Characterizing Renal Involvement in Light Chain Amyloidosis on ^{124}I-Evuzamitide PET/MRI Imaging

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BACKGROUND

- ^{124}I-evuzamitide (AT-01) is a novel pan-amyloid PET radiotracer that is renally excreted and undergoes rapid dehalogenation of unbound tracer, allowing amyloid-bound tracer imaging of target organs.
- In a cohort of patients with light chain (AL) amyloidosis, transthyretin amyloidosis, and a control non-amyloid population, we sought to characterize renal amyloid fibril deposition through ^{124}I-evuzamitide PET/MRI imaging.

METHODS

- The study was approved by the OHSU IRB and conducted under an FDA-approved IND.
- For patients who did not have a primary renal amyloid presentation, the diagnosis of renal AL amyloidosis was based on standard clinical, laboratory, biopsy, and imaging criteria according to guidelines, in addition to the presence or absence of alternative explanations for renal disease. The diagnosis was confirmed in 6 patients, and strongly suspected in 3 patients.
- All patients underwent PET/MRI with ^{124}I-evuzamitide.
- Renal uptake was quantified using standardized uptake value ratio (SUVR), defined as the ratio of renal SUV / left ventricular blood pool SUV.
- Renal SUVR and uptake pattern were then compared between renal AL amyloidosis patients and non-renal AL controls.
- Proteinuria was not systematically assessed at the time of the PET/MRI scan.

Table 1: Baseline Characteristics Stratifying by Renal AL Amyloidosis vs. Control

Variable	Total (n=50)	Renal AL Amyloidosis (n=9)	Controls (n=41)	p-value
Age (years)	72.0 ± 9.1	69.9 ± 7.8	72.6 ± 9.4	0.384
Male Sex (%)	37 (74%)	5 (56%)	32 (78%)	0.164
Cardiac Amyloidosis (%)	34 (68%)	5 (56%)	29 (71%)	0.377
Underlying Phenotype for Controls:				
Extra-renal AL Amyloidosis			3 (7%)	
Transthyretin Amyloid Cardiomyopathy (ATTR-CM)	–	–	27 (66%)	–
LVH/HCM			4 (10%)	
Hereditary Transthyretin Carrier			5 (12%)	
Orthopedic Amyloid Deposits			2 (5%)	
^{124}I-evuzamitide administered activity (mCi)	1.05 ± 0.02	1.05 ± 0.01	1.04 ± 0.01	0.504
Mean Renal SUV	5.8 ± 5.6	12.5 ± 11.0	4.3 ± 1.3	0.056
Mean LV Blood Pool SUV	4.0 ± 1.1	3.7 ± 0.8	4.1 ± 1.2	0.291
Mean Renal SUVR (Kidney / LV Blood Pool)	1.2 (0.9, 1.6)	1.9 (1.4, 4.8)	1.0 (0.8, 1.4)	**<0.001**
eGFR (mL/min)	48.7 ± 14.9	36.5 ± 14.7	51.3 ± 13.7	0.018
Creatinine (mg/dL)	1.20 ± 0.51	1.60 ± 0.90	1.11 ± 0.33	0.148

RESULTS

- 50 patients were enrolled from January through August, 2023. All subjects completed the study protocol. 9 (18%) of patients had renal AL amyloidosis.
- The baseline characteristics are shown in Table 1.
- In one patient with renal AL amyloidosis requiring kidney transplant:
  - Native AL-affected kidney: Renal SUVR = 12.8, Figure 1A
  - Unaffected transplanted kidney: Renal SUVR = 0.86, Figure 1B
- Median renal SUVR was 1.9 (1.4, 4.8) in renal AL amyloidosis vs. 1.0 (0.8, 1.4) in non-renal AL controls (p<0.0001), Figure 2.
- As demonstrated in Figure 1A, patients with renal AL amyloidosis generally had more homogenous kidney uptake whereas non-renal AL controls generally had a heterogenous pattern, Figure 3.

