# Application of MRI to Chronic Kidney Disease (CKD): evidence to date

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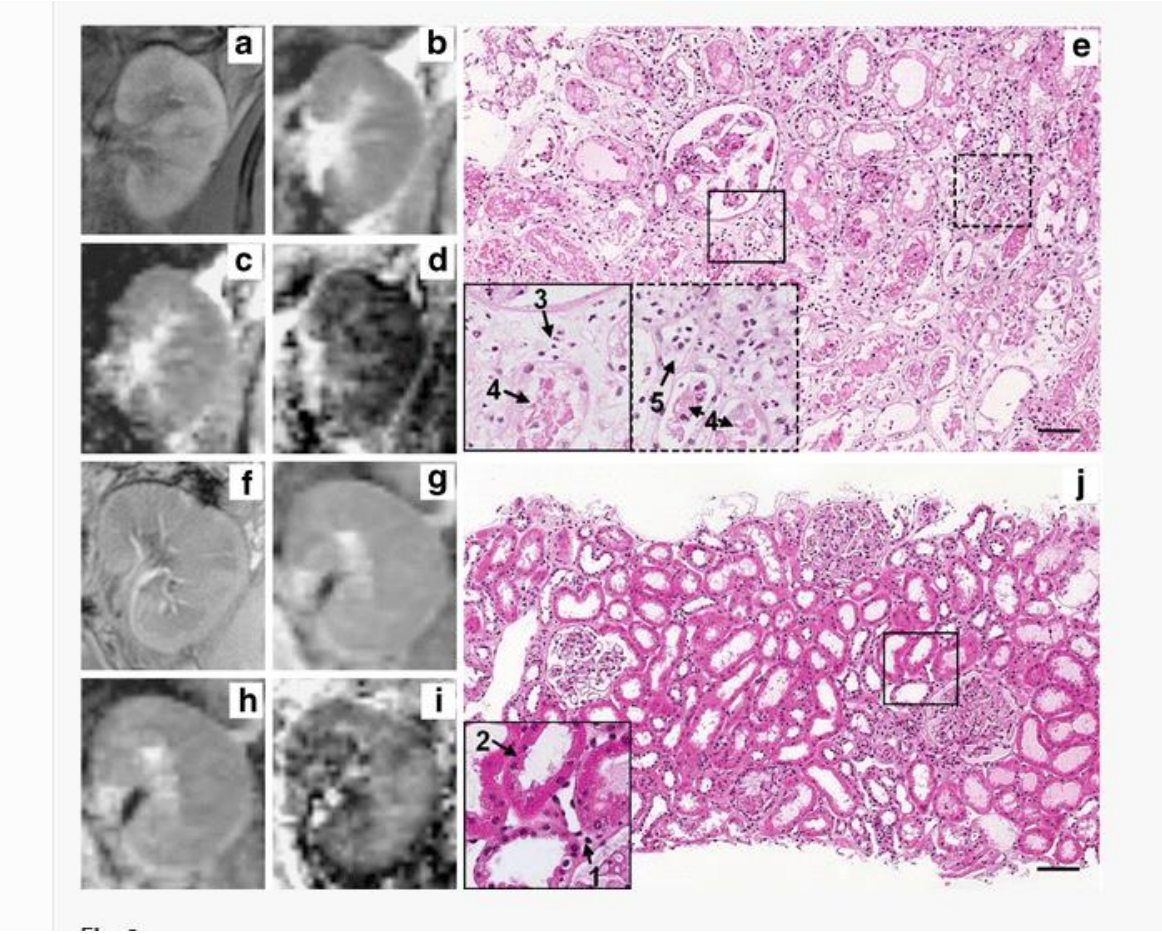
*Nottingham 2019*

# Current evidence for MRI in CKD

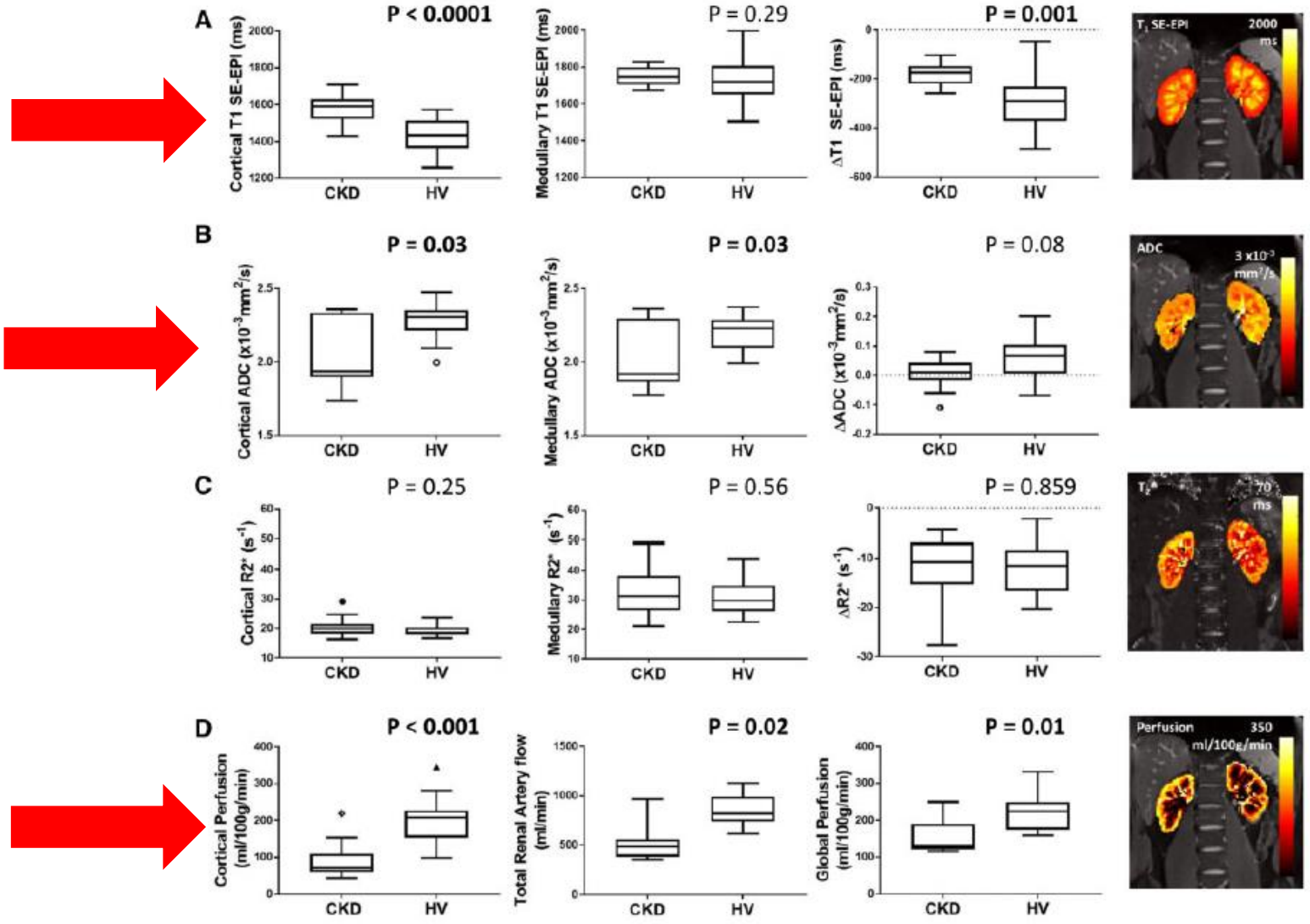
- Recognize a sick kidney
- Evaluate non invasively the histology
  - Ct in lung/fibroscan in liver, MRI in heart
- Follow non invasively the evolution of a disease
- Predict prognosis

