



Westmead Hospital



The University of Sydney
AUSTRALIA

iIF/TA as a Surrogate Marker for Renal Graft Loss

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Aim

- To determine if iIF/TA is predictive of graft loss
- To identify the histological and clinical events leading to iIF/TA at 12 months

Study Population

- Patient Cohort: Simultaneous Kidney Pancreas Transplant recipients
- Protocol biopsies done at 0, 1, 3, 12, 36 and 60 months after transplant

i-IF/TA definition

Mononuclear cell infiltration in areas of tubular atrophy and interstitial fibrosis (normally excluded)

Semi-quantitative assessment i-IF/TA score:

i-IF/TA 0: mononuclear cells involving <10% of combined areas of tubular atrophy and interstitial fibrosis

i-IF/TA 1: 10-25% of the combined areas of tubular atrophy and interstitial fibrosis

i-IF/TA 2: 26-50%

i-IF/TA 3: > 50% of damaged cortex

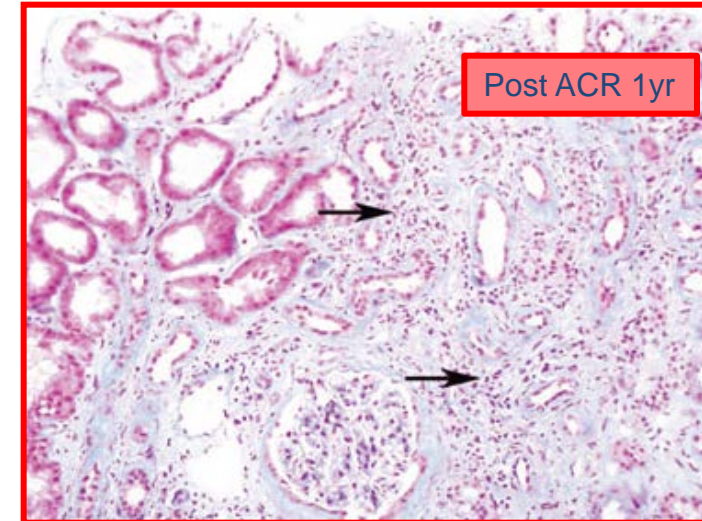
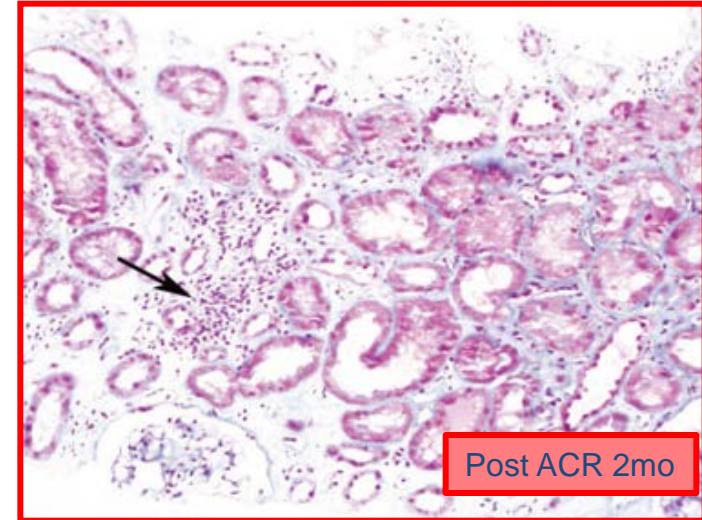
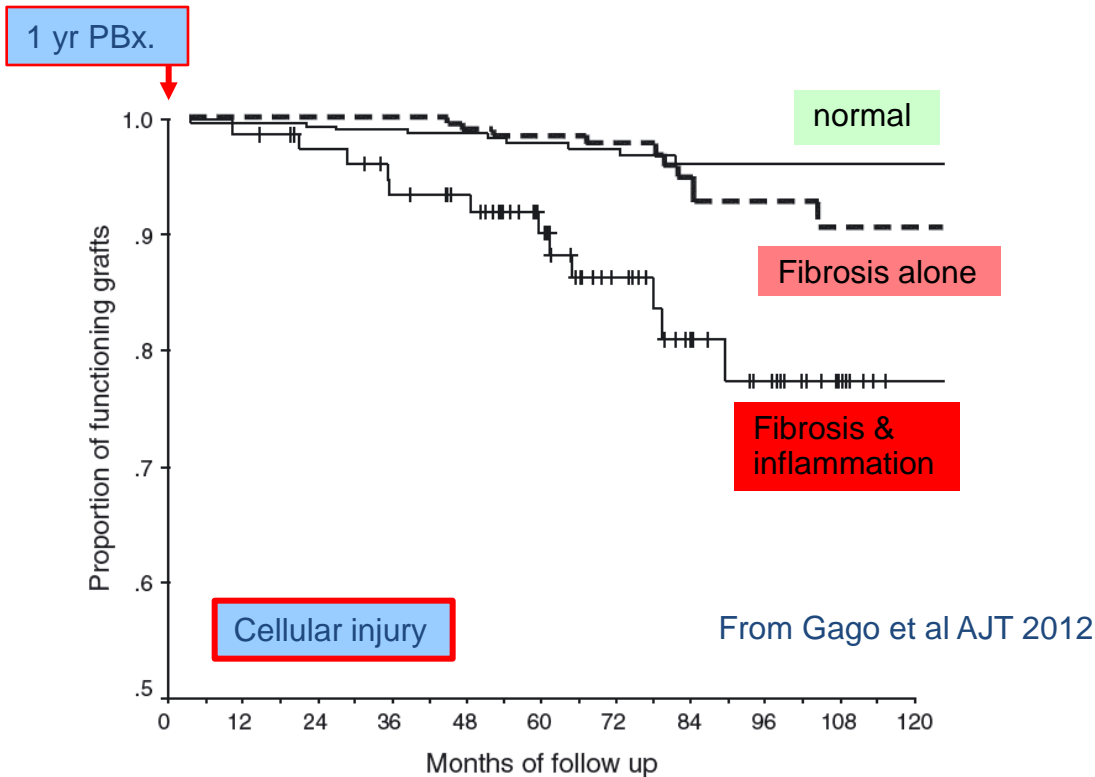
Inflammation & fibrosis

