Applications of MRI to renal transplantation - evidence to date

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Introduction

- Renal transplantation is the therapy of choice for patients with end-stage renal diseases
- Episode of acute allograft dysfunction is reported in approximately 30%–40% of patients
- Early detection of allograft dysfunction is mandatory for a good outcome, but might be challenging in clinically asymptomatic patients

Introduction

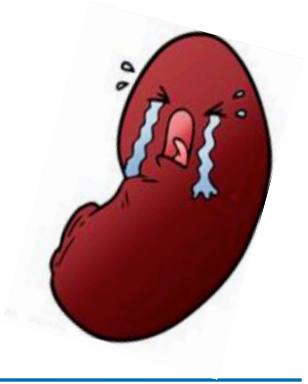
- Standard procedure in case of unclear allograft dysfunction is invasive renal biopsy

- Low risk of biopsy associated major complication (0.4% and 1%), one graft lost in approximately 2,500 biopsies (Schwarz *et al.,* 2005)

- Elevated risk of complications: patients >60 years, low glomerular filtration rate (GFR) (<60 ml/min/1.73 m^2), hypertension, acute renal dysfunction (Tøndel *et al.,* 2012)

Possible complications

- Lymphogenic (lymphocele) and urological (urinoma, urin leckage)
- Vascular (ishemia)
- Acute allograft rejection (AAR) (oedema, inflammation) and chronic allograft rejection (CAR) (fibrosis)
- Acute tubular necrosis (ATN)
- Drug induced by ciclosporine, virustatika etc. (fibrosis)



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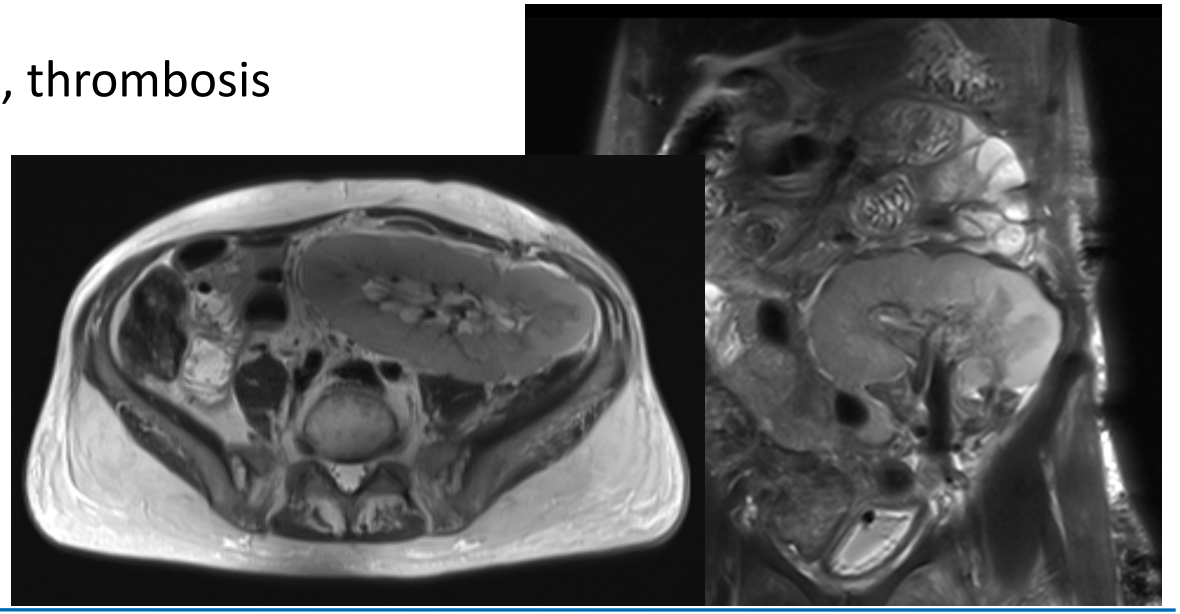
Investigation protocol