# Diffusion MRI in healthy and sick kidneys




*Eisenberg, 2006; Thoeny, Radiology 2005 and 2006*

# Multiparametric MRI in CKD




22 patients G3/4, 22 healthy volunteers

*Buchanan, NDT, 2019*

# Current evidence for MRI in CKD

- Recognize a sick kidney
- Evaluate non invasively the histology
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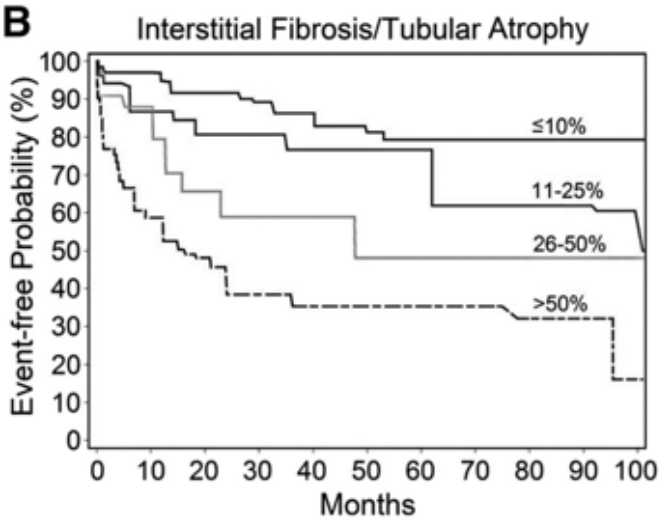
# Why should we evaluate fibrosis in the kidney?

- IF associates to eGFR
- If predicts the evolution of renal disease
- Treatment choice  in selected cases

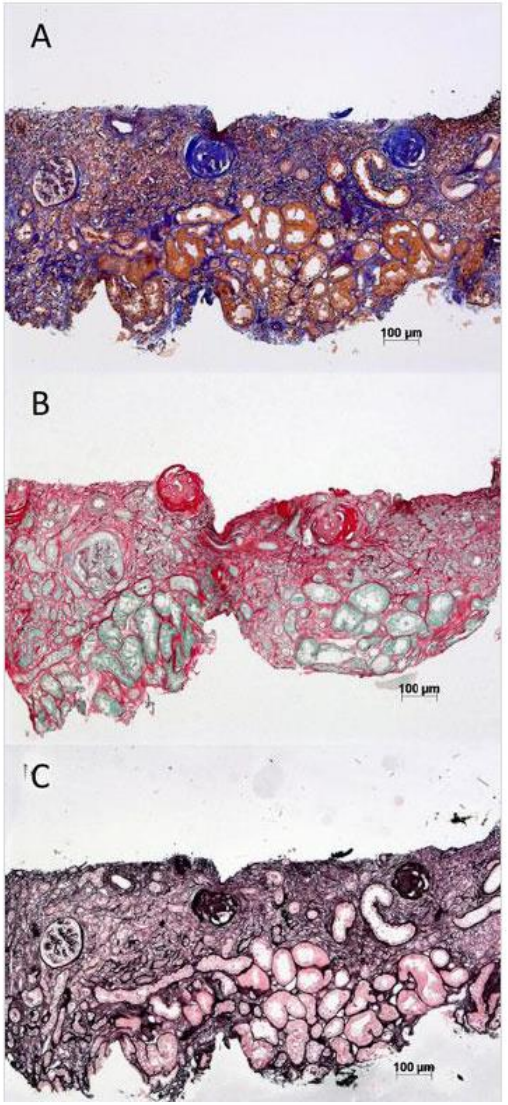



| | | | | | |
|---|---|---|---|---|---|
| Interstitial fibrosis/tubular atrophy | | | | | |
| Minimal (≤10%) | 249 | 4.3 | — | — | — |
| Mild (11%–25%) | 142 | 8.6 | 1.85 [1.13 to 3.05] | 1.63 [0.96 to 2.75] | 1.34 [0.78 to 2.31] |
| Moderate (26%–50%) | 118 | 18.2 | 3.71 [2.34 to 5.88] | 2.99 [1.83 to 4.90] | 2.14 [1.24 to 3.69] |
| Severe (>50%) | 158 | 38.3 | 7.15 [4.73 to 10.8] | 5.07 [3.17 to 8.09] | 3.42 [1.99 to 5.87] |

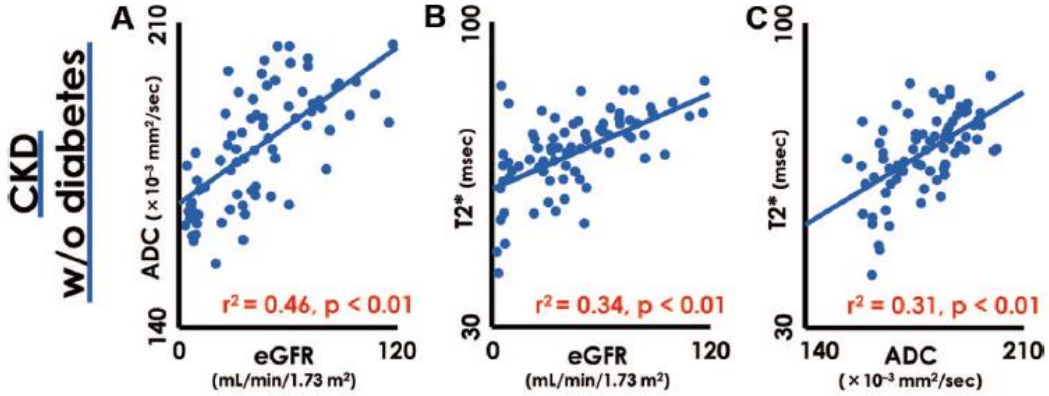
*Srivastava, JASN, 2018*

# Histological evaluation of IF

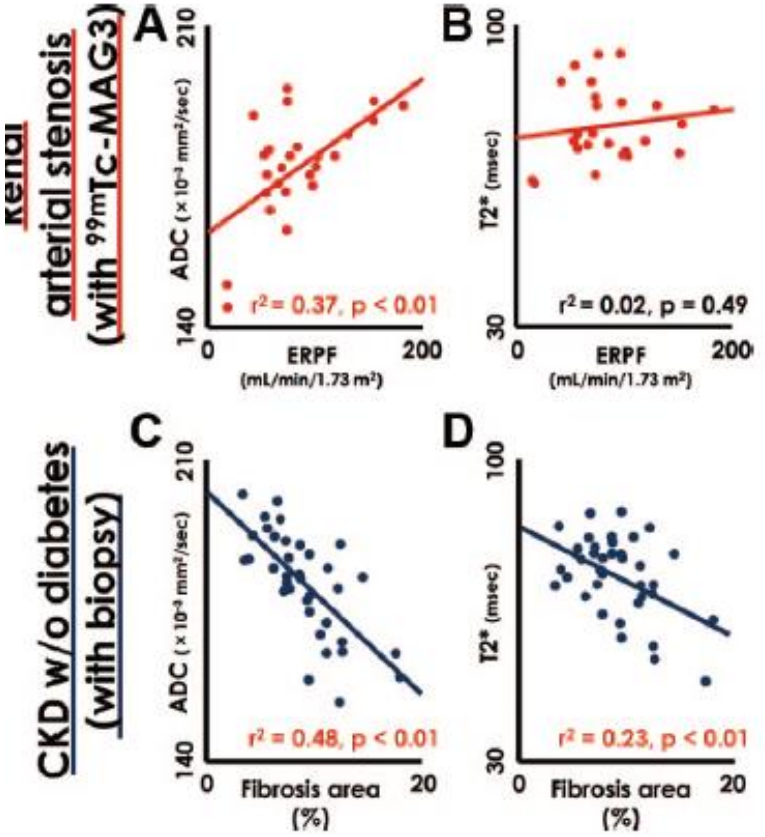
- Standard stainings: trichrome Masson, sirius red, silver
- Visually most of the time
- Automatization in developpment
- Focal and bleeding risk



