# Assessment of Renal Fibrosis Using Magnetization Transfer MRI

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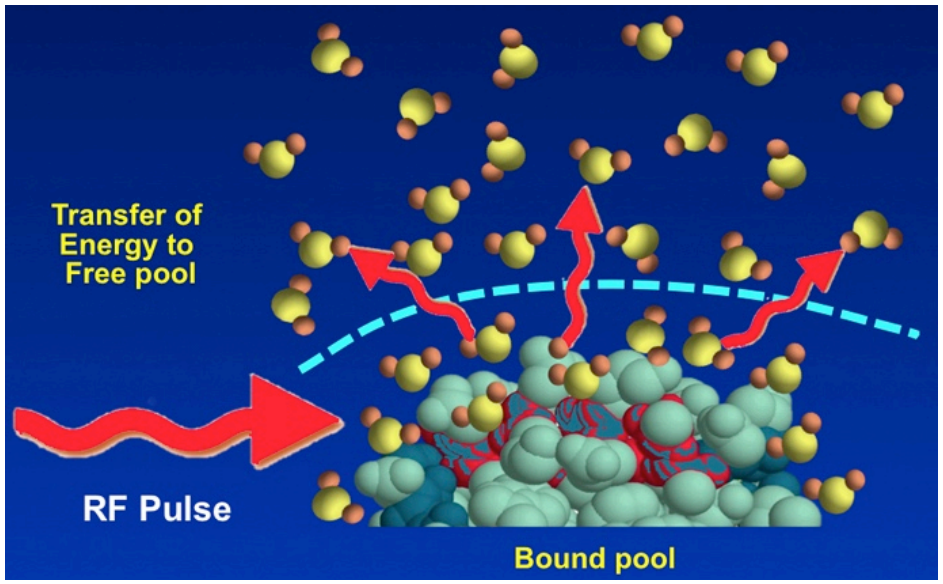
# Development of Renal fibrosis

- Consistent predictor of an irreversible loss of renal function
- Accumulation of extracellular matrix is a common denominator of progressive fibrosis
  - macromolecules like fibronectin, collagens type I, III, and IV, elastin, thrombospondin, vitronectin, laminin, proteoglycans, glycoproteins
- A noninvasive, direct, specific method is needed
  - improve early diagnosis and gauge progression of renal injury or success of therapy

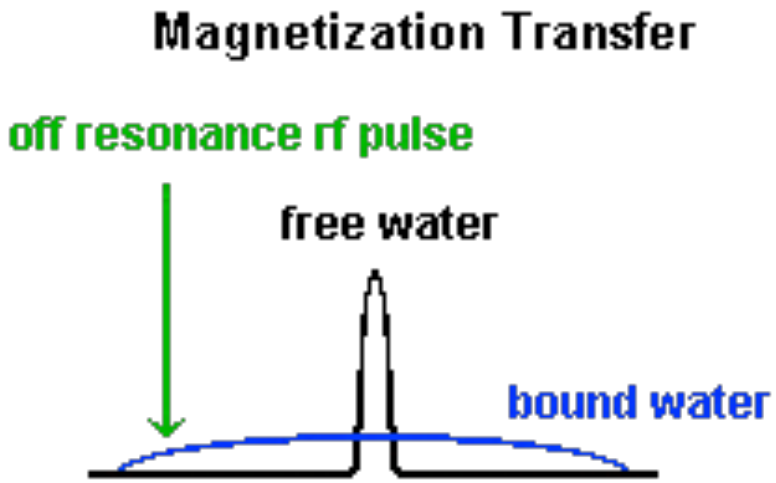

 

# Magnetization transfer imaging (MTI)

- Molecular MRI based on co-existence of 2 tissue proton pools:
  1. Observable, free water pool (freedom to perfuse / diffuse)
  2. Invisible, restricted water pool (bound to local molecules).




- An off-resonance MT can render restricted molecules 'visible'
- *Longitudinal magnetization of restricted water molecules is saturated using a selective radio-frequency (RF) pulse*





# Evaluation of MTI contrast

- Due to their saturation, exchanged molecules do not participate in the MR signal of the free water pool
  - a detectable decrease in free water signal at the readout
  - proportional to restricted pool size and exchange rate
- In scar tissue collagen is the main target macromolecule

- Optimal MTI parameters depend on
  - Collagen type
  - Tissue type
  - Magnetic field

MTI
stands for
Magnetization transfer imaging
...
by allacronyms.com



# Experimental Validation

- Hypothesis: MTI can detect renal fibrosis
  - correlate with kidney function and oxygenation in renovascular disease