- Anatomical imaging
- DWI/DTI
- ASL
- BOLD
- T1 and T2 mapping
- Other methods

Anatomic imaging

- T2 HASTE in three spatial directions for anatomical imaging

$\Rightarrow$ Possible diagnosis of:
lymphocele, urinoma, thrombosis



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DWI/DTI

- 23 DWI/DTI studies in transplants (August 2017)
- ADC, D, D* in mm^2/s
- FA dimensionless
- *f* in %

- **ADC** correlates with allograft function (eGFR) and degree of allograft rejection in the biopsy (Kaul *et al.,* 2014)
- ***f* (IVIM)** significantly reduced in allografts with acute rejection (Eisenberger *et al.*, 2010)
- **FA** (medulla) correlates with eGFR and is significantly lower in patients, whose allograft function did not recover in comparison to patients with reversible allograft dysfunction (Lanzman *et al.,* 2013)

DWI/DTI

- DWI parameters might further improve the assessment of the severity of renal allograft dysfunction and help to decide when to perform biopsy

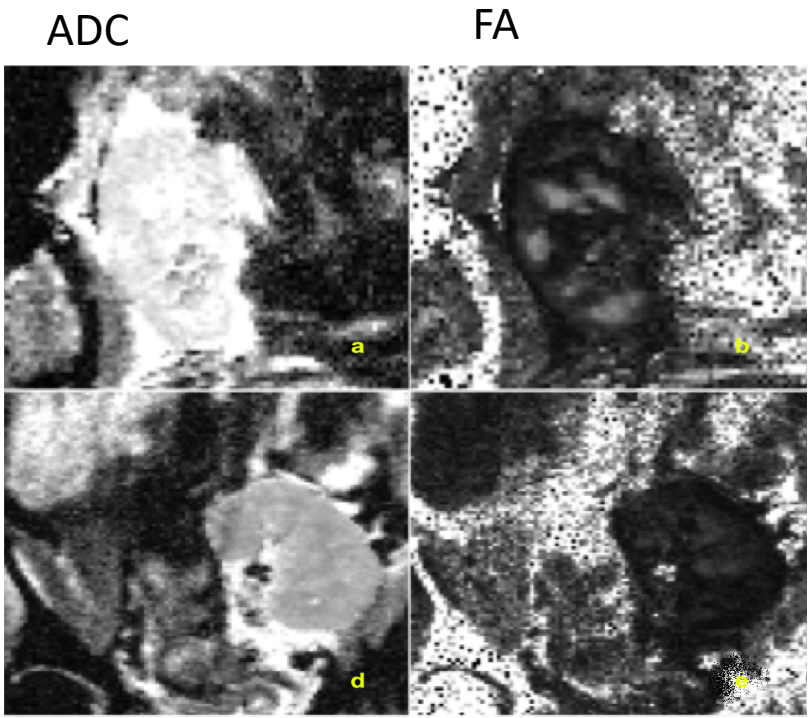
- No differentiation of various underlying pathologies responsible for the impaired renal function

$\Rightarrow$ Possible diagnostic value: ATN, AAR, degree of fibrosis (CAR), reversibility of graft dysfunction