# Diffusion MRI and fibrosis

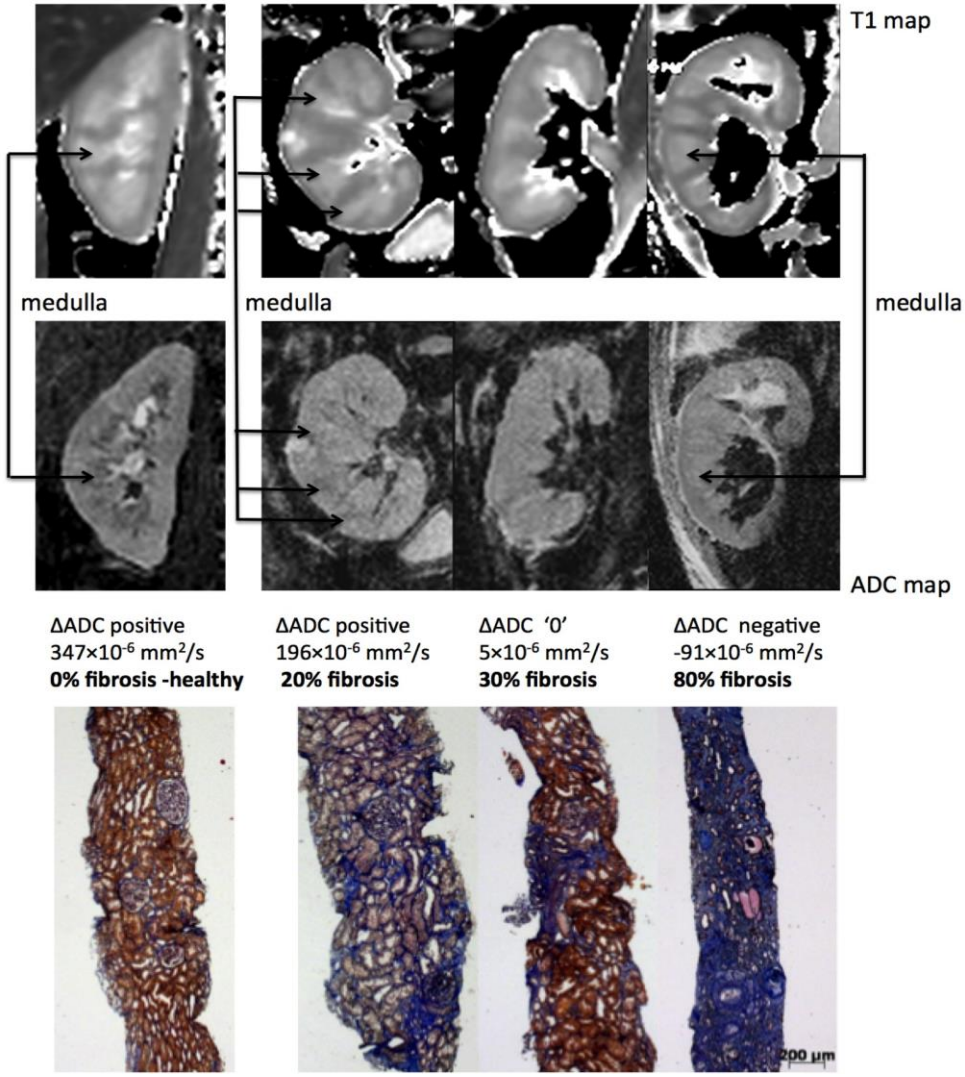



142 Patients with diabetic nephropathy (43), AKI (23), CKD non diabetic (76)

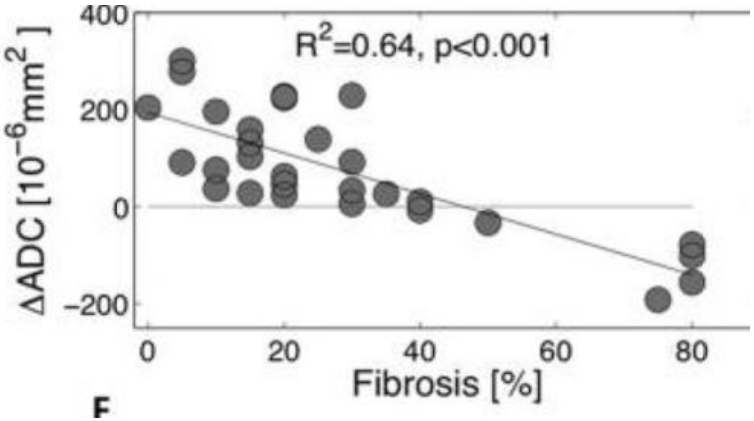



*Inoue, JASN, 2011*

# Correcting for the medulla: ΔADC

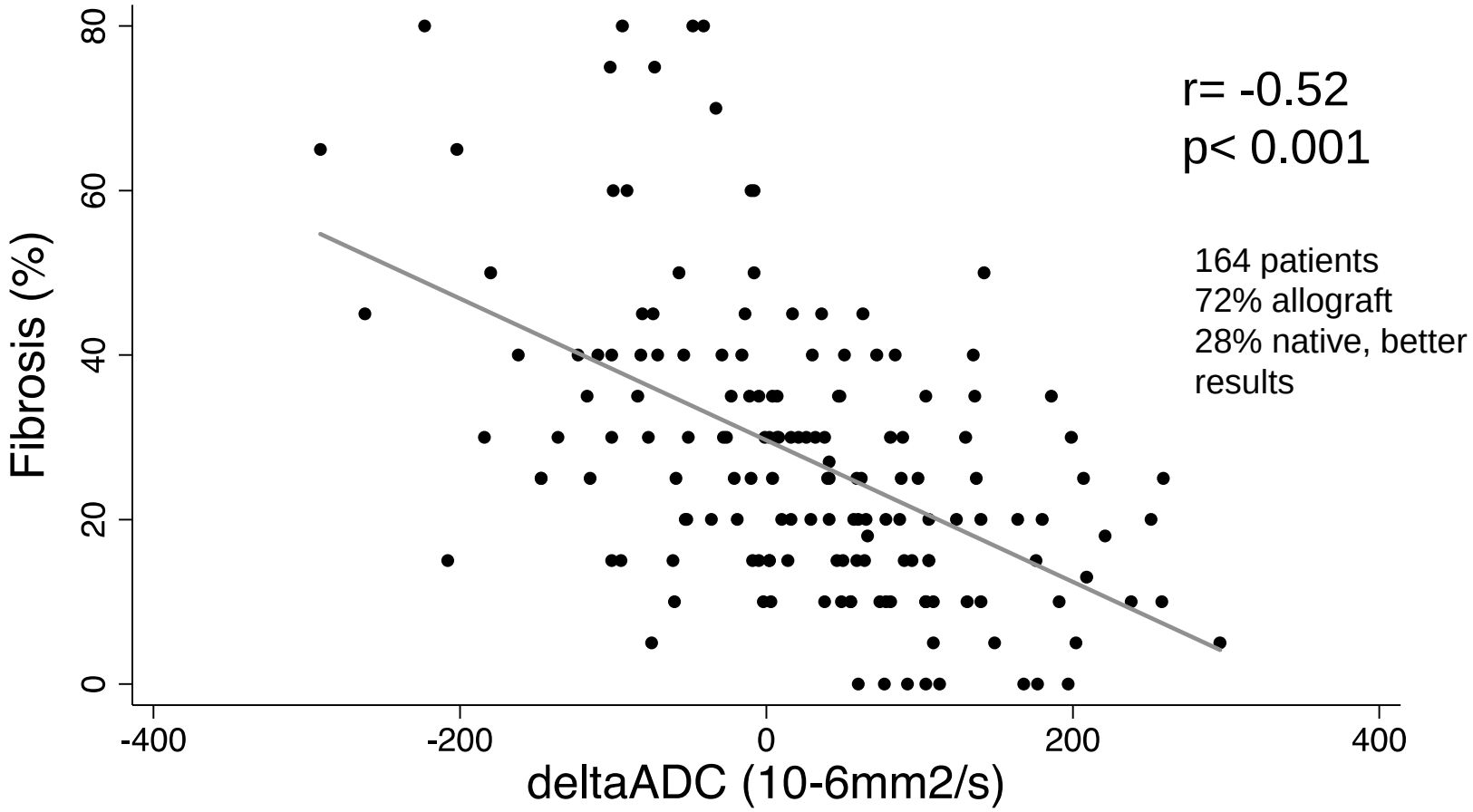



**∆ADC =**
**(ADC cortex) – (ADC medulla)**



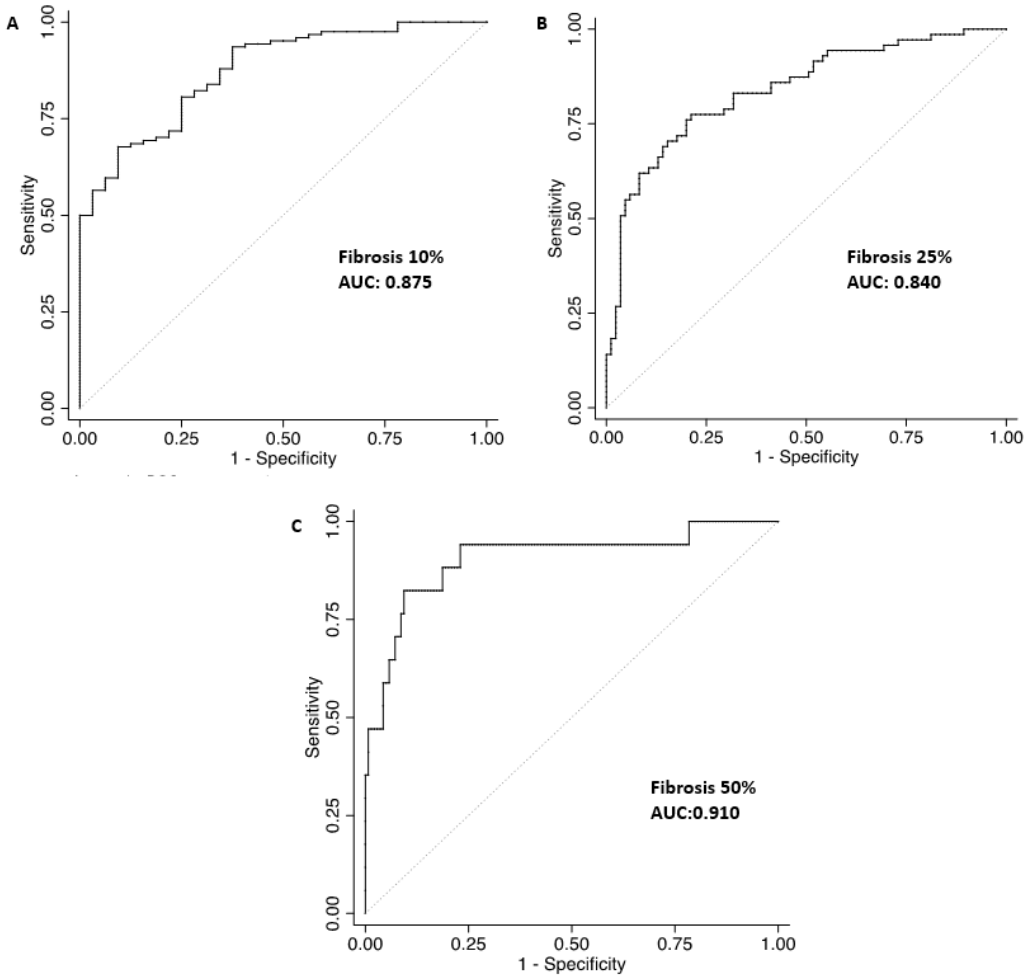

*Friedli I et al. Sci Rep. 2016 Jul*
*Fridli et al., JMRI, 2017*