**7T and 16.4T:**

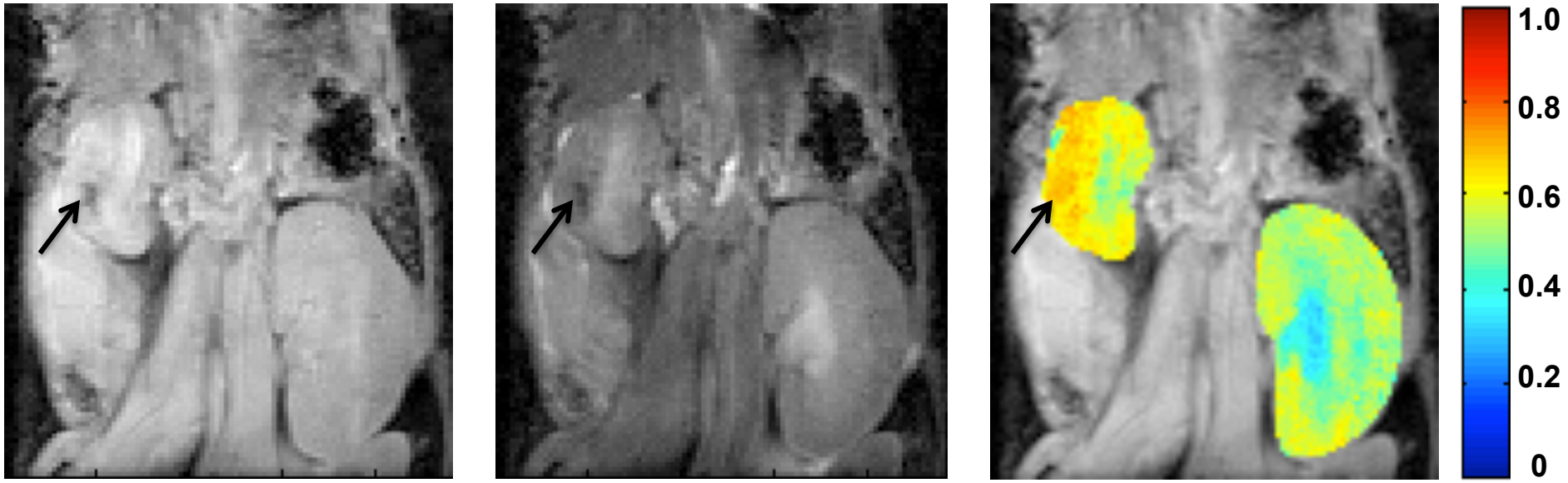
- Ex vivo: excised mouse kidneys
- In vitro: collagen phantom
- In vivo: unilateral murine renal artery stenosis (RAS)
- Longitudinal: at 2, 4, & 6 wks of unilateral murine RAS

**3T:**

- In vitro: collagen phantom
- In vivo: unilateral swine RAS
- In vivo: prediction/detection of reversal of swine RAS