Causes:

- Re-transplant, subclinical inflammation
- Prior ACR (not DSA), DGF, BKVAN

Outcome

- Graft loss HR 4.33 (2.49-7.53) $P < 0.001$

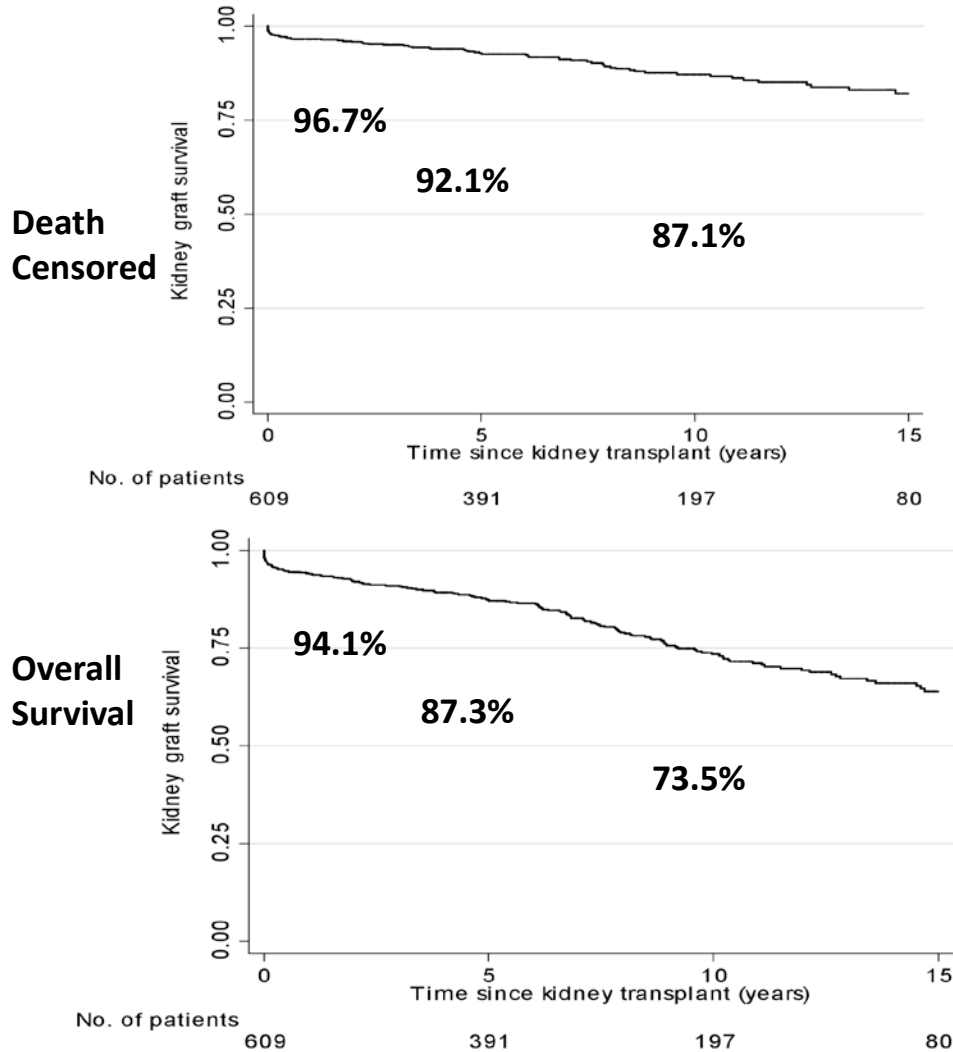


Prospective cohort study
N=795 kidney Tx. (TXG excluded)
Classified by 1 year BFC
IF/TA +/- Banff i ("GIF+i")

Patient Characteristics – SPK recipients

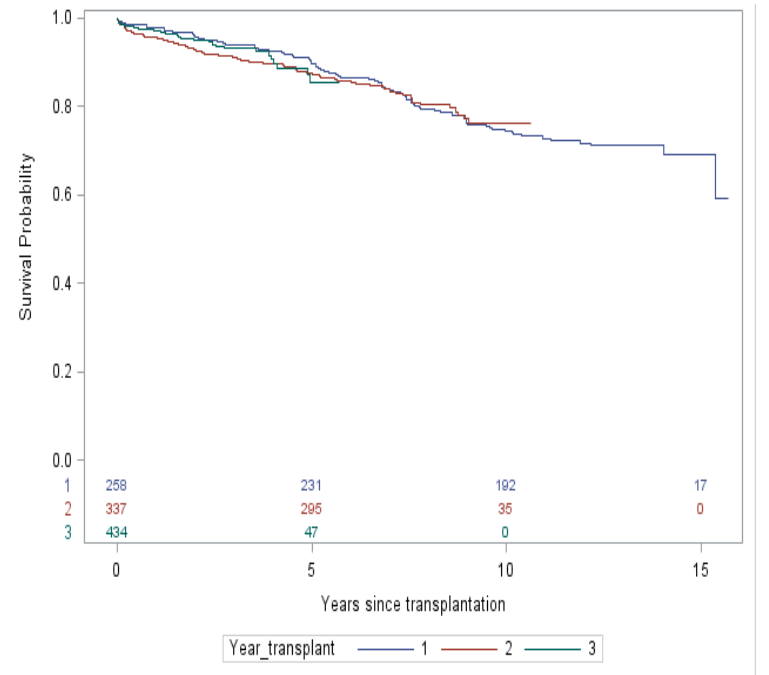
- 301 patients
- Recipient age (years) 38.1±7.0
- Total HLA mismatch score 4.5±1.2
- Total ischemia time (hours) 11.3±3.0
- Donor age (years) 27.0±9.7
- Induction therapy 190/89/19
(none/basiliximab/antilymphocyte)
- Early acute cellular rejection 158 (53%)
- Early vascular rejection 44 (14.6%)
- Early humoral rejection 55 (18.2%)
- Antilymphocyte treatment 78 (26.0%)
- Patient follow up (years) 10.4±6.2

