RENAL ^{123}I-MIBG SCINTIGRAPHY SUGGESTS FUNCTIONAL SYMPATHETIC REINNERVATION IN HUMAN KIDNEY ALLOGRAFTS

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BACKGROUND

Kidney transplantation is the only durable therapy for end stage renal disease, but allograft nephropathy remains an important clinical problem. Sympathetic denervation might be involved in the pathogenesis of allograft nephropathy. At time of transplantation the allograft is entirely denervated, but histological evidence suggests reinnervation after transplantation. However, the functional significance of this reinnervation is unknown. Assessment of functional sympathetic nerves in human organs is possible with ^{123}I-metaiodobenzylguanidine (^{123}I-MIBG) scintigraphy. MIBG is a noradrenaline analogue that accumulates in adrenergic tissue. When labelled with ^{123}Iodine, MIBG can be visualized. Cardiac ^{123}I-MIBG imaging is routinely used for the measurement of cardiac sympathetic activity in chronic heart failure patients. Uptake reflects the density/intactness of the neural tissue within the organ. Wash-out rate is thought to reflect sympathetic activity.
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PATIENT CHARACTERISTICS (n = 5)

Age (years)	54 (range 38-83)	Antihypertensive drugs	5/5
Years after transplantation	23 (11-35)	Calcium antagonists	0/5
Bilateral nephrectomy	1/5	Beta blocking agents	0/5
Plasma creatinine (µmol/L)	95 (63-157)	Prednisolone	5/5
Creatinine clearance (ml/min)	89 (56-118)	Calcineurine inhibitor	0/5
Proteinuria (g/24hr)	0.23 (0.12-038)	Mycophenolatemophetil	4/5

METHODS

Five patients were studied with an renal allograft in situ for ≥ 10 years. All patients had a creatinine clearance ≥ 50 ml/min and were not prescribed alpha or beta blocking agents. Immunosuppressive and antihypertensive agents were continued throughout the study. Anterior and posterior planar semi-wholebody images were performed at 15 minutes and 4 hours after the intravenous administration of 185 MBq ^{123}I-MIBG. A ^{123}I vial with a known amount of radioactivity was included in the planar images as a reference. In addition, 4 hours after administration of ^{123}I-MIBG, single positron emission computed tomography (SPECT)-CT (low dose) was made. Figure 1 shows the fused SPECT-CT image. Regions of interest (ROIs) were manually drawn in transverse CT images, following kidney cortex contours of native and allograft kidneys, excluding the calyces. ROIS were then fused into volumes of interest (VOIs) and copied to the co-registered SPECT (Figure 2, Hybrid Viewer™, Hermes Medical Solutions, Stockholm, Sweden). Mean counts/voxel expressed ^{123}I-MIBG uptake. ROIs in adipose tissue served as background reference. Relative renal uptake of ^{123}I-MIBG was calculated as:

$$(\text{uptake } ^{123}\text{I-MIBG}_{kidney} - \text{uptake } ^{123}\text{I-MIBG}_{adipose}) / \text{uptake } ^{123}\text{I-MIBG}_{adipose.}$$

Washout-rates (WORs) were calculated by creating geometric means of anterior and posterior planar semi-wholebody images. ROIs were drawn in the mediastinum, myocardium, native kidneys and renal allograft. Relative uptake in the organs was calculated as % of the injected dose of ^{123}I-MIBG. WORs in the myocardium, native left kidney and renal allograft were deducted from 15 minutes and 4 hour images. For WORs, the non-specific wash-out in the mediastinum served as reference.

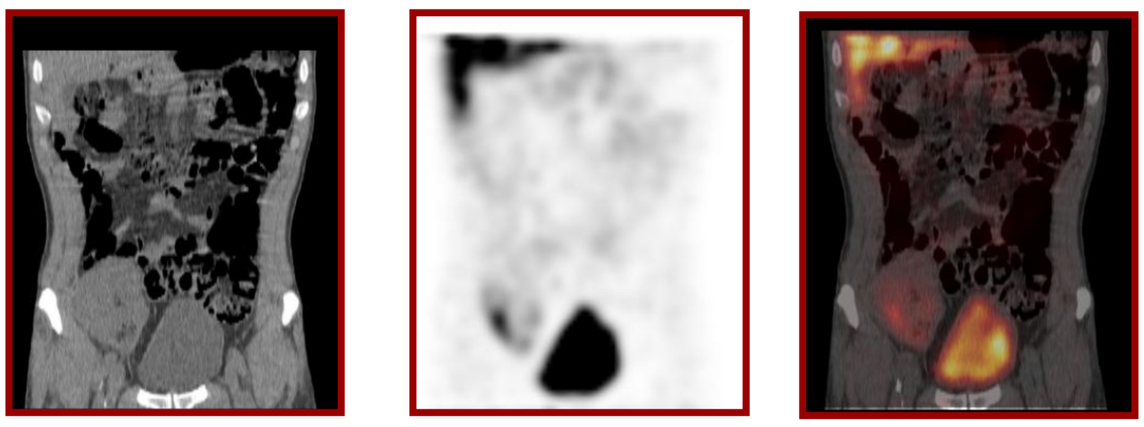
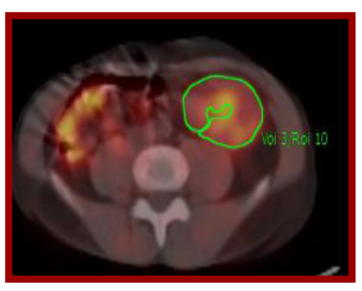
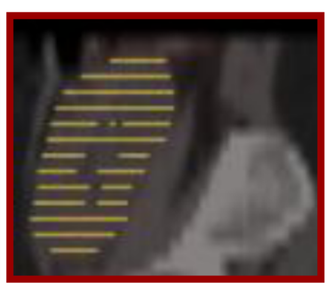