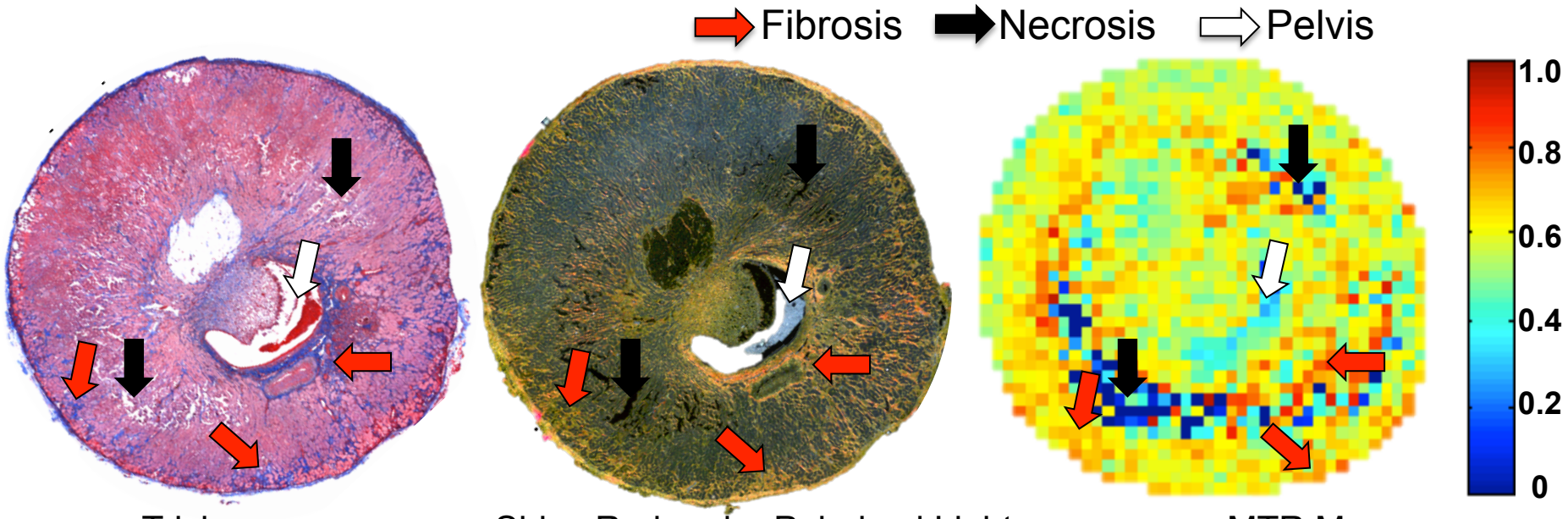
# MTR Maps of Murine RAS Kidneys

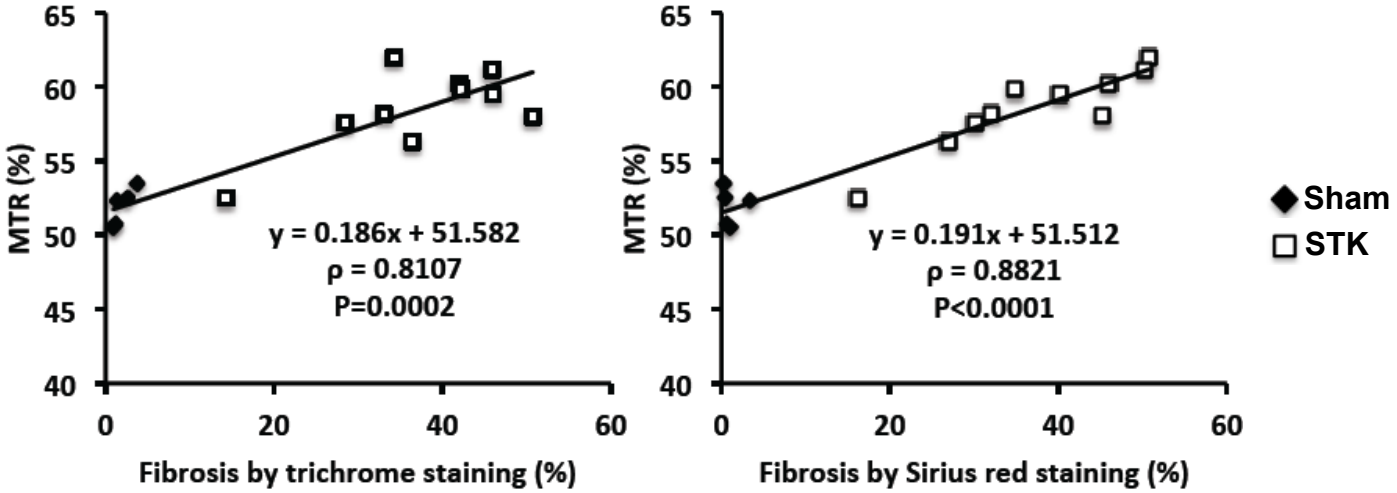



**Baseline** **MT-Weighted** **MTR Map**

# MTI for Fibrosis Measurement in Murine RAS

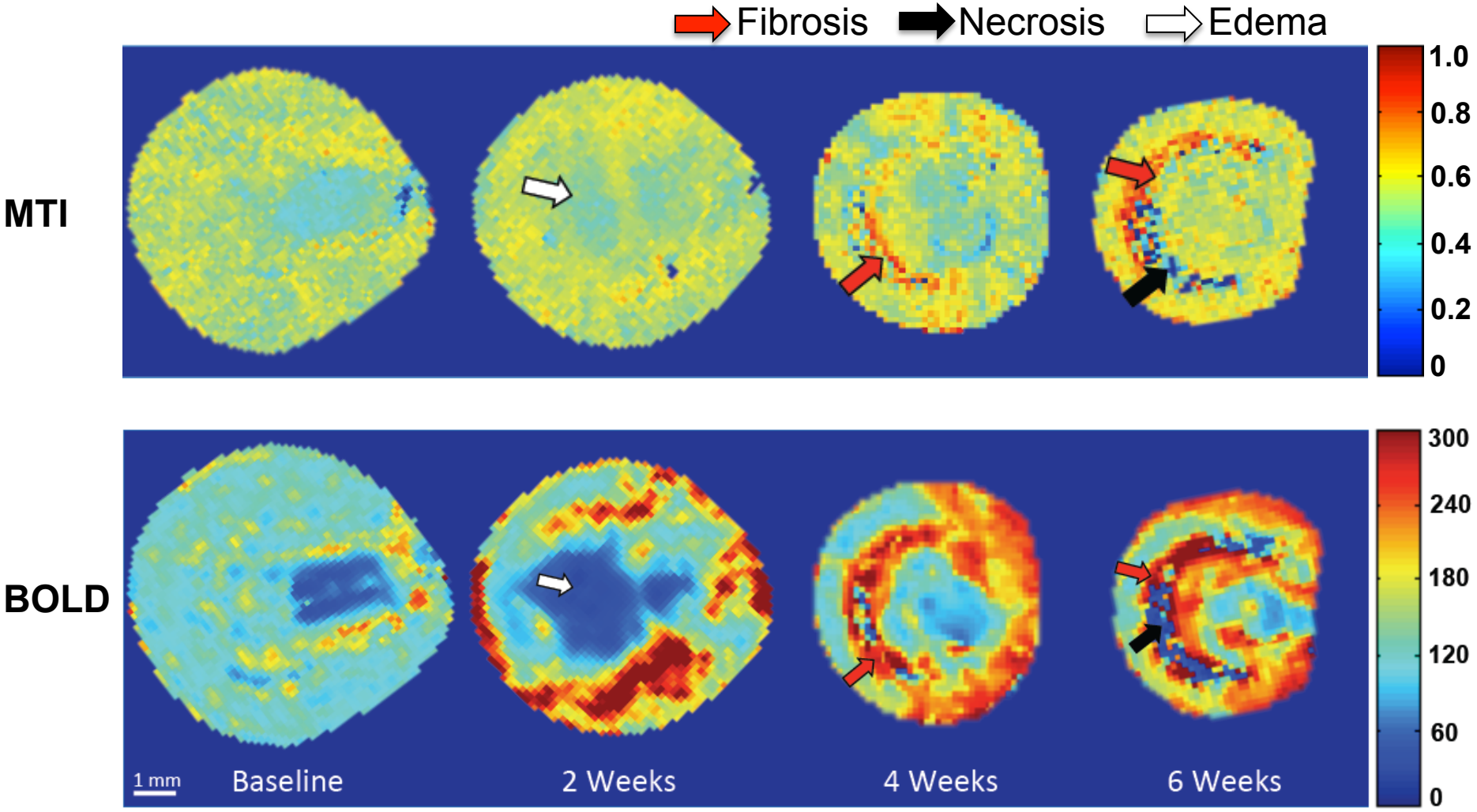





Jiang K, et al… Lerman LO. *Radiology*: 160566, 2016.