Kidney Graft Survival in SPK Recipients

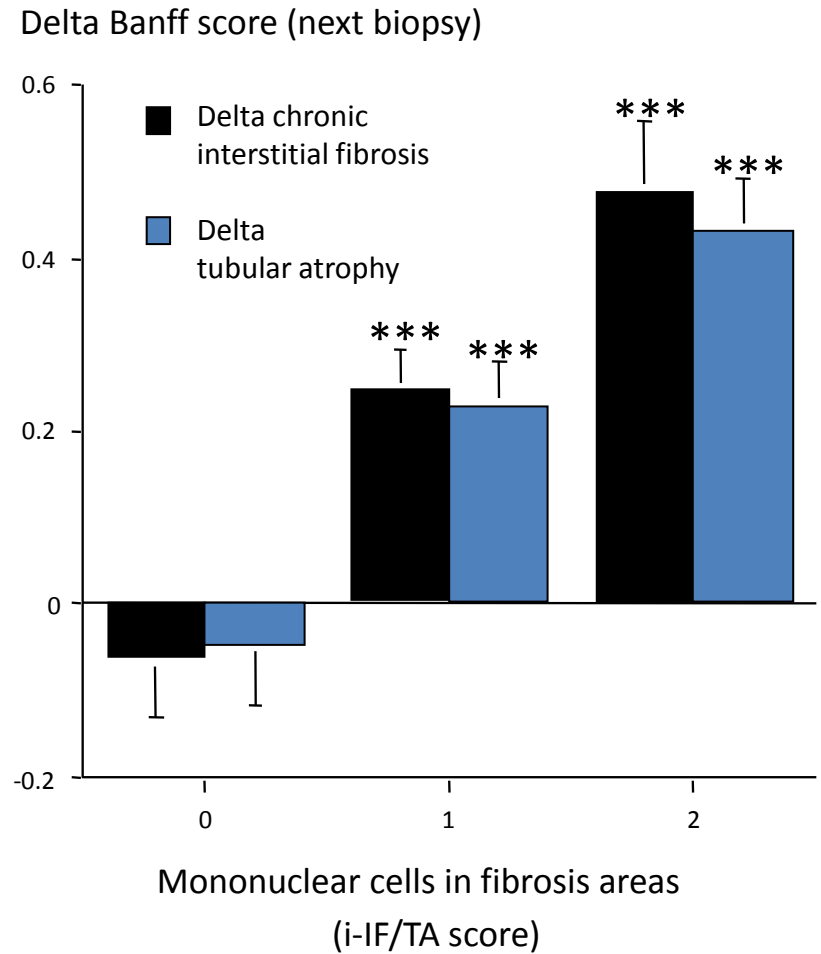
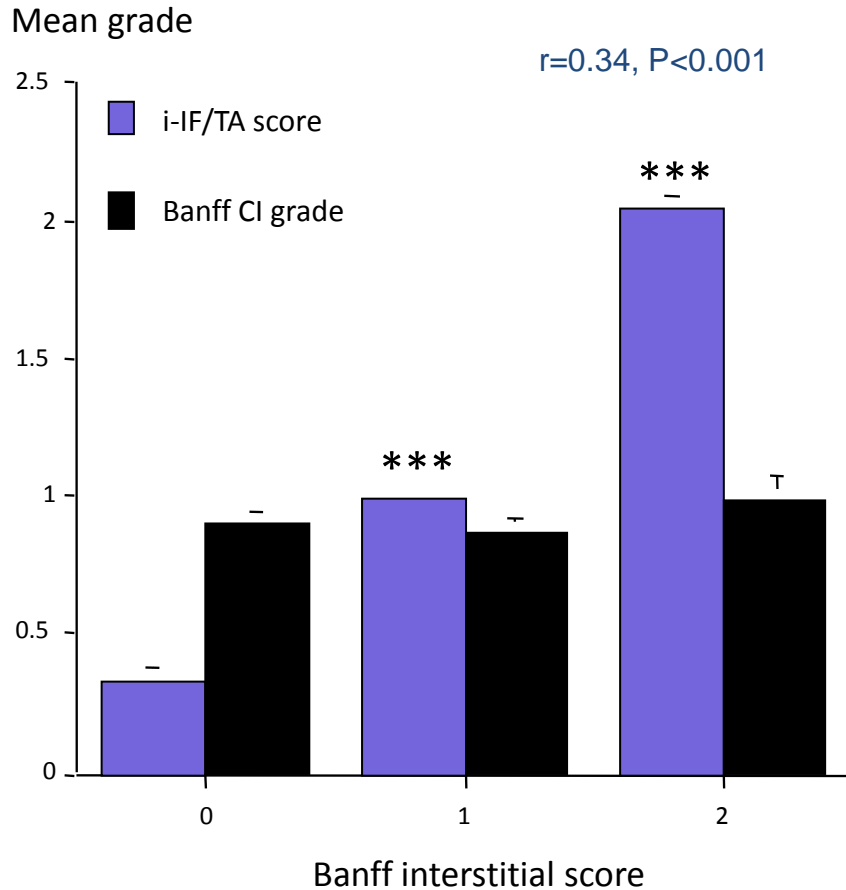


