INTRODUCTION
Pathogenesis of radiocontrast nephropathy is poorly understood [1]. Based on clinical observations, a role for endothelial dysfunction is speculated [1,2]. Nitric oxide and prostaglandins are important mediators released by the endothelium. Recently, it was shown inhibition of these two factors was necessary and sufficient to predispose rats to severe renal injury following radiocontrast administration [3]. We have previously demonstrated that BOLD MRI can evaluate the intrarenal oxygenation noninvasively in humans [4,5]. More recently, we have implemented a multiple gradient recalled echo (mGRE) sequence to perform BOLD MRI in rat kidneys [6]. The technique is ideally suited to follow changes in medullary oxygenation owing to the relatively low tissue pO2 [1]. Here, we have investigated whether BOLD MRI would be sensitive to changes in renal medullary oxygenation following pharmacological inhibition of nitric oxide and prostaglandin synthesis in the same model as in Ref.3.

METHODS
Animal preparation: Six anesthetized (Inactin 100 mg/kg) rats were studied. The femoral vein of the rats were canulated for the administration of pharmacological agents, nitric oxide inhibitor, L-NAME (No-nitro-L-arginine methyl ester, 10 mg/kg) and prostaglandin inhibitor, indomethacin (10 mg/kg). Two sets of experiments were performed where agents were administered in reversed orders.

n = 3, Baseline – L-NAME – Indomethacin
n = 3, Baseline – Indomethacin – L-NAME

Imaging: All studies were performed on a 1.5 T whole body MR scanner (Vision, Siemens Medical Systems, Erlangen, Germany) using a multiple gradient recalled echo (mGRE) sequence (TR/TE/FA= 60 msec/10-56 ms/30°, Acq=1, FOV=125 mm, Thickness= 3 mm, Matrix= 160*256) to acquire 16 T2* weighted images [6]. An R2*=(1/T2*) map was reconstructed online based on the signal in the sixteen T2* weighted images. A flexible wrist coil was used to receive the signal. Rats were placed on their right side to reduce the susceptibility artifacts on the kidneys caused by the bowel gas. We obtained baseline BOLD MRI data and followed the R2* changes every three minutes after administration of the pharmacological agents. We acquired images for 15 min following the injection of each of the pharmacological agents.

RESULTS

Figure 1a shows an example of the R2* maps of the right kidney before and after administration of L-NAME followed by indomethacin. Figure 1b plots the corresponding R2* values in the cortex and medulla. Table 1 shows ΔR2* for cortex and medulla at 15 and 30 minutes after baseline for each of the two sets of experiments performed.

Table 1. ΔR2* ± sd of the medulla and cortex at 15 min after injection of each pharmacological agent.

<table>
<thead>
<tr>
<th></th>
<th>Medulla</th>
<th>Cortex</th>
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<tbody>
<tr>
<td>L-NAME</td>
<td>4.86±3.92</td>
<td>2.10±3.12</td>
</tr>
<tr>
<td>L-NAME+Indo</td>
<td>16.71±3.37</td>
<td>7.24±4.31</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>11.10±10.0</td>
<td>0.83±0.86</td>
</tr>
<tr>
<td>Indo+L-NAME</td>
<td>18.63±3.46</td>
<td>6.43±4.51</td>
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</table>

DISCUSSION
As seen in the Figure 1, this mGRE sequence [6] provides sufficient spatial resolution to differentiate the cortex and medulla in rat kidney. Figure also shows that R2* increases markedly in the medulla following administration of L-NAME and indomethacin, while cortical R2* changes only minimally. Similar additive effects were also observed for the indomethacin-L-NAME series (Table 1). The changes in medullary R2* values are consistent with the changes in the regional blood flow following administration of these agents [3]. Agmon et al report relative changes in cortical blood flow of comparable magnitude to those in the medulla. However, BOLD MRI is less sensitive to changes in blood flow and hence in blood pO2 in the cortex owing to its relatively high baseline pO2 [3]. The observed changes in R2* of the medulla are consistent with invasive pO2 measurements following NO inhibition by LNMMA [7] and indomethacin [8].

In conclusion, BOLD MRI can evaluate noninvasively the medullary oxygenation changes in rat kidneys that are predisposed to acute renal failure. This technique could have valuable applications in evaluating therapeutic/preventive strategies being proposed for ARF in a pre-clinical setting [9] or preventive measures for radiocontrast nephropathy.

ACKNOWLEDGEMENTS:
The work of supported in part by a Grant-in-aid from the American Heart Association (PVP), and National Institutes of Health, DK 53221 (PVP) and DK 18078 (FHE).

REFERENCES