# MTI vs. BOLD-MRI



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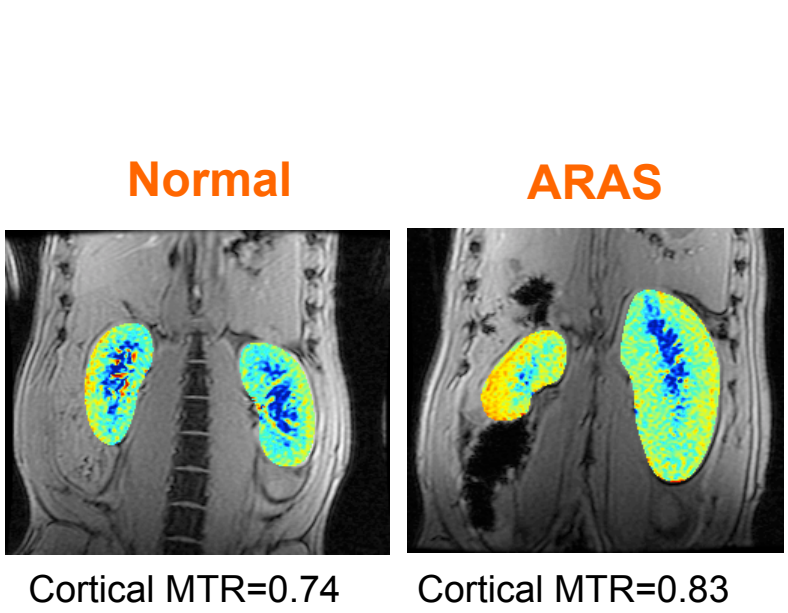
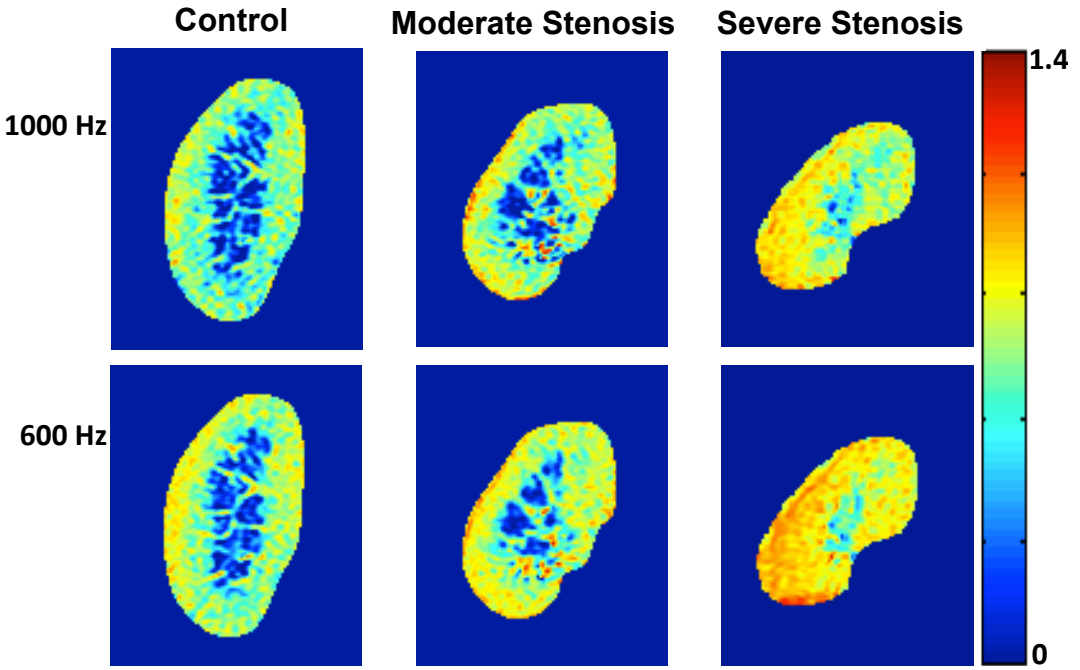
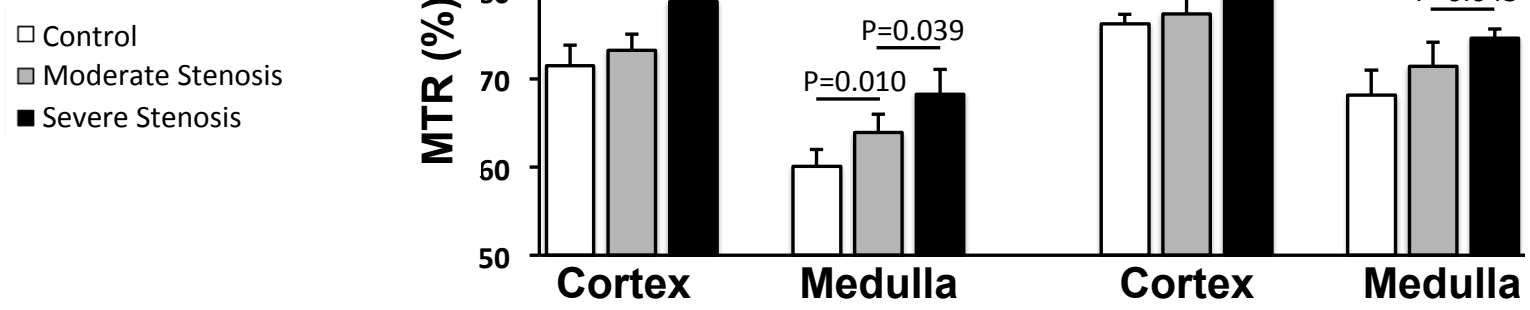
# 3.0 Tesla MRI