Figure 1. Left panel CT scan, middle panel SPECT and right panel the fused SPECT-CT

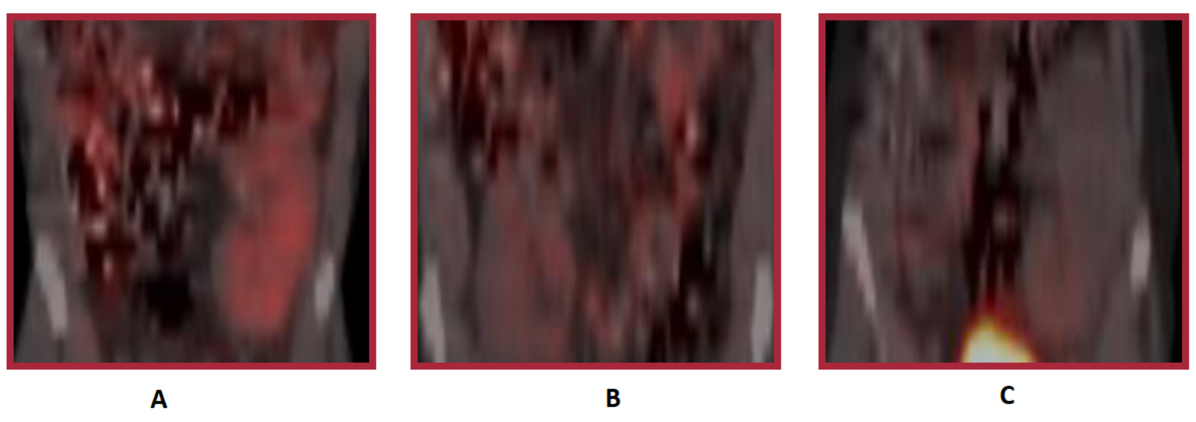


2a.

Figure 2a. A manually drawn region of interest (ROI) in transverse CT images (green line) of the kidney allograft.
Figure 2b. Sagittal view of the kidney allograft: combined ROIs in transverse CT images (yellow lines) create a volume of interest (VOI).



2b.



A B C D E

Figure 3: SPECT-CT ^{123}I-MIBG images of patients with various lengths of time after kidney transplantation.

A = 11 years **B** = 18 years
C = 20 years **D** = 32 years
E = 35 years

RESULTS

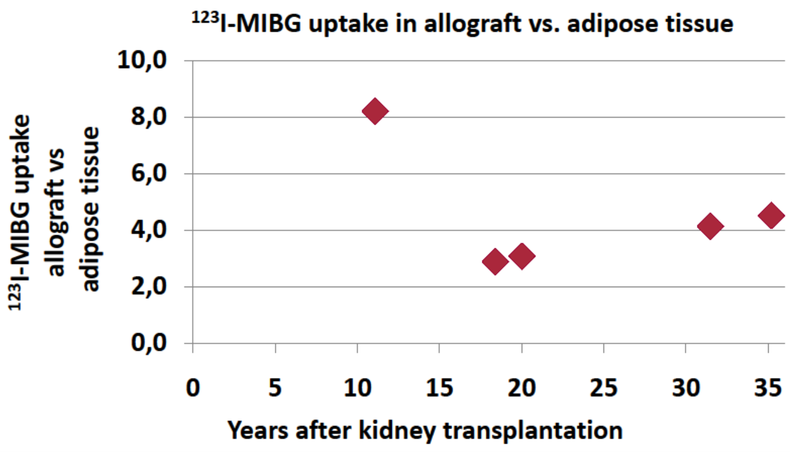


Figure 4: Uptake of ^{123}I-MIBG in the kidney allograft in years after transplantation.

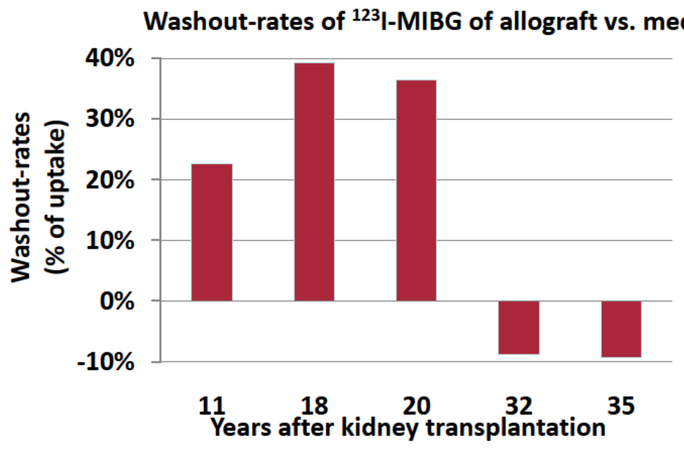


Figure 5: Washout rates (WORs) of ^{123}I-MIBG in the allograft. Negative WORs can reflect an increase in ^{123}I-MIBG uptake.

CONCLUSION

Based on renal allograft uptake and washout of ^{123}I-MIBG, these data suggest functional sympathetic reinnervation in long surviving human renal allografts. This is in line with histological evidence of reinnervation of the renal allograft. However, the use of renal ^{123}I-MIBG scintigraphy for this specific purpose, should be further validated.

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