DWI/DTI

Good allograft function
eGFR > 60 ml/min/1.73 m^2

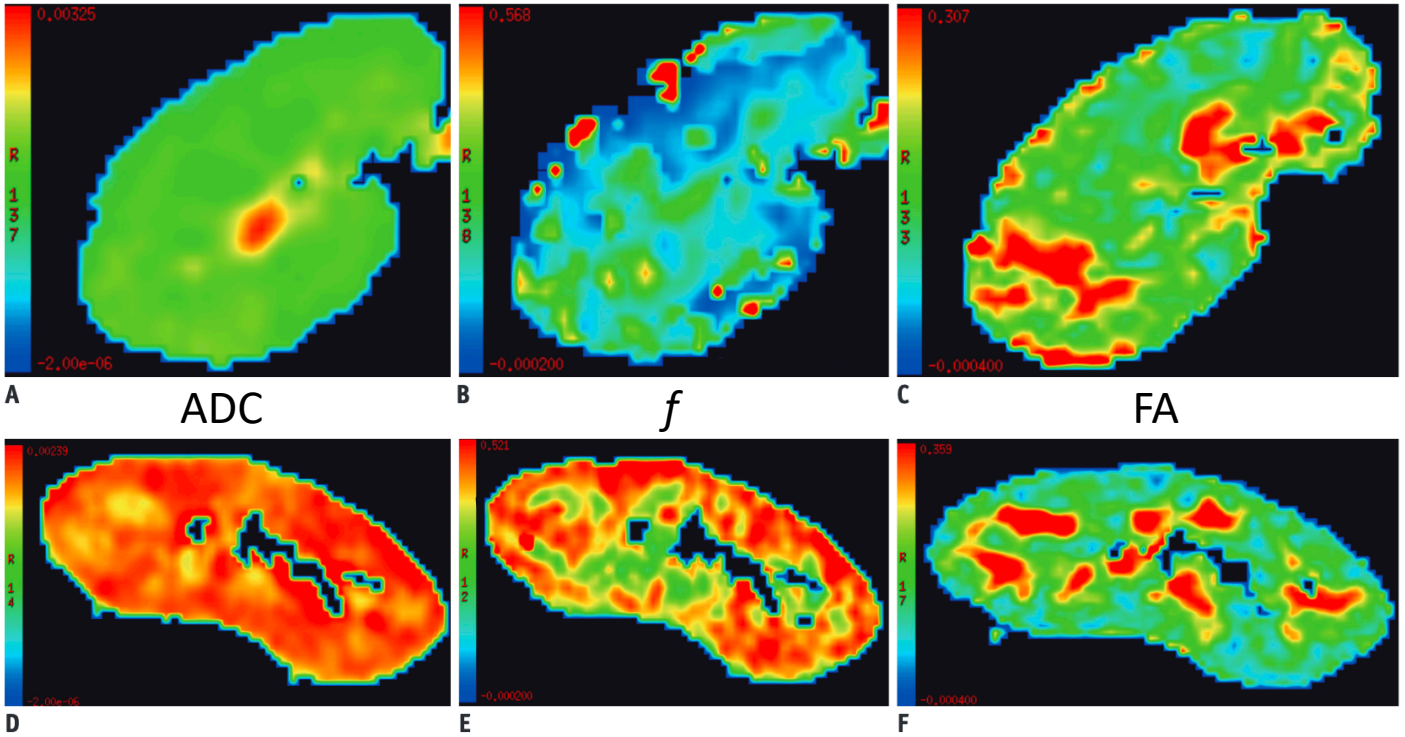
Poor allograft function
eGFR = 15 ml/min/ 1.73 m^2



Ljimani et al., „Functional MRI of transplanted kidney“, Abdom Radiol (NY). 2018 Oct;43(10):2615-2624

DWI/DTI

Poor allograft function
eGFR = 20
ml/min/ 1.73 m^2



Good allograft function
eGFR = 100
ml/min/ 1.73 m^2

Yu et al., „Multiparametric Functional Magnetic Resonance Imaging for Evaluating Renal Allograft Injury“, Korean J Radiol. 2019 Jun;20(6):894-908.

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ASL

- 6 ASL studies in transplants (January 2018)
- Perfusion in ml/100g/min

- **ASL** perfusion in cortex correlates significantly with eGFR (Heusch *et al.,* 2014)
- **ASL** perfusion differ between patients with early and delayed graft function after transplantation (Hueper *et al.,* 2015)
- **ASL** perfusion can be used to determine filtration fraction and could potentially act as a biomarker of renal functional reserve in potential living kidney donors (Cutajar *et al.,* 1988)

ASL

- **ASL** perfusion correlates with the percentage of affected tubules in kidney biopsies (Hueper *et al.,* 2014)
- **ASL** perfusion in the cortex of affected allografts decrease compared to stable allograft function two years after transplantation (Niles *et al.,* 2016)