# MTI with Moderate and Severe RAS



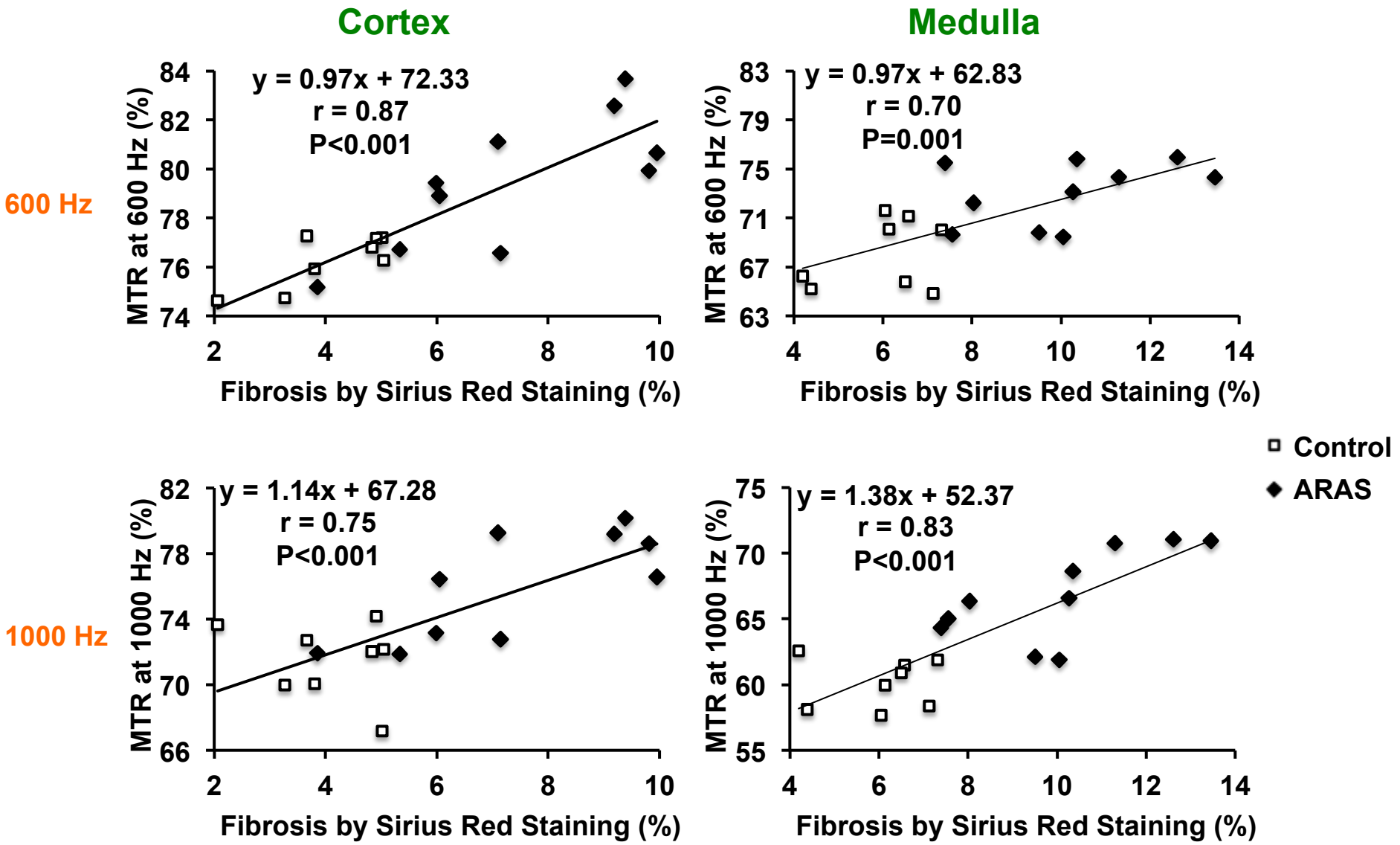




Jiang K, et al. Invest Radiol 52: 686-692, 2017



# Correlation between MTR and Renal Fibrosis



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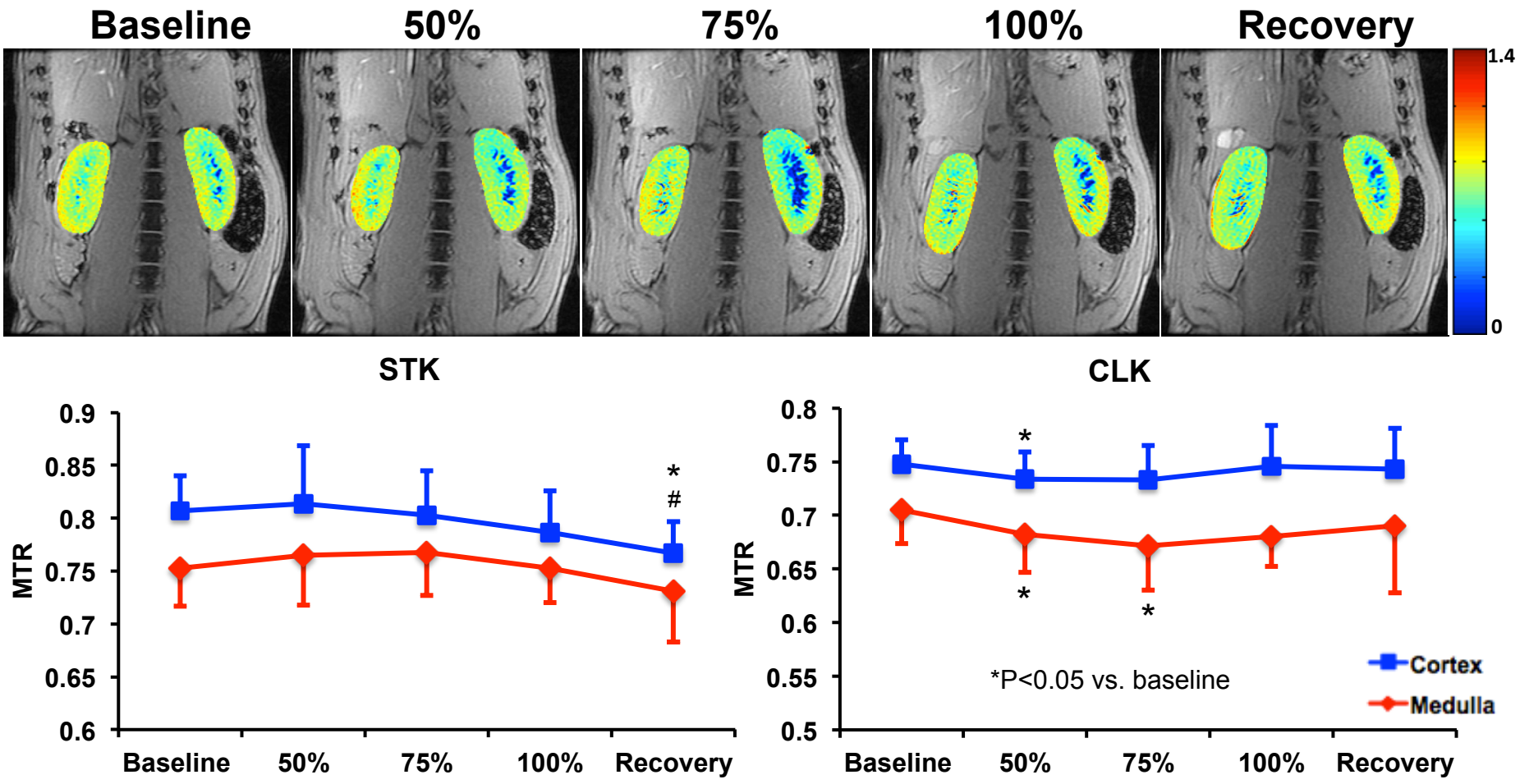
# MTI: Hemodynamic Stability



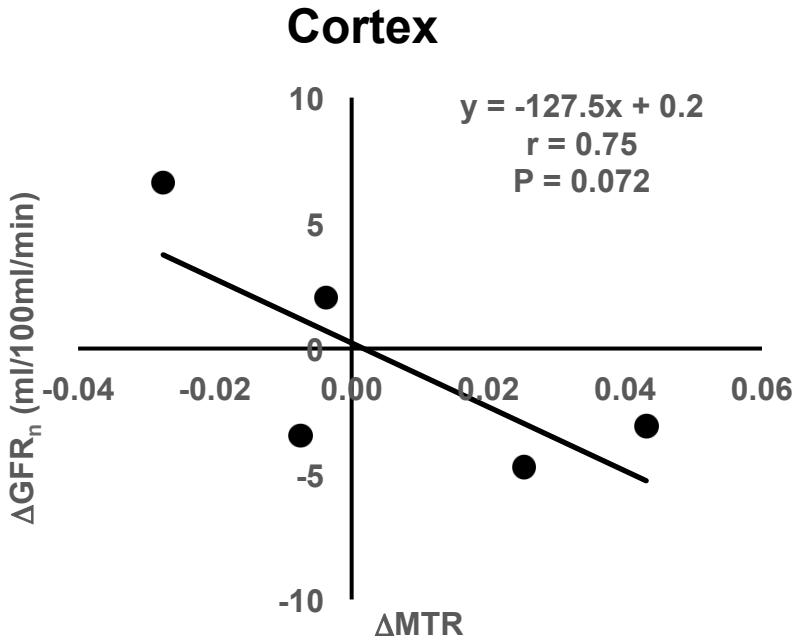

