

# Quantitative Evaluation of Acute Renal Transplant Dysfunction with Low-Dose 3D MR Renography

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## Introduction:

Major causes of acute graft dysfunction are either anatomic or intrinsic causes such as acute rejection, acute tubular necrosis (ATN), and calcineurin inhibitor (CI) immunosuppressive drug toxicity. Therapeutic strategies are radically different depending on the diagnosis. Early characterization of the underlying cause of graft dysfunction is important, because delayed treatment can lead to irreversible loss of nephrons and hasten graft loss over time (1). Unfortunately, biopsies are invasive and painful and can result in complications such as bleeding, infection, and, rarely, graft loss. Our group has proposed low-dose 3D magnetic resonance (MR) renography for measuring renal function based on a multi-compartmental tracer kinetic renal model (2, 3). The purpose of this study was to assess quantitative low-dose 3D magnetic resonance (MR) renography to diagnose acute transplant dysfunction.

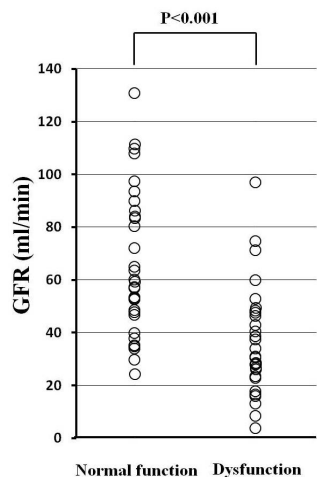
## Materials and Methods:

Low-dose 3D MR renography was performed in 63 consecutive renal transplant recipients. Three subjects with Cr > 8.0 mg/dl (who were examined preceding the FDA advisory about nephrogenic systemic fibrosis) were excluded because of insufficient renal enhancement during low-dose MR renography. Therefore we examined 60 patients (41 men, 19 women; age range, 22-71 years), of whom 31 patients had clinically normally functioning transplants, and 29 patients had acute dysfunction (Table 1) proved by biopsy (n=22) or determined by consensus assessment of all clinical data by an experienced team of 2 transplant surgeons and one nephrologist (n=7). According to an IRB-approved protocol, MR renography was performed at 1.5 T (Avanto or Symphony, Siemens) with 3D FLASH oblique coronal sequence (TR/TE/flip angle=2.84/1.05/12°, 1.7x1.7x2.5 mm<sup>3</sup> voxel, 3 s acquisition time) acquired repeatedly during intermittent breath-holding for 10 min after 4 ml Gd-DTPA and 20 ml saline flush, injected at 2 ml/s. (Following Dec 2006, all subjects with GFR < 30 ml/min based on MDRD estimator were excluded from participation because of the risk of NSF.) In addition to MR renography, all subjects underwent routine T1- and T2-weighted imaging and contrast-enhanced MR angiography,

venography, and urography for routine anatomic assessment. Glomerular filtration rate (GFR), mean transit time for vascular (MTT-A), mean transit time for tubules (MTT-T) and mean transit time for whole kidney (MTT-K) were calculated using the multi-compartmental tracer kinetic renal model applied to Gd concentration vs. time curves for renal cortex and medulla (3). GFR and the ratio of MTT-A to MTT-K (MTT-A/K), MTT-T to MTT-K (MTT-T/K) were compared between transplanted kidneys with normal, acute rejection, ATN, chronic rejection and drug toxicity. Statistical analysis was performed by using ANCOVA. P<0.05 was considered to indicate a significant difference.