Kidney Transplant alone Graft Survival

Overall graft survival 2000 – 2015 at Westmead



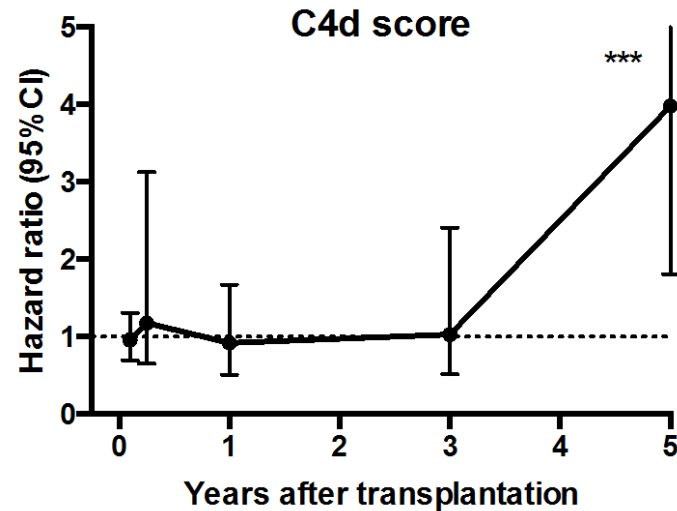
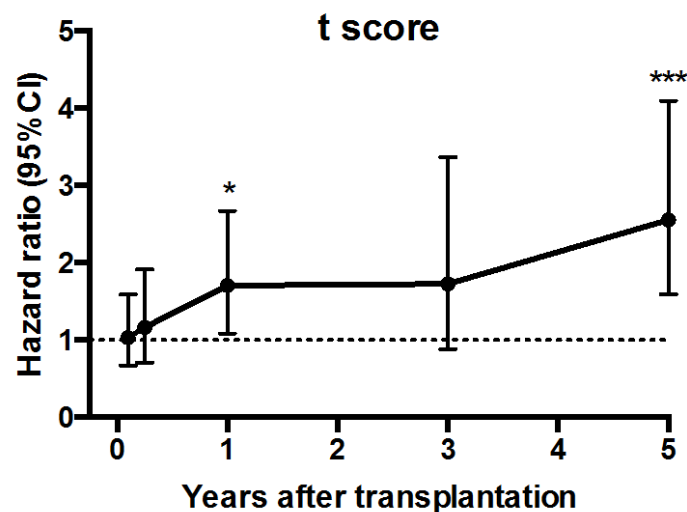
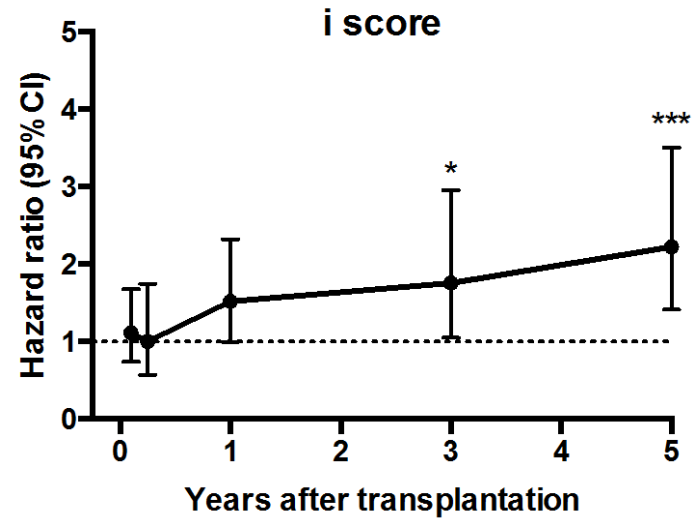
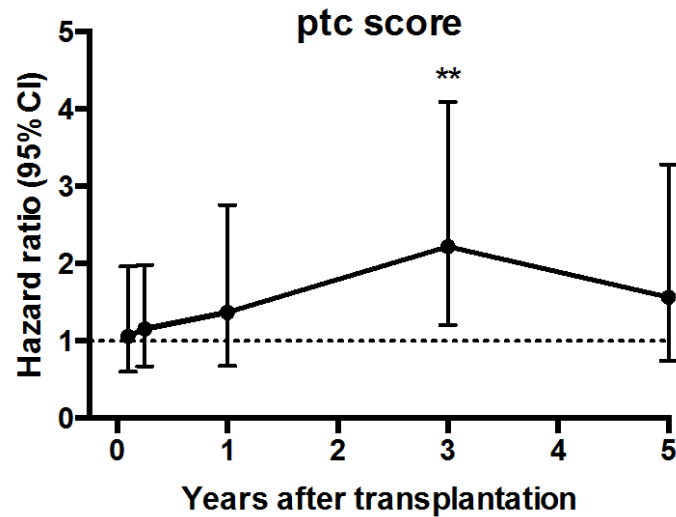
i-IFTA: Further Tubulointerstitial Damage