- STK cortical MTR largely stable over a range of RBF
  - slight drop at recovery
- A transient decrease in CLK MTR, due to increased fluid?

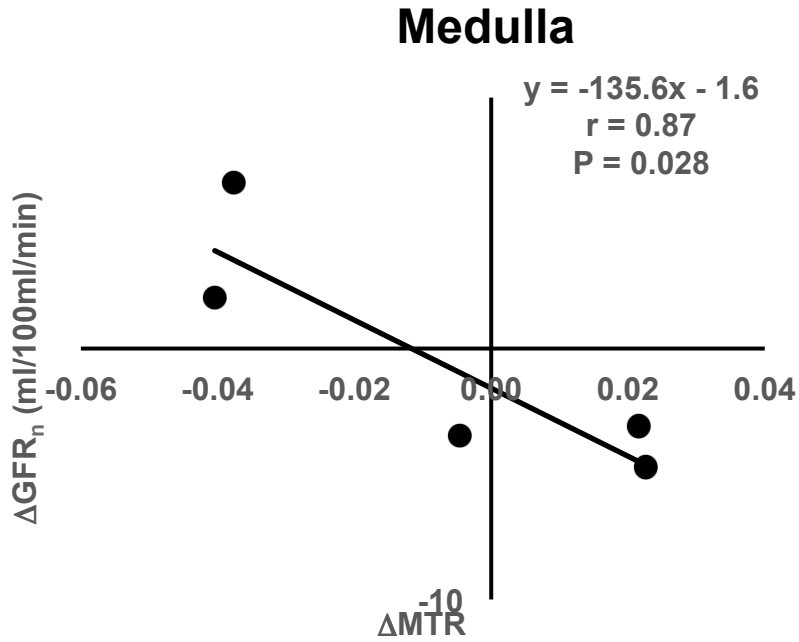
*P<0.05 vs. baseline
#P<0.05 vs. 50%

Offset Frequency at 600 Hz

# MTI in Predicting Renal Recovery

- Pigs studied after 6 wks of RAS and again 4 wks after PTRA
- ΔMTR correlates well with renal $\Delta GFR_n$