# ΔADC external validation




*Berchtold et al., NDT 2019*

# Combining ΔT1 and ΔADC



# Bold, diffusion and aterial spin labelling

103 kidney allograft recipients

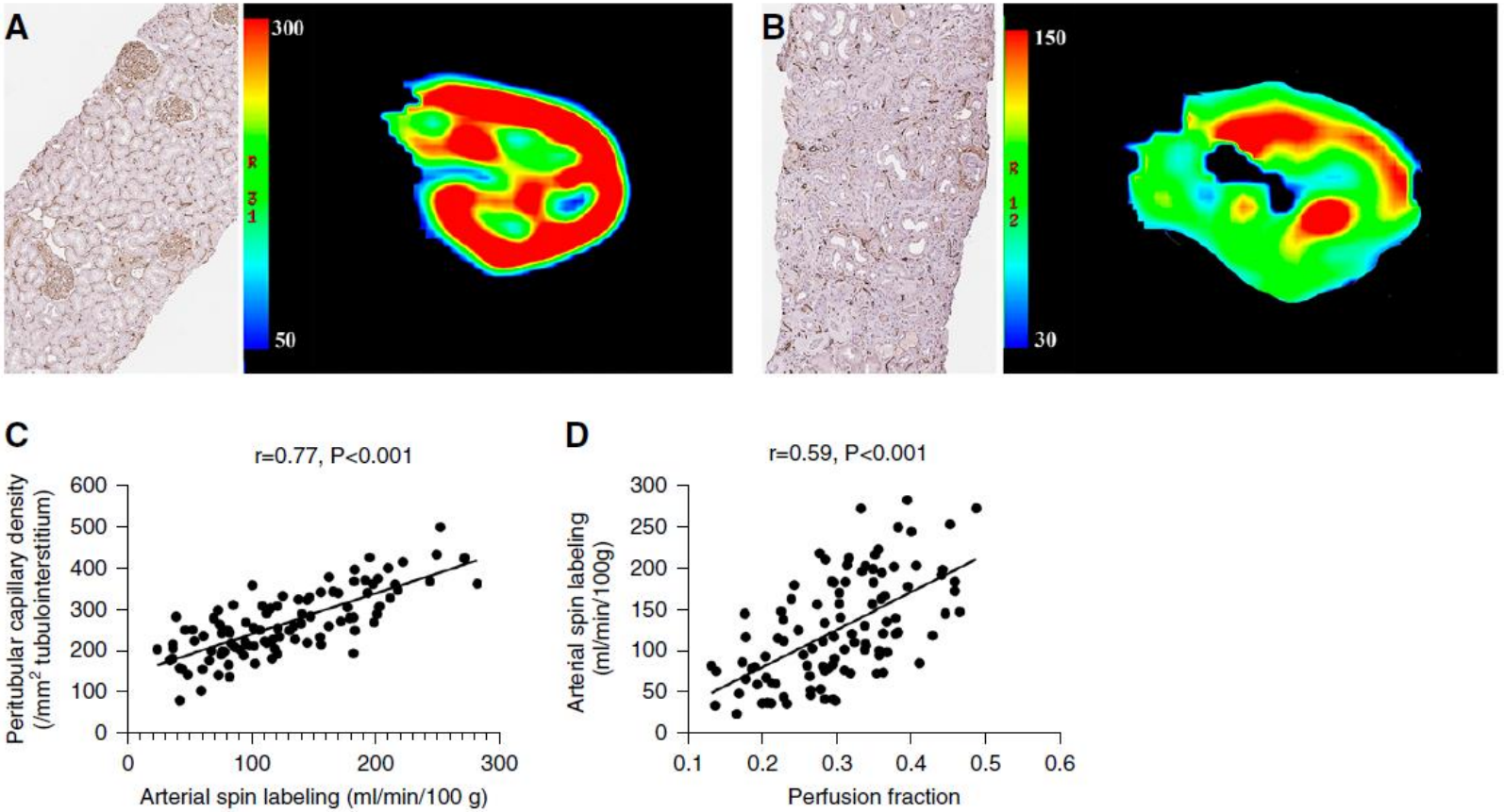
**Table 2. Performances of eGFR and functional magnetic resonance imaging measurements for the differentiation of ≤25% versus >25% interstitial fibrosis and >50% versus ≤50% interstitial fibrosis among kidney transplant patients with allograft injury**