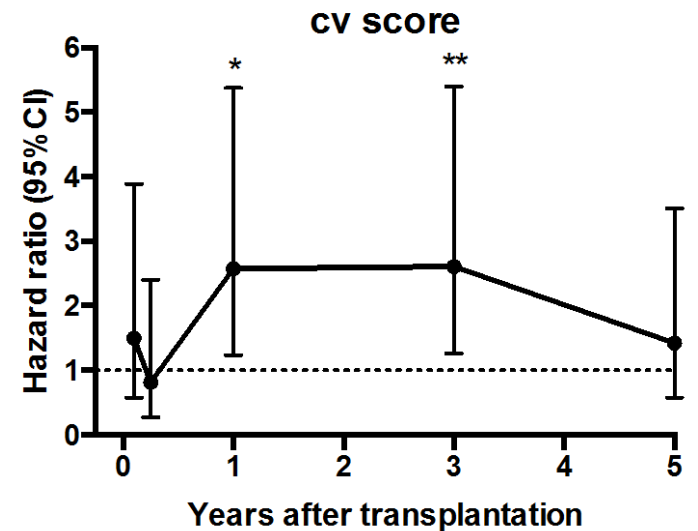
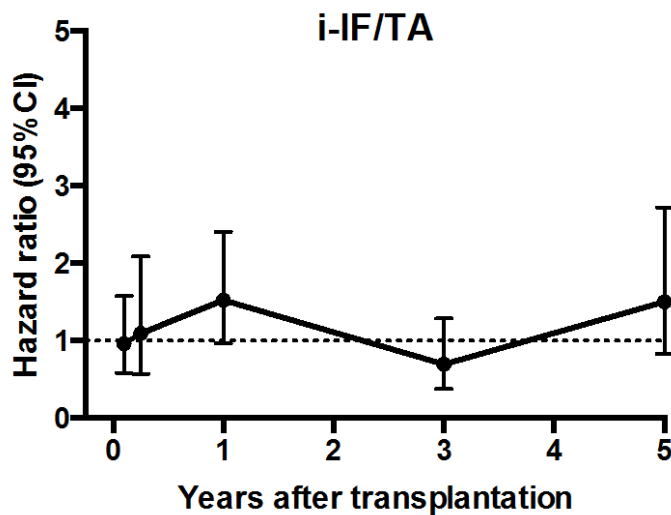
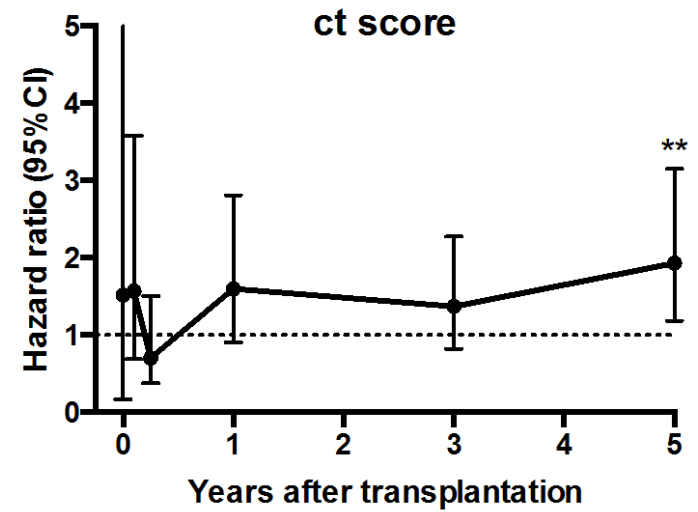
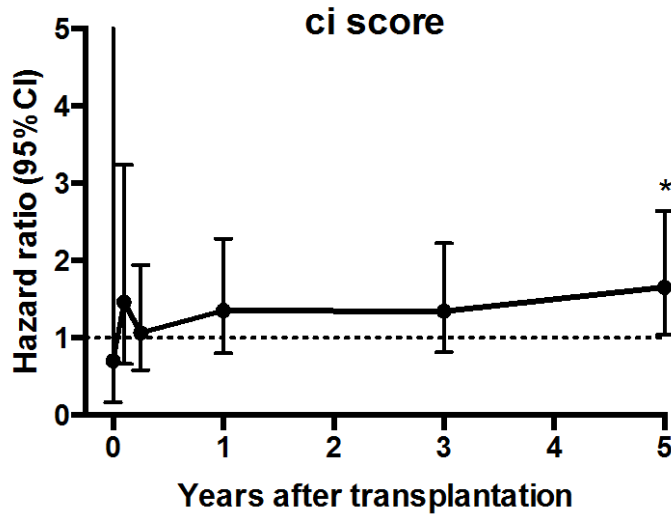
Same biopsy