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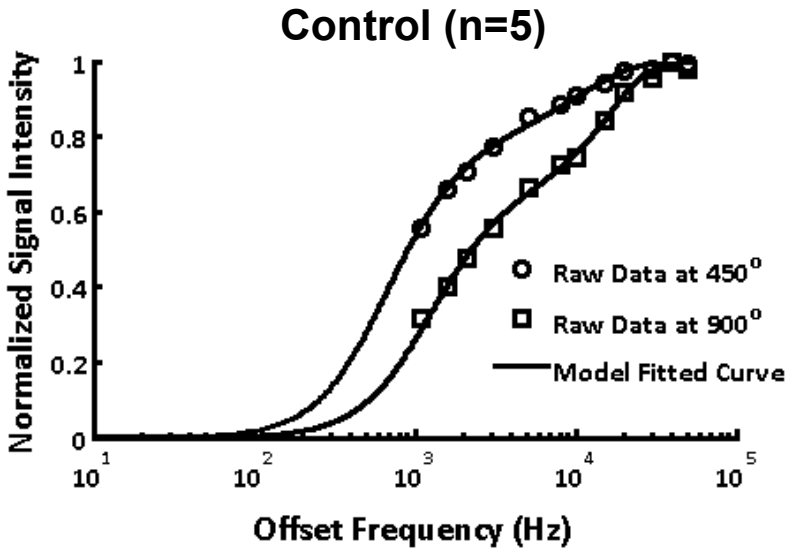
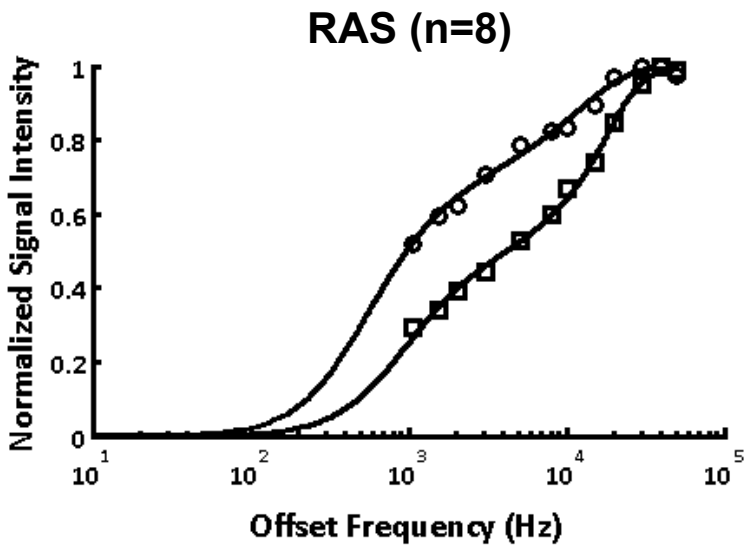
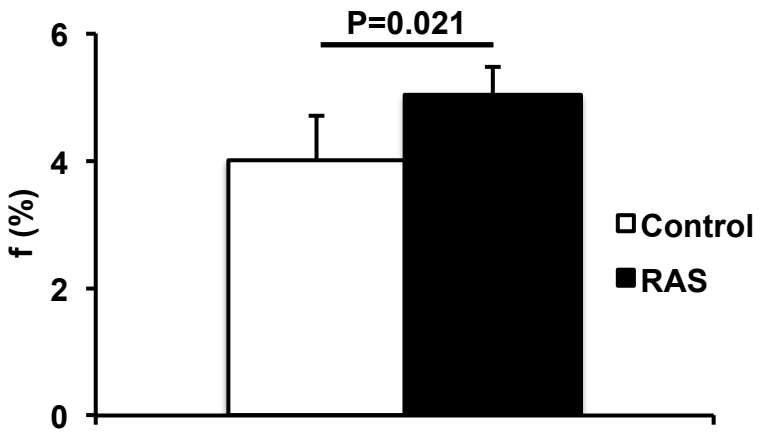
# Quantitative MT (qMT)

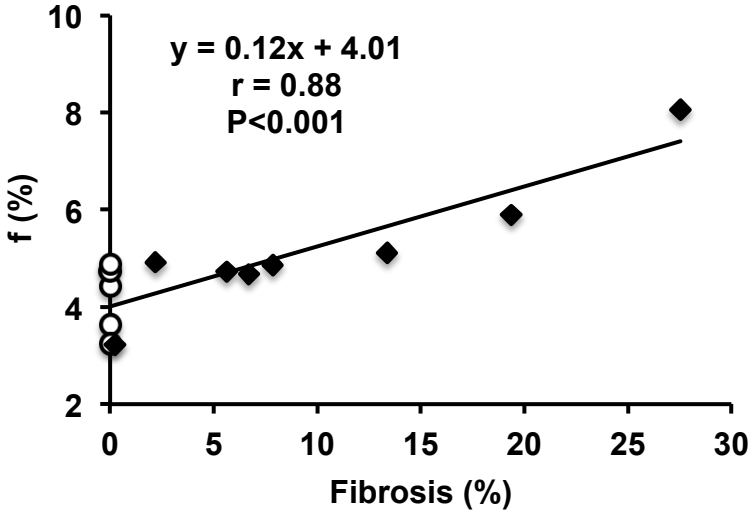

 