| Measurements | Correlations with Interstitial Fibrosis | ≤25% versus >25% Interstitial Fibrosis | | | | >50% versus ≤50% Interstitial Fibrosis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Cutoff | AUC (95% CI) | Sensitivity (95% CI) | Specificity (95% CI) | Cutoff | AUC (95% CI) | Sensitivity (95% CI) | Specificity (95% CI) |
| Apparent diffusion coefficient | rho=−0.77; $P<0.001$ | 199×10$^{-3}$mm$^2$/s | 0.87 (0.79 to 0.93) | 76% (62% to 87%) | 84% (70% to 93%) | 191×10$^{-3}$mm$^2$/s | 0.88 (0.80 to 0.93) | 86% (64% to 97%) | 72% (61% to 81%) |
| Arterial spin labeling | rho=−0.83;; $P<0.001$ | 101 ml/min per 100 g | 0.92 (0.85 to 0.97) | 94% (85% to 99%) | 78% (63% to 88%) | 82.9 ml/min per 100 g | 0.94 (0.87 to 0.98) | 95% (76% to 99.9%) | 87% (77% to 93%) |
| Perfusion fraction | rho=−0.66 $P<0.001$ | 0.299 | 0.81 (0.72 to 0.88)[a] | 76% (62% to 87%) | 78% (63% to 88%) | 0.285 | 0.86 (0.78 to 0.92) | 91% (70% to 99%) | 72% (61% to 81%) |
| BOLD | rho=0.61; $P<0.001$ | 18.10 Hz | 0.79 (0.69 to 0.87)[b] | 79% (64% to 89%) | 72% (57% to 84%) | 18.14 Hz | 0.85 (0.76 to 0.92) | 91% (70% to 99%) | 69% (58% to 80%) |
| eGFR[c] | rho=−0.79; $P<0.001$ | 38 ml/min per 1.73 m$^2$ | 0.91 (0.84 to 0.96) | 91% (80% to 97%) | 78% (63% to 88%) | 38 ml/min per 1.73 m$^2$ | 0.91 (0.84 to 0.96) | 95% (76% to 99.9%) | 72% (61% to 81%) |
| eGFR[d] | rho=−0.79; $P<0.001$ | 38 ml/min per 1.73 m$^2$ | 0.93 (0.85 to 0.97) | 89% (77% to 97%) | 83% (69% to 92%) | 38 ml/min per 1.73 m$^2$ | 0.90 (0.82 to 0.95) | 95% (76% to 99.9%) | 68% (56% to 79%) |

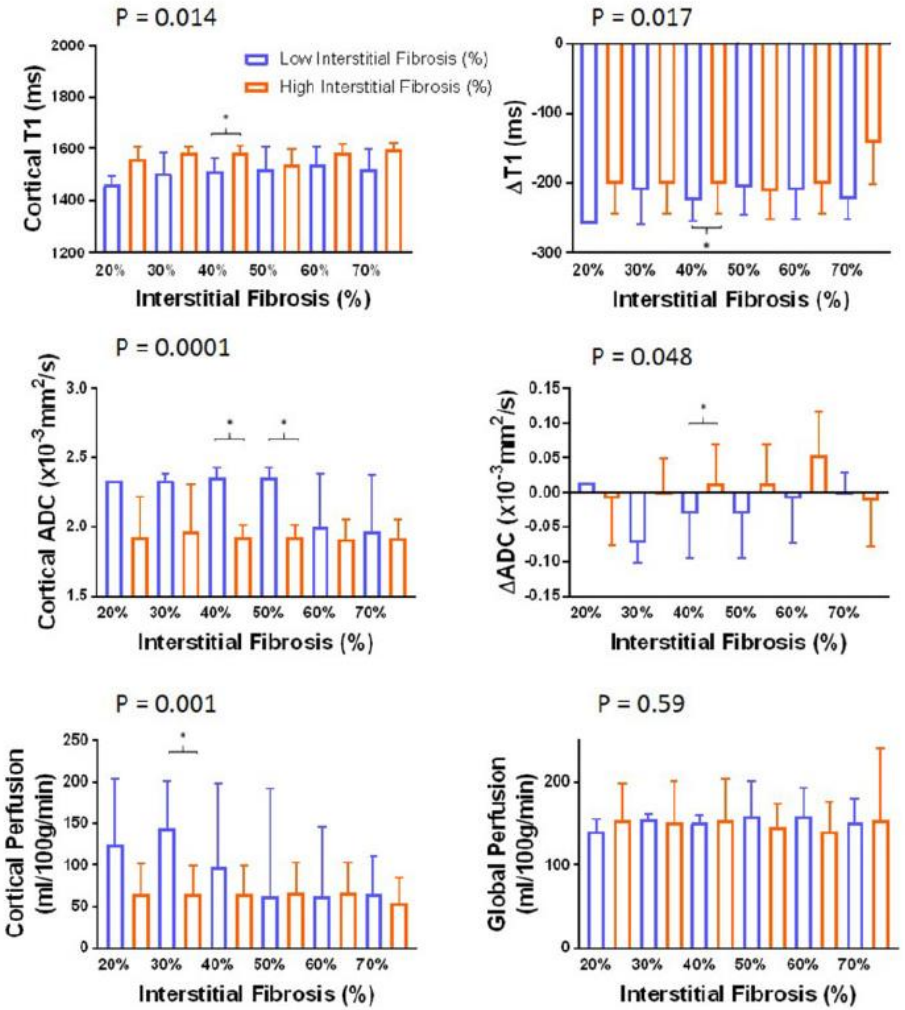
eGFR calculated by the CKD Epidemiology Collaboration equation AUC, area under the curve; 95% CI, 95% confidence interval; BOLD, blood oxygen level–dependent.
[a]Represented $P<0.05$ by comparing the AUC of perfusion fraction to that of eGFR.
[b]Denoted $P<0.01$ by comparing the AUC of BOLD to that of eGFR.
[c]Indicated that data were analyzed from all 103 patients with allograft injury.
[d]Denoted that data were analyzed from 93 patients with BOLD results.