Biopsy-pairs n=849, next biopsy

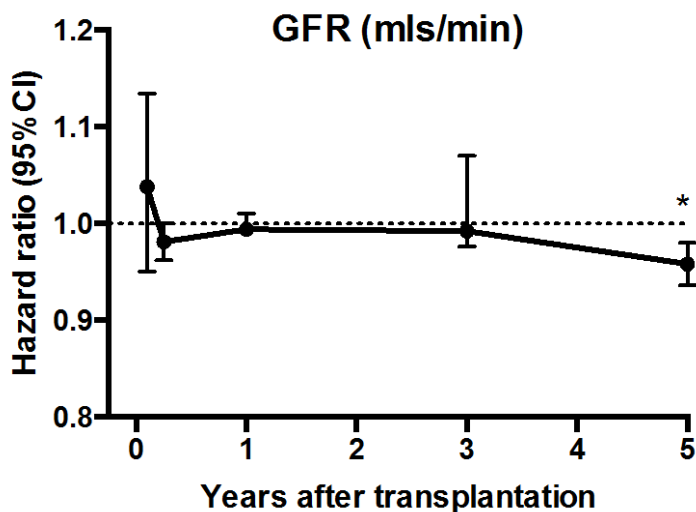
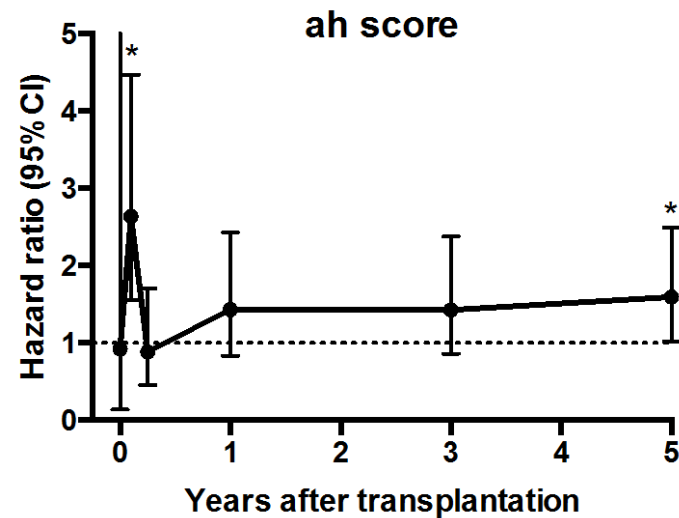
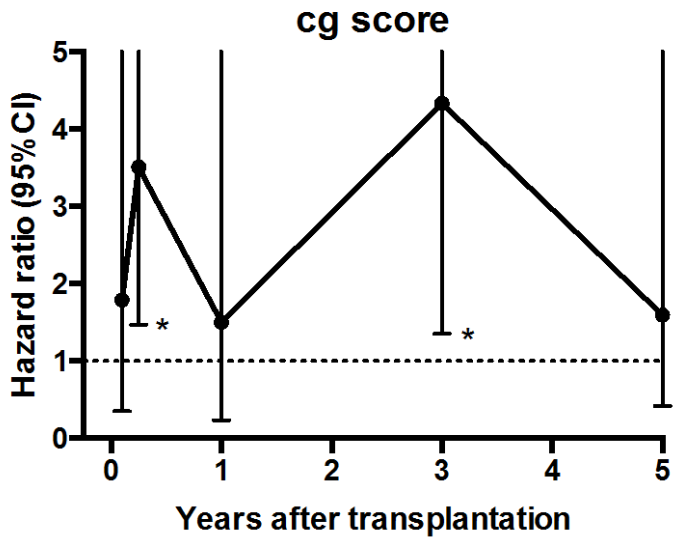
Risk of death censored graft loss according to Banff scores - univariate



Risk of graft loss according to chronic Banff Scores – univariate



Hyalinosis & GFR were not predictors of graft loss



Multivariate model of 1 yr histopathology predicting death censored graft loss

Based on our analysis 1 year protocol biopsy
– best time point to predict long term graft loss

Comprehensive model 1: at one year post-transplant

	HR	95%CI	P value
Banff features			
Fibrointimal thickening (cv)	3.055	1.387-6.728	0.006
Inflammatory fibrosis (i-IF/TA)	1.805	1.110-2.935	0.017
Transplant glomerulopathy (cg)	2.563	0.347-18.955	0.357

Prevalence rates of iIF/TA on 1yr protocol biopsies

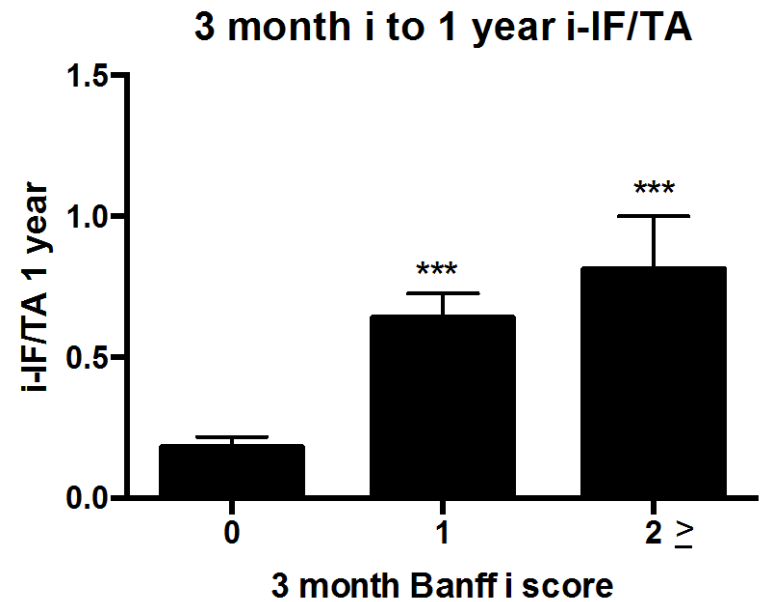
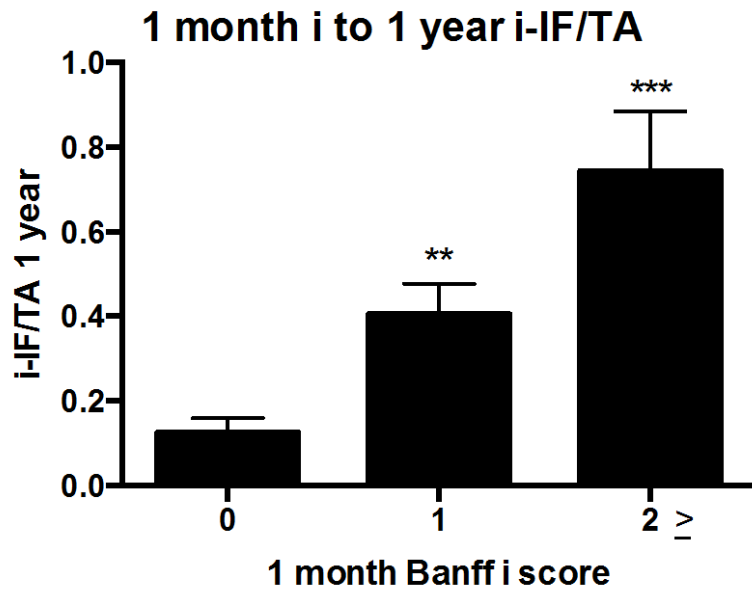
i-IF/TA Score	0	1	2	3
No. Biopsies	187	59	10	3