# In Vivo qMT at 16.4T: Renal Cortex

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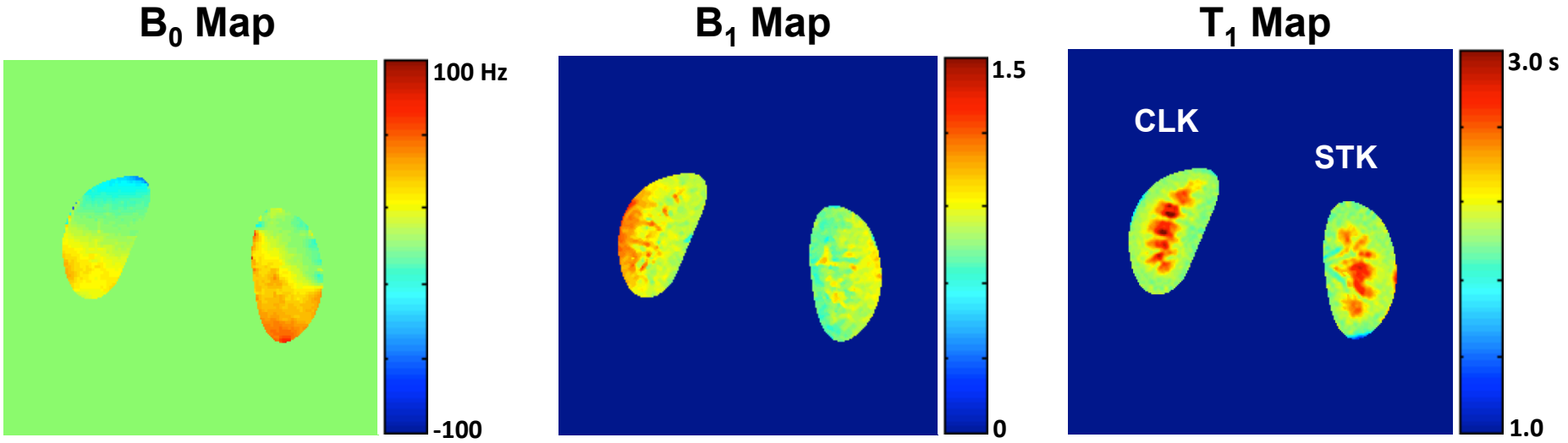
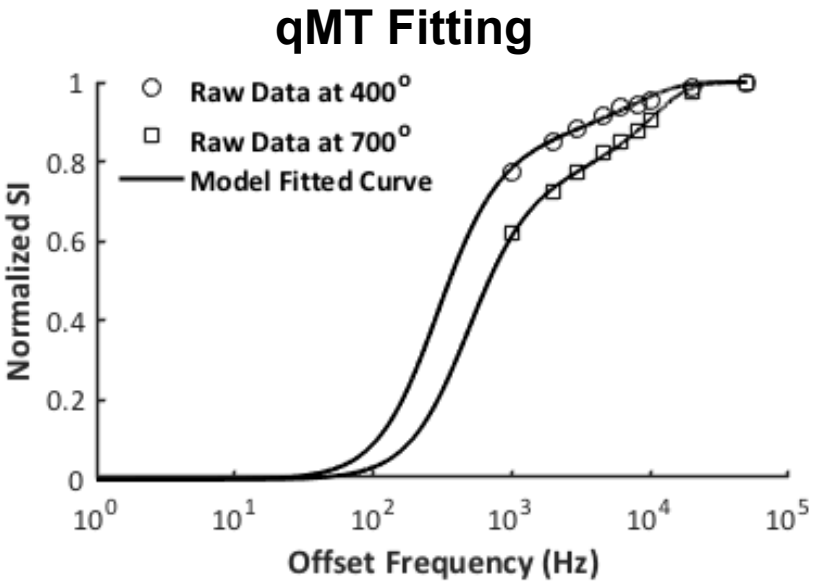
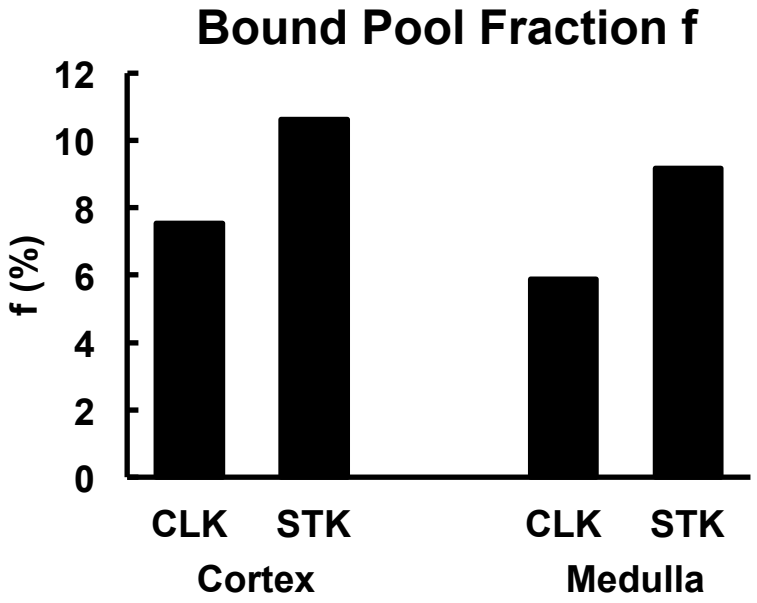
# Feasibility of qMT in Swine Kidney at 3.0 T

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# Conclusions:
## MTI for Detection of Kidney Fibrosis

- In vivo MTR (16.4T, 7T, 3T) correlates well with renal fibrosis determined by histology May allow detection/monitoring of renal disease
- May allow quantitative reproducible measures
- Need to establish sensitivity and specificity; application to other models
- *Cost, availability, contraindications, vendor dependence, application in human subjects?*


 