**Table 1**

|                   | Acute rejection | ATN         | Chronic rejection | Drug toxicity |
|-------------------|-----------------|-------------|-------------------|---------------|
| n                 | 12              | 8           | 6                 | 3             |
| Age (y)           | 44.9 ± 14.8     | 52.3 ± 14.2 | 46.3 ± 16.4       | 47.3 ± 8.3    |
| Creatinin (mg/dl) | 3.1 ± 1.0       | 2.7 ± 0.7   | 2.9 ± 1.3         | 2.7 ± 1.2     |
| Diagnosis         |                 |             |                   |               |
| Biopsy (n)        | 10              | 7           | 3                 | 2             |
| Clinical (n)      | 2               | 1           | 3                 | 1             |



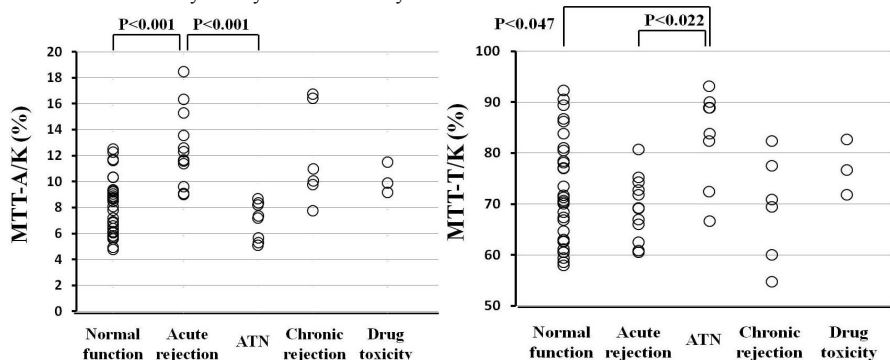
**Fig 1.** Scatterplots show GFR in normal function kidney and dysfunction kidney.

## Results:

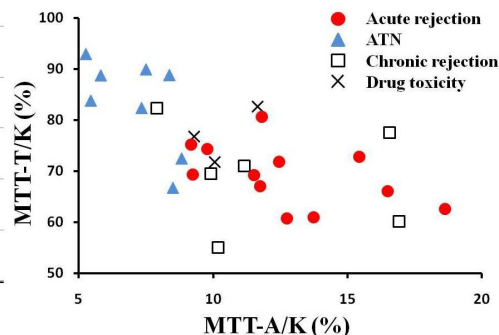
Average GFR was 36.4 ± 20.8 ml/min in the group with acute dysfunction, compared with 65.9 ± 27.6 ml/min in the normal functioning group (P<0.001) (Fig 1). MTT-A/K was significantly higher in acute rejection group (mean 12.7 ± 2.9 %, range 9.2 – 18.6 %) than in normal function group (mean 8.3 ± 2.2 %, range 4.9 – 12.7 %) (P<0.001) or in ATN group (mean 7.1 ± 1.4 %, range 5.3 – 8.8 %) (P<0.001) (Fig 2a). MTT-T/K was significantly higher in ATN group (mean 83.2 ± 9.2 %, range 66.7 – 92.9 %) than in the normal function group (mean 72.4 ± 10.2 %, range 58.2 – 92.1 %) (P=0.047) or in acute rejection group (mean 69.2 ± 6.1 %, range 60.7 – 80.6 %) (P=0.022) (Fig 2b). Distribution of MTT-A/K and MTT-T/K in each disease is shown in Fig 3. The measure MTT-A/K was itself able to perfectly discriminate ATN from acute rejection. In particular, the diagnostic test that classified patients as acute rejection when MTT-A/K 9.0% and as ATN otherwise achieved 100% diagnostic accuracy.

## Conclusion

Our findings of delayed vascular transit times in acute rejection are consistent with histopathologic data. Similarly, our results showing delayed tubular transit times in ATN compared with normal or acute rejection are also consistent with the known impaired tubular function in ATN (4). Using our low-dose MR renography method, we found the pattern of high MTT-A/K and low MTT-T/K in acute rejection compared with ATN. For our sample, MTT-A/K alone was able to perfectly discriminate ATN from acute rejection. We found no parameters that could predict diagnoses of drug toxicity, although our results are limited by small sample size. Our method of MR renography with the multi-compartmental tracer kinetic renal model is promising for the diagnosis of acute transplant renal dysfunction and can be performed as a component of routine anatomic imaging of the transplanted kidney.



**Fig 2.** Scatterplots show the relationship between MTT-A/K and each dysfunction (a) and between MTT-T/K and each dysfunction (b).



**Fig 3.** Distribution of MTT-A/K and MTT-T/K in each dysfunction.

## References

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