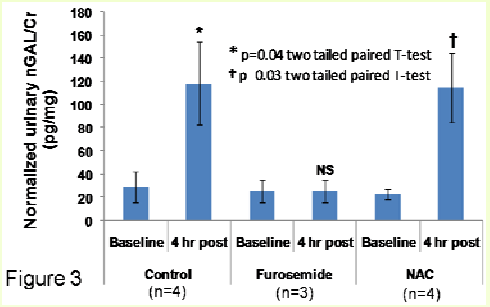


Figure 3 summarizes the urine NGAL measurements obtained at baseline and 4 hour post-contrast. Note that there is a significant increase at 4 hrs in both control and rats treated with NAC suggesting AKI, while there is no change in those treated with furosemide.

## Conclusions

This data reconfirm that acute changes in kidney tissue oxygenation can be monitored following iodinated contrast administration using BOLD MRI. Furthermore, for the first time, the observations with BOLD MRI in the model of CIAKI have been compared with an independent biomarker for CIAKI, urinary NGAL. This suggests that the large increase in R2* following contrast administration is associated with renal injury. Similar increase in R2* and the elevation of NGAL was prevented in the FUR group indicating protection from injury (Figure 3). NAC (at the dose used) was not effective in providing protection from injury.

Future studies should optimize dose of furosemide and NAC for efficacy. Since NGAL has been shown to detect CIAKI in humans, these observations can be translated to humans. Further studies are also warranted to define the threshold R2* value associated with risk of developing AKI.

## References

1. Radiology. 2013;267:106-18.
2. Radiology. 2013;267:86-93.
3. JMRI. 2012;36:1162-7.

Work supported in part by a grant from NIDDK, R01-053221