Figure 1: Renal SUVR of Native AL-affected Kidneys vs. Transplanted Unaffected Kidney in One Patient with Renal AL Amyloidosis

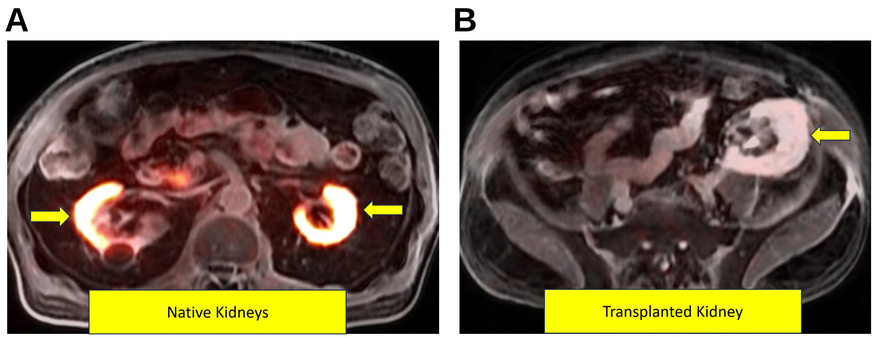


Figure 2: Renal SUVR in Renal AL Amyloidosis vs. Control

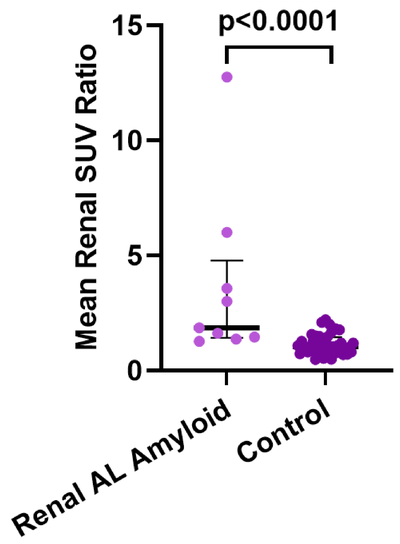
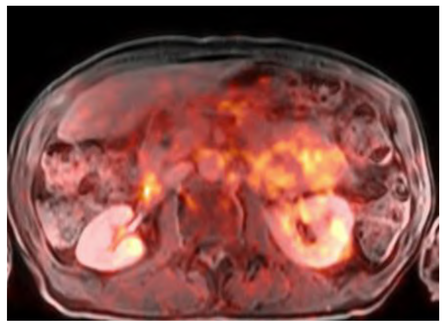
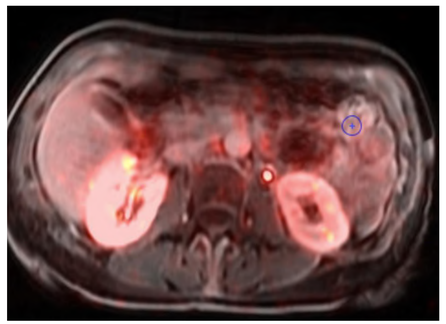
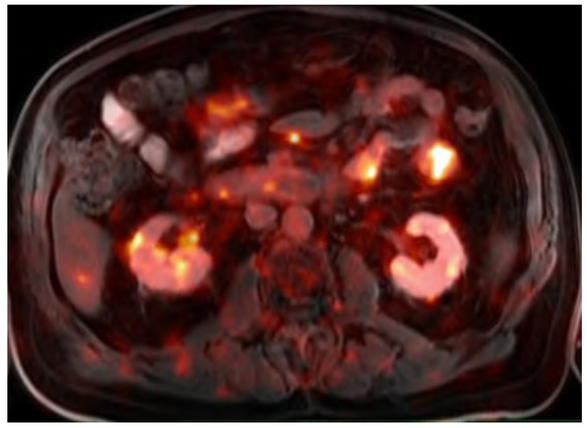


Figure 3: Heterogenous ^{124}I-evuzamitide Uptake in Three Non-Renal AL Control Patients







CONCLUSIONS

- Renal AL amyloid deposition can be accurately detected using ^{124}I-evuzamitide (AT-01) PET/MRI.
- Renal SUVR differentiated patients with and without clinical renal amyloidosis.
- Additionally, pattern of uptake between renal AL amyloidosis compared to the non-renal AL control population differed, providing evidence for qualitative descriptors in addition to quantitative approaches.
- Further work is needed to define diagnostic thresholds in a larger consecutive cohort of patietns with renal amyloidosis. Additionally, histopathological correlation might provide additional insights.

DISCLOSURES & FUNDING

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