Prevalence of graft loss according to pathology

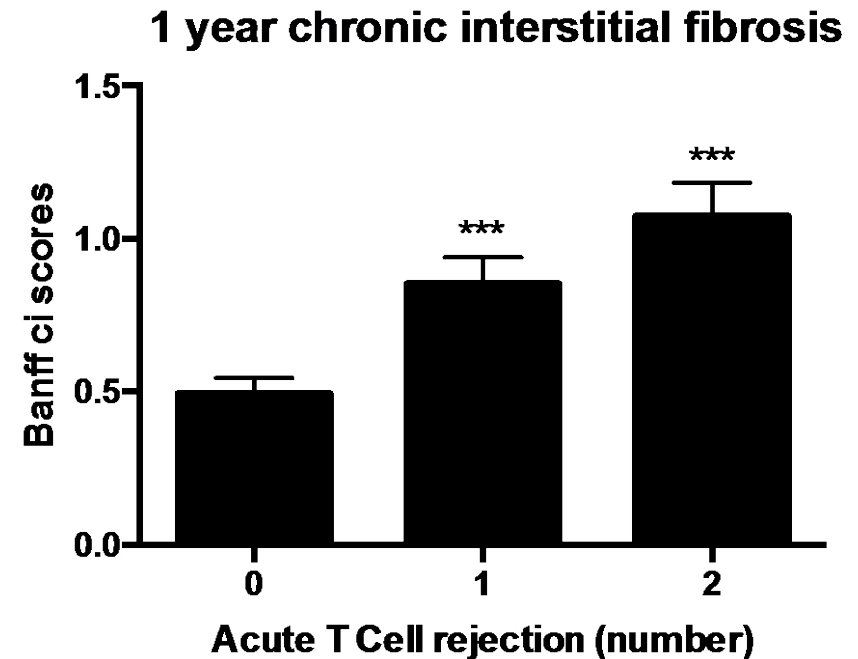
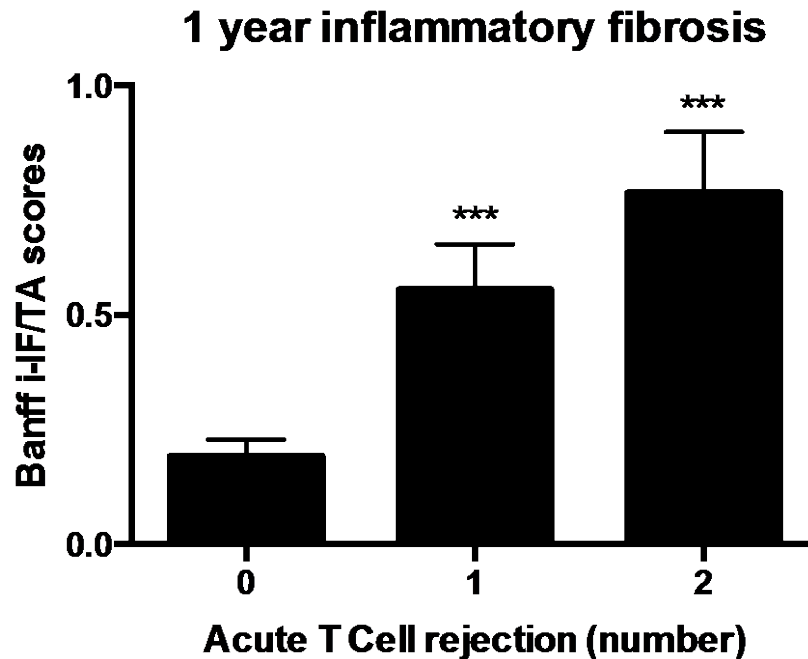
Histology	Graft Loss Score = 0	Graft loss Score ≥ 1
i-IF/TA	12/183 (6.6%)	14/72 (19.4%)
cg	27/256 (10.5)	2/10 (20%)
cv	16/205 (7.8%)	9/42 (21.4)