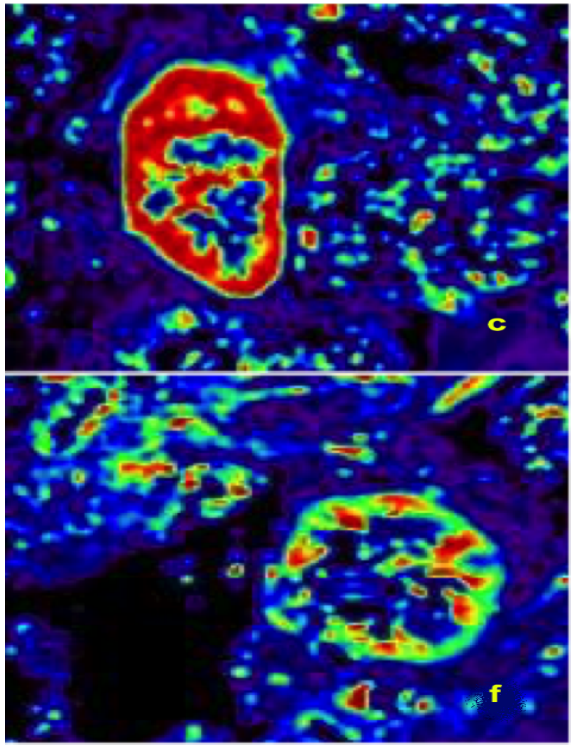
- Low SNR

$\Rightarrow$ Possible diagnostic value: predicative factor for allograft outcome, CAR and long-term monitoring, renal functional reserve in donors

ASL

Good allograft function
eGFR > 60 ml/min/ 1.73 m^2

Poor allograft function
eGFR = 15 ml/min/ 1.73 m^2



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Investigation protocol

- Anatomical imaging
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BOLD

- 15 BOLD studies in transplants (December 2017)
- R2* in 1/s

- **R2*** in medulla lower during acute rejection compared with normally functioning transplants and transplants with ATN (Sadowski *et al., 2005)*
- **R2*** in cortex higher in ATN compared with acute rejection and with normally functioning transplants (Sadowski *et al., 2005)*
- **R2*** c/m - ratio marker to distinguish between ATN, acute rejection and normally functioning transplants

BOLD

- **R2*** in medulla an important tool for the detection of subclinical chronic allograft damage and long-term monitoring (Niles *et al.,* 2016)

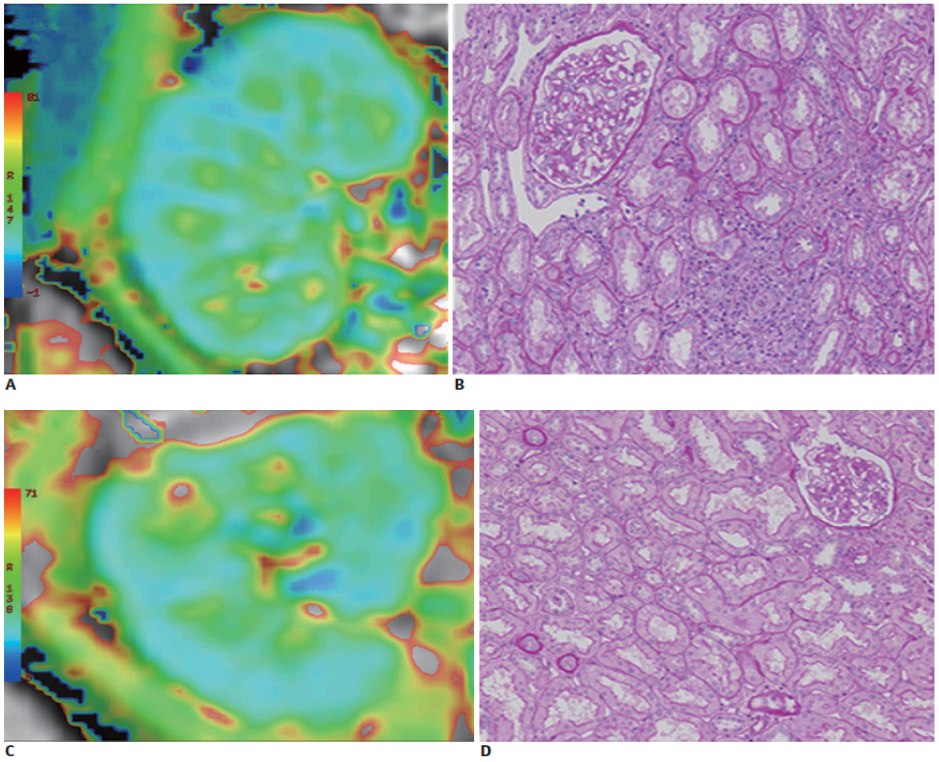
- BOLD MRI cannot distinguish the changes in oxygenation caused by perfusion alterations from those attributed to oxygen consumption alterations