*Wang CJASN 2019*

# Arterial spin labeling and capillary rarefaction



# Multiparametric MRI in CKD

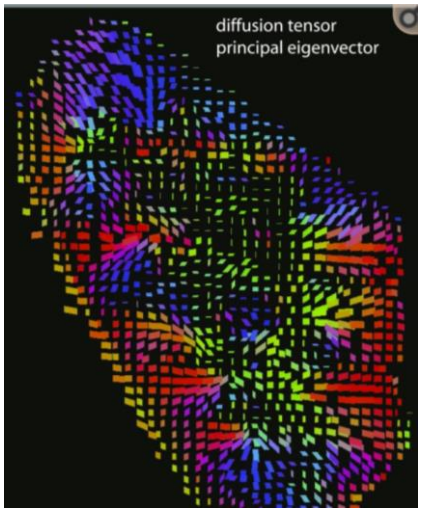



22 patients G3/4, 22 healthy volunteers

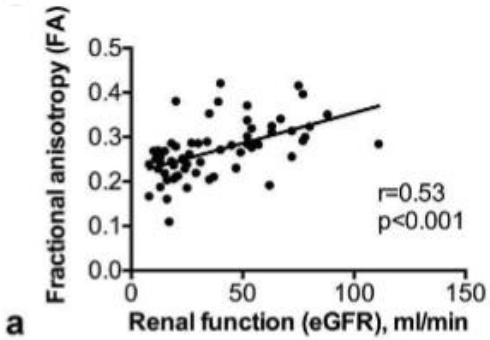
Different fibrosis cutoff

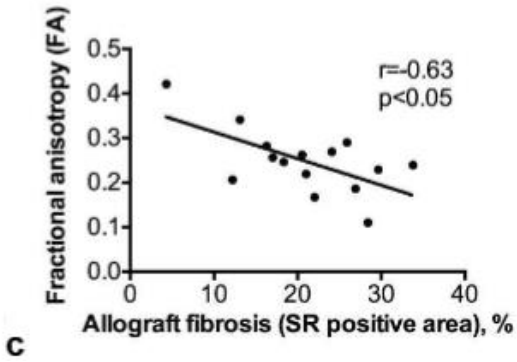
*Buchanan, NDT, 2019*

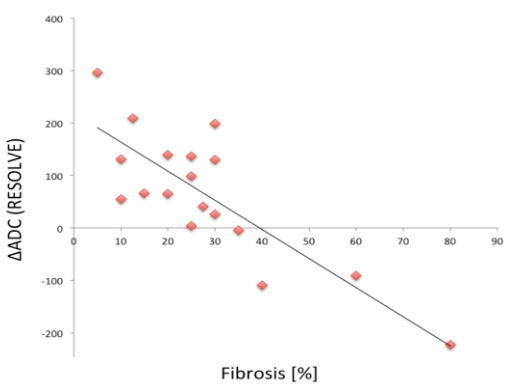
# Diffusion tensor MRI

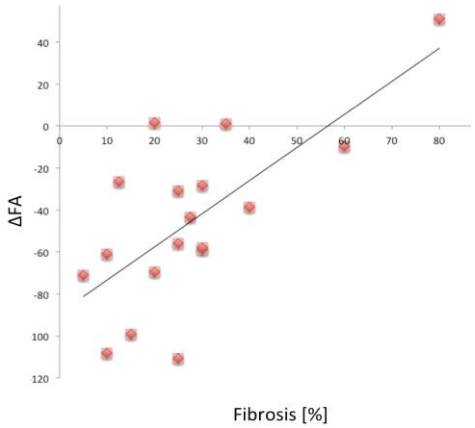



- Diffusion in selected directions( 10-20 directions)
- Measures fractional anisotropy (FA),



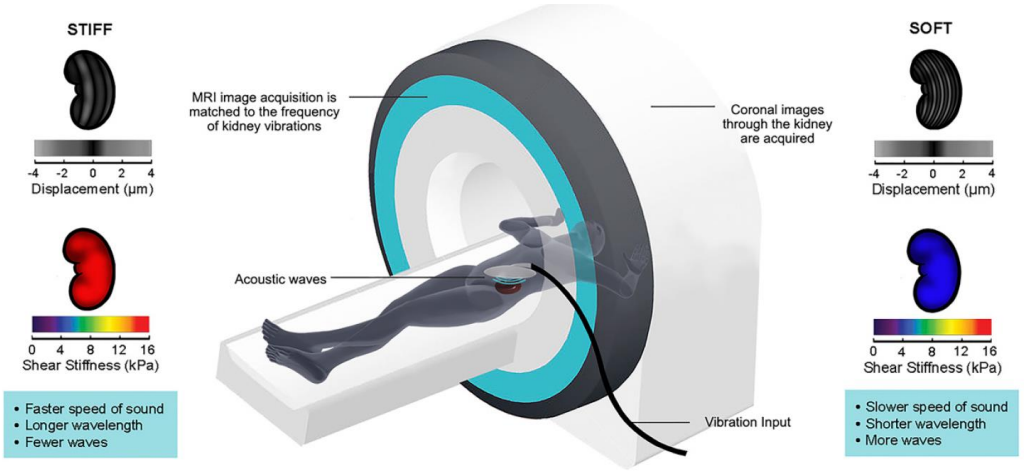




*Hartung, JMRI, 2016*

# MRI elastography




16 allograft recipients with biopsy

| Groups of Measures | Spearman rho or $r^2$ | *P* Value |
|---|---|---|
| Whole-kidney MRE stiffness versus Banff fibrosis score | Rho =0.67 | <0.01 |
| Whole-kidney MRE stiffness versus baseline eGFR | Rho =−0.65 | <0.01 |
| Whole-kidney MRE stiffness versus history of prior or current rejection | Rho =0.39 | 0.13 |
| Whole-kidney MRE stiffness versus slope of eGFR change over the 12-mo follow-up period | Rho =−0.70 | 0.004 |
| Baseline eGFR versus slope of eGFR change over the 12-mo follow-up period | Rho =0.63 | 0.01 |
| Baseline urine albumin-to-creatinine ratio versus slope of eGFR change over the 12-mo follow-up period | Rho =−0.65 | 0.01 |
| Whole-kidney MRE stiffness as a predictor of the slope of eGFR change over the 12-mo follow-up period (regression analysis) | $r^2$=0.48 | 0.03 |