Average follow up 10 years

i-IF/TA correlates with early pathological processes

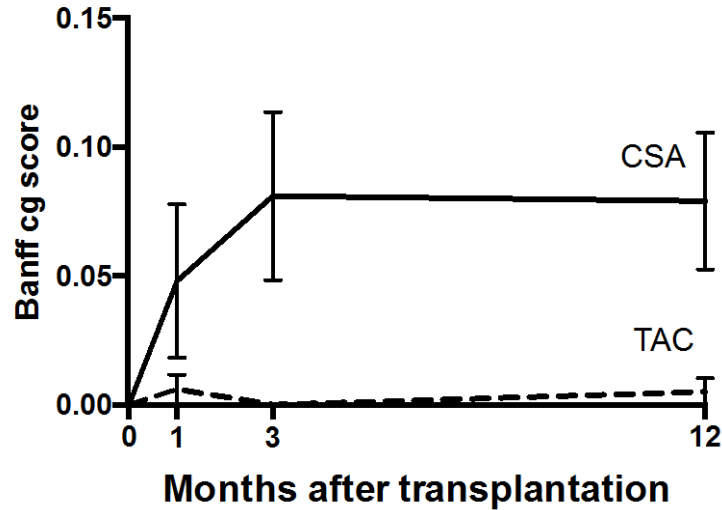


Early rejection types & chronic phenotypes

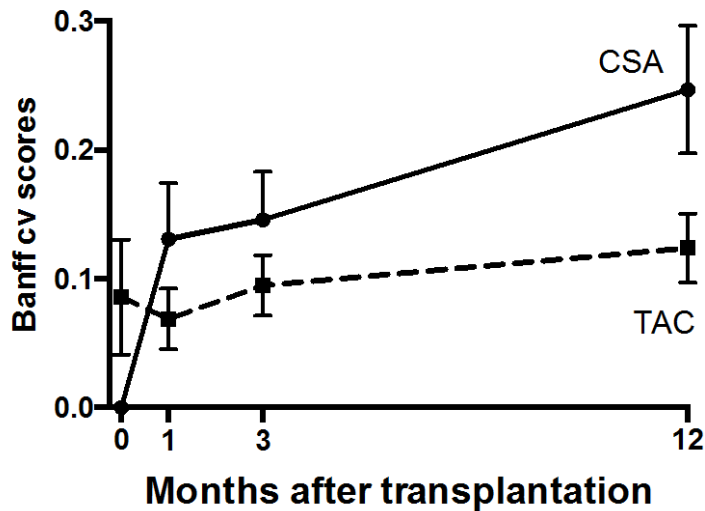


Era and Immunosuppression modify biopsy findings

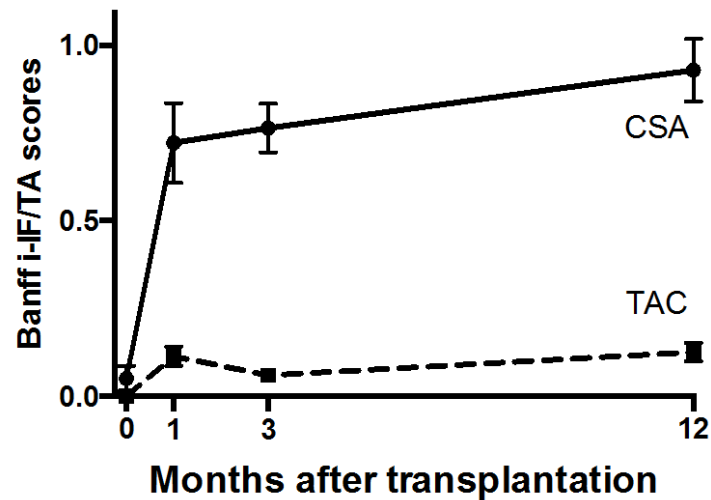
Transplant glomerulopathy



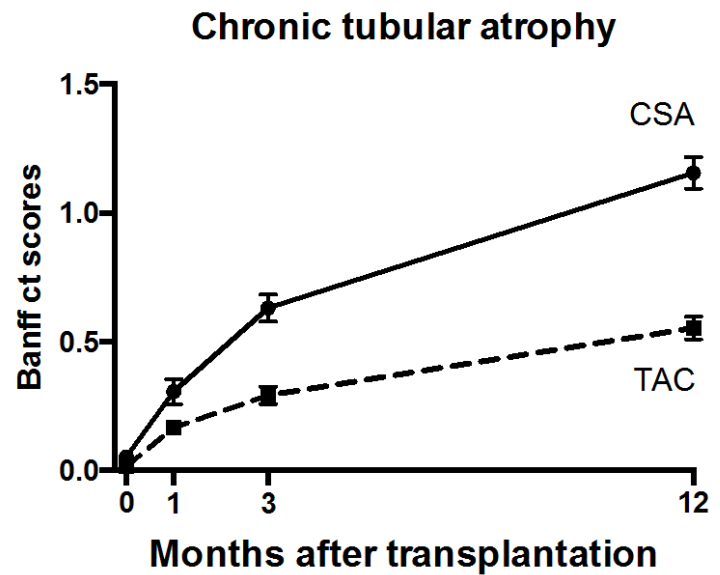
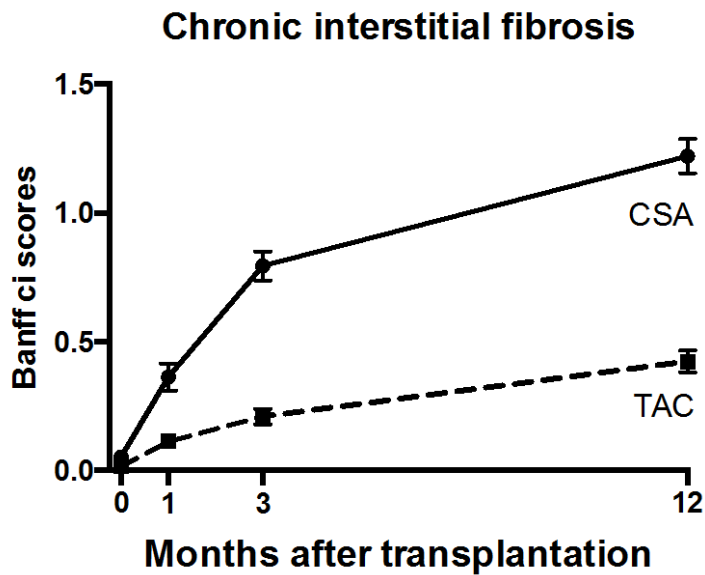
Fibrointimal hyperplasia



Inflammatory fibrosis



Era and Immunosuppression modify risk of chronic histological change



iIF/TA potential Surrogate marker for long term graft loss

- Predictive of graft loss (associated with clinical harm)
- Linked to prior clinical events that are consistent with an increased risk of graft loss ie early ACR/SCR
- Aim to validate these findings in kidney transplant recipients