$\Rightarrow$ Possible diagnostic value: ATN vs AAR, CAR, long-term monitoring especially of drug therapy

BOLD

Acute rejection

Good allograft function



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Investigation protocol

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T1 and T2 mapping

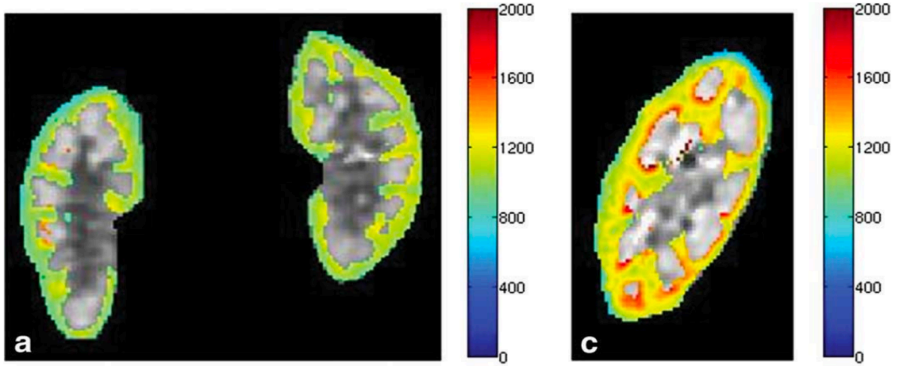
- 3 T1 studies, no T2 studies in transplants (Oktober 2017)
- T1 and T2 in ms

- **T1** in cortex strongly correlate with eGFR (Huang *et al.,* 2011)
- **T1** c/m – ratio show moderate correlation with renal interstitial fibrosis and eGFR (Friedli *et al.,* 2016)

- Low specificity as fibrosis and oedema both influence T1
- No specificity for different pathologies due to low study number

$\Rightarrow$ Possible diagnostic value: interstitial fibrosis, evaluation of transplant function

T1 and T2 mapping



nativ

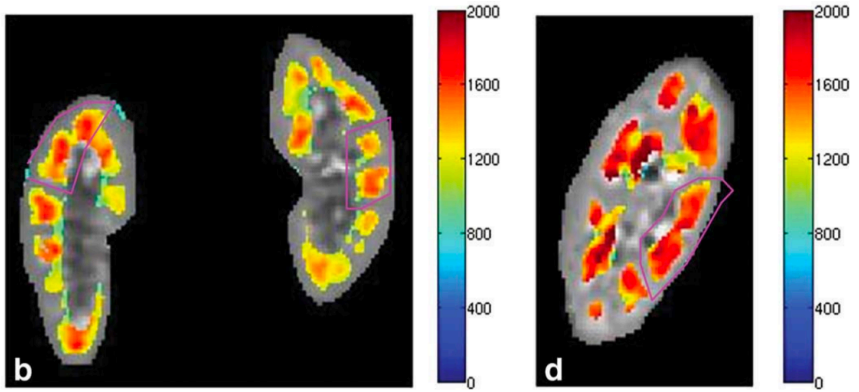
transplant

Cortex

Medulla

nativ

transplant



Huang et al., „Measurement and comparison of T1 relaxation times in native and transplanted kidney cortex and medulla“, Volume33, Issue5, May 2011, Pages 1241-1247

Overview

IMAGING TECHNIQUE	ATN		AAR		CAR	
	C	M	C	M	C	M
DWI/DTI ADC	↓	↓	↓	↓	↓	↓
FA	-	-	↓	⇊	↓	⇊
f	-	↓	-	↓	-	-
ASL PERFUSION	↓	-	↓	↓	-	-
BOLD R2*	↑	-	-	⇊	-	↓
T1	ratio↓		ratio↓		ratio↓	