*Kirpalani, CJASN, 2017*

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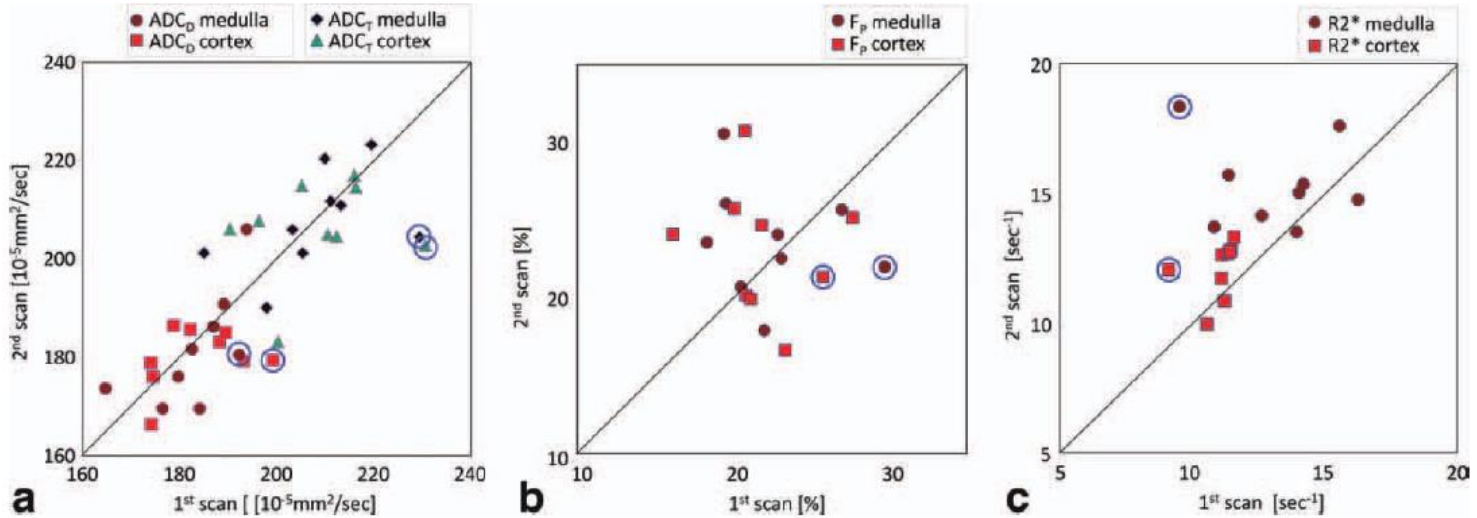
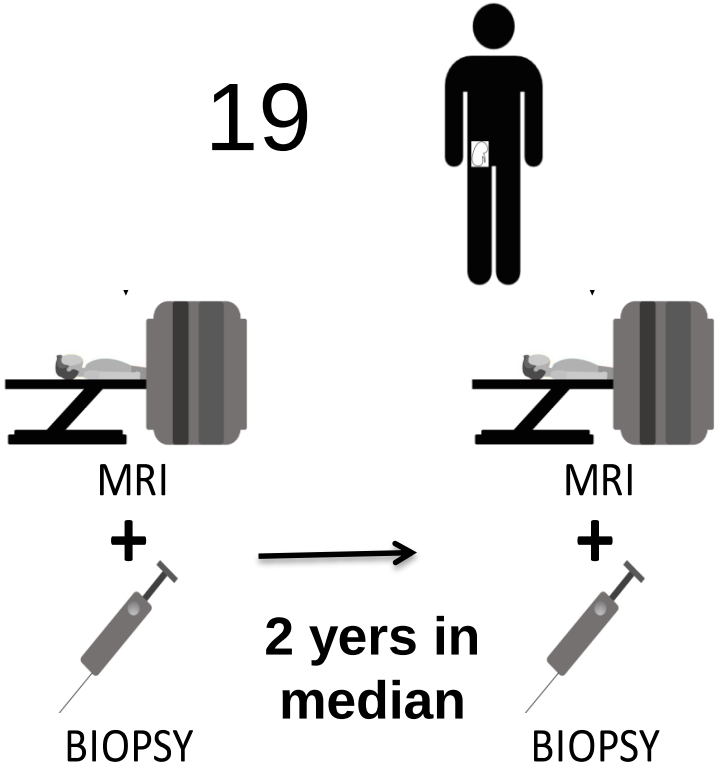
# Can MRI be used to follow a patient?





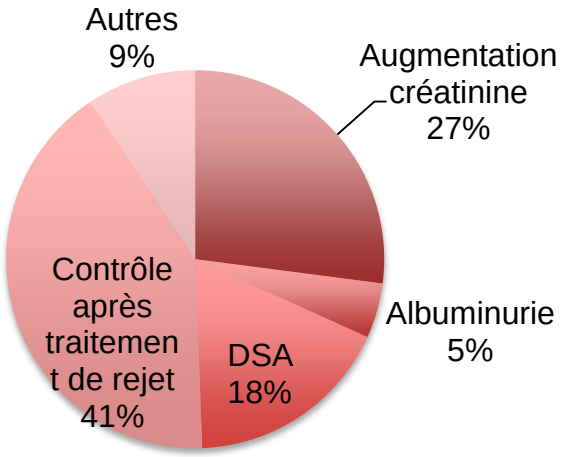

Nine allograft patients, first imaging at 7 +/- 3 months, second at 32+/-2 months

# Can MRI be used to follow a patient?



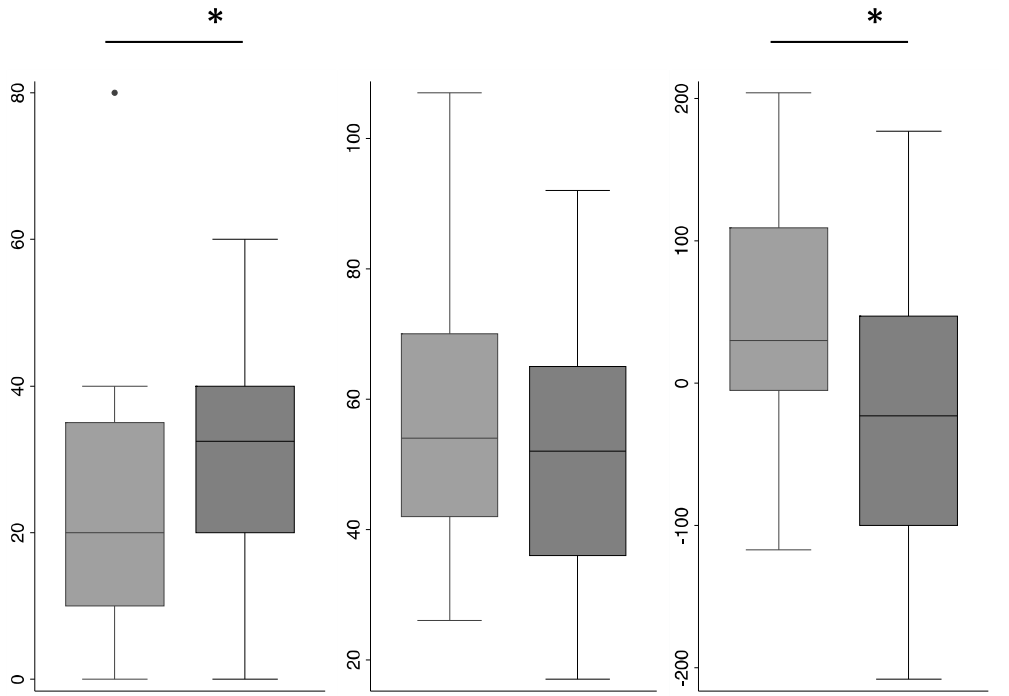

**First biopsy**: 12.4 months (IQR: 12.0-49.1)
- Protocol biopsy(53%)
- Indication biopsy(47%).

**Second biopsy**: 38.4 months (IQR: 23.7-75.5)
- Protocol (11%)
- Indication (89%)




*L. Berchtold et al, accepted in NDT*

# Diffusion MRI detects fibrosis aggravation before creatinine elevation




| | FIBROSIS (%) | | eGFR (ml/min/1.72m2) | | MRI ΔADC ($10^{-6}mm^2/s$) | |
|---|---|---|---|---|---|---|
| | Baseline | Follow-up | Baseline | Follow-up | Baseline | Follow-up |
| Values | 20 (10-35) | 32.5 (20-40) | 54 (42-70) | 52 (36-65) | 30 (-5 – 109) | -23 (-100-47) |
| Paired T-test | *p=0.03 | | p=0.19 | | *p=0.005 | |

*L. Berchtold et al, accepted*

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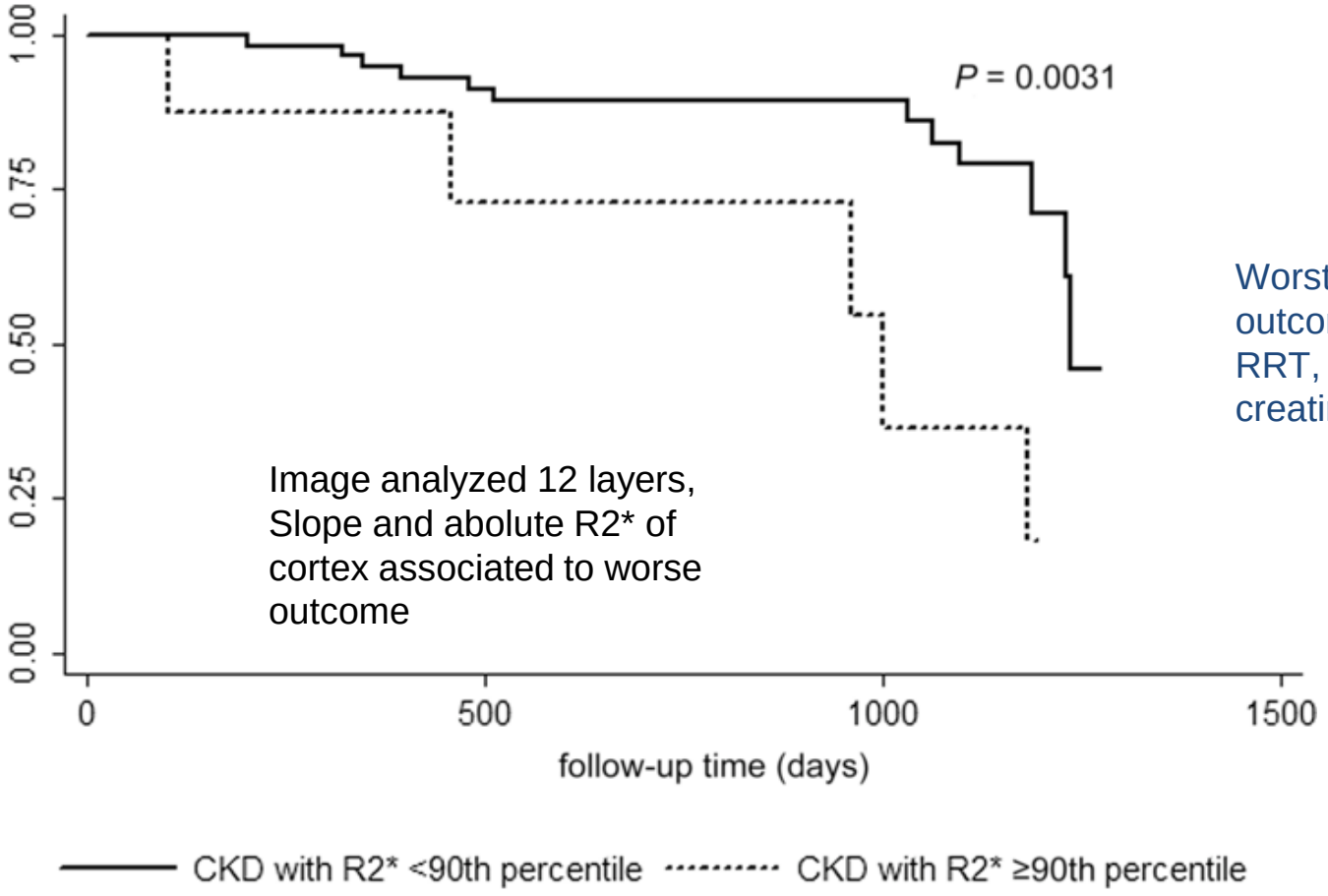
# Can MRI predict CKD evolution?




Worst renal outcome : RRT, +30% creatinine

BOLD MRI in 112CKD patients, 47 with HBP, 24 controls
patients followed 3 years in median

*Pruijm et al., KI, 2018*

# Can MRI predict eGFR slope?

*92 patients, native kidneys, 42% diabetes, mean eGFR 49 ml/min/1.73 m2, followed mean 5.13 years. Correlation to eGFR slope*

| A. Univariate | | 95% CI | | | |
|---|---|---|---|---|---|
| | Estimate | Lower | Upper | *t*-value | P-value |
| Age (per year) | −0.031 | −0.071 | 0.009 | −1.520 | 0.132 |
| Gender (male) | 0.000 | −0.634 | 0.634 | 0.000 | 0.999 |
| Diabetes mellitus | −0.667 | −1.290 | −0.045 | −2.130 | 0.036* |
| Mean blood pressure (per 10 mmHg) | −0.072 | −0.139 | −0.006 | −2.170 | 0.033* |
| Treatment with ACE-I/ARB | −0.535 | −1.180 | 0.110 | −1.650 | 0.103 |
| eGFR (per mL/min) | 0.009 | −0.013 | 0.031 | 0.800 | 0.425 |
| Urine protein:creatinine ratio | −1.154 | −1.492 | −0.816 | −6.780 | <0.001* |
| Uric acid (per 10 μmol/L) | −0.538 | −1.004 | −0.073 | −2.300 | 0.024* |
| T2* (per ms) | 0.076 | 0.004 | 0.149 | 2.080 | 0.040* |
| ADC (per $\times 10^{-3} mm^2/s$) | 2.598 | −2.123 | 7.319 | 1.090 | 0.277 |

| B. Multivariate | | 95% CI | | | |
|---|---|---|---|---|---|
| | Estimate | Lower | Upper | *t*-value | P-value |
| Age (per year) | −0.018 | −0.060 | 0.025 | −0.840 | 0.405 |
| Gender (male) | 0.080 | −0.474 | 0.634 | 0.290 | 0.775 |
| Diabetes mellitus | −0.464 | −1.028 | 0.100 | −1.640 | 0.105 |
| Mean blood pressure (per 10 mmHg) | −0.031 | −0.087 | 0.025 | −1.100 | 0.273 |
| Treatment with ACE-I/ARB | −0.259 | −0.832 | 0.315 | −0.900 | 0.372 |
| eGFR (per mL/min) | −0.027 | −0.052 | −0.003 | −2.200 | 0.031* |
| Urine protein:creatinine ratio | −1.084 | −1.447 | −0.720 | −5.940 | <0.001* |
| Uric acid (per 10 μmol/L) | −0.493 | −0.987 | 0.001 | −1.990 | 0.051 |
| T2* (per ms) | 0.104 | 0.035 | 0.174 | 2.980 | 0.004* |
| ADC (per $\times 10^{-3}$ $mm^2/s$) | −1.714 | −6.111 | 2.683 | −0.780 | 0.440 |

*Sugiyama, NDT, 2018*

# Summary

- Large improvement in MRI methodology for the evaluation of CKD patients:
- *Better assessment of renal fibrosis, perfusion and oxygenation*
- *Follow up of patients*
- *Prognosis assessment*

# The challenges remaining are among others

- *Use multiparametric MRI and combine complementary sequences*
- *Homogenize the technologies used*
- *Homogenize and automatize the quantification*
- *Apply it in everyday practice?*
  *vasculitis w/o biopsy ( anca, pla2r?)*
  *before liver/heart transplantation*
  *diabetic patients ….*

# Thank you for your attention

*Nephrology*
Lena Berchtold
Chantal Martinez
Pierre-Yves Martin

*Pathology*
Solange Moll

*Collaborators*
Hariett Thoeny
Menno Pruijm

*Radiology*
Jean-Paul Vallée
Iris Friedli
Lindsey Crowe

*European the Cooperation in Science and Technology (COST) Action PARENCHIMA (www.renalmri.org)*