Investigation protocol

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MRA

- Contrast free techniques TOF-MRA and SSFP
- Very good correlation to digital subtraction angiography (DSA) (Lanzman *et al.,* 2009)
- Often overestimates the degree of RAS of renal allografts

$\Rightarrow$ Possible diagnostic value: assessment of vascular abnormalities in renal allografts

MRA

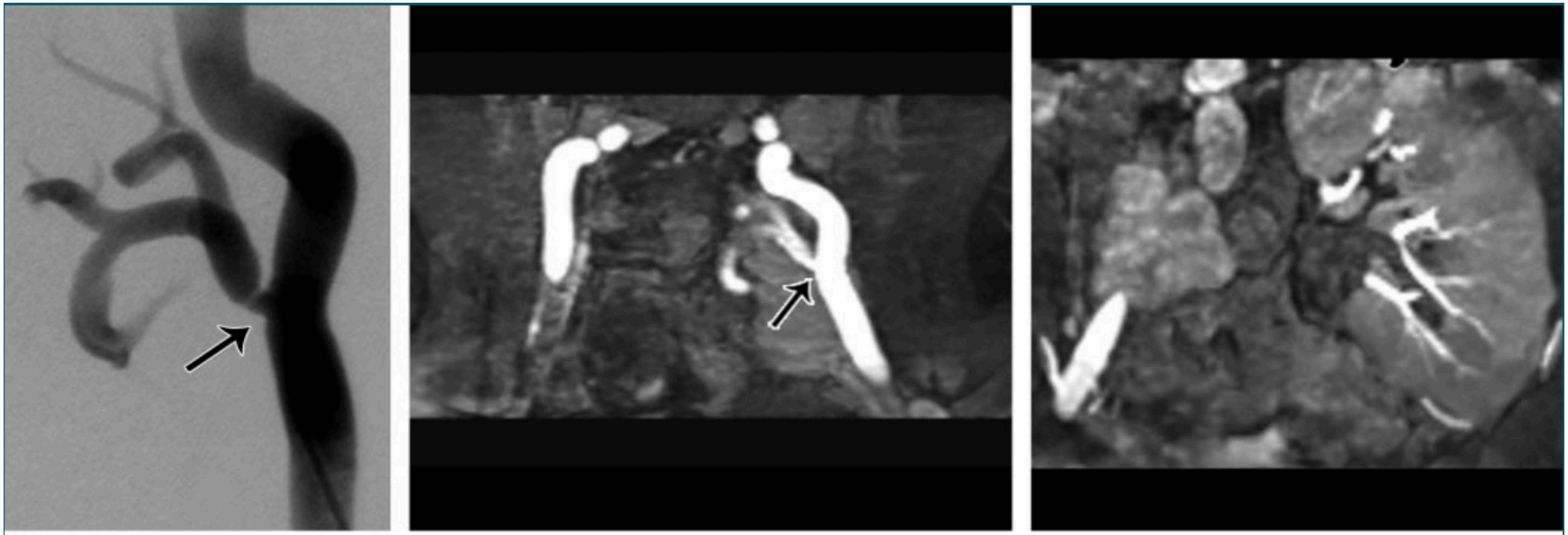


Figure 4: Images in 31-year-old man (living donor recipient) suspected of having TRAS at US. **(a)** DSA shows relevant TRAS (grade 3, arrow) at anastomosis with external iliac artery. **(b)** Extent of stenosis (arrow) is depicted correctly on coronal MIP reconstructions but signal loss is seen in main transplant artery. **(c)** Note excellent contrast of parenchymal branches on coronal MIP reconstructions.

Lanzman et al., „ECG-gated nonenhanced 3D steady-state free precession MR angiography in assessment of transplant renal arteries: comparison with DSA“, Radiology. 2009 Sep;252(3):914-21.

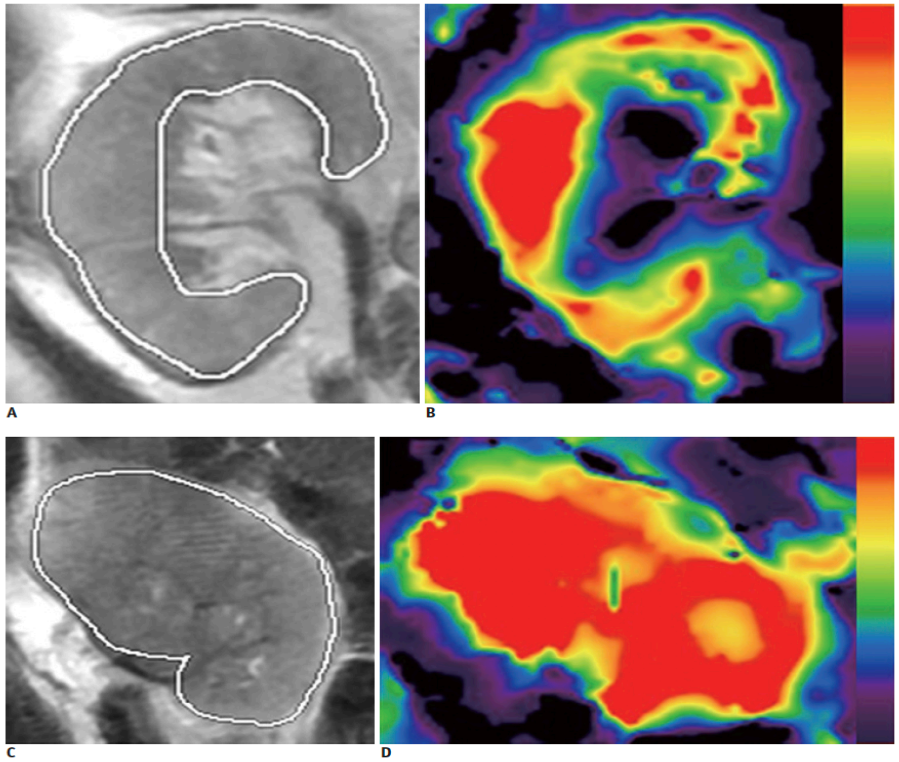
New methods

- Chemical-exchange-saturation-transfer (**CEST**) shows increased contrast ratios from cortex to medulla in allografts with acute allograft rejection compared with healthy controls (Kentrup *et al.,* 2017)
- **^{23}Na** - based MRI shows significant lower ^{23}Na concentration and corticomedullary sodium gradient in transplanted kidneys in comparison with native kidneys (Moon *et al.,* 2014)
- Quantitative susceptibility mapping (**QSM**) deliver information on renal tissue microstructure (Xie *et al.,* 2013)
- Quantitative mapping of the longitudinal relaxation time in the rotating frame (**$T_1\rho$**) significant correlates with the degree of renal fibrosis (Rappachi *et al.,* 2015)
- Magnetic resonance elastography (**MRE**) a reliable tool for the assessment of whole kidney stiffness (Kirpalani *et al.,* 2017)

New methods

Poor allograft function
eGFR = 15 ml/min/ 1.73 m^2

Good allograft function
eGFR = 89 ml/min/ 1.73 m^2



MRE

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Conclusion

IMAGING TECHNIQUE	DIAGNOSTIC VALUE
DWI/DTI	ATN, AAR, degree of fibrosis (CAR), reversibility of graft dysfunction
ASL	Predicative factor for allograft outcome, CAR and long-term monitoring, renal functional reserve in donors
BOLD	ATN vs AAR, CAR, long-term monitoring especially of drug therapy
T1/T2 MAPPING	Interstitial fibrosis, evaluation of transplant function
MRA	Assessment of vascular abnormalities in renal allografts
CEST	Tissue microenvironment
^{23}NA-MRI	Corticomedullary sodium gradient
QSM	Local susceptibility, tubulus tracking
$T_1\rho$	Fibrosis
MRE	Fibrosis

Conclusion

- All MRI techniques deliver diverse information about the renal allografts
- Multicenter validation of functional MR-techniques is urgently needed (increasing sample size)
- Cut-off values for different pathologies
- More PR for the techniques
- Multiparametric examination protocol will improve the monitoring of renal allografts and detection of different causes of allograft dysfunction (acquisition time about 30 min)

Thank you very much for your attention!