

^{99m}Tc -p5+14 (AT-05) is a pan-amyloid imaging agent that effectively detects cardiac amyloid by both planar and SPECT/CT imaging at 1 h post-injection with a high signal-to-background ratio

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BACKGROUND

- Cardiac amyloidosis is most commonly associated with the deposition of misfolded transthyretin (ATTR) or immunoglobulin light chains (AL). Early and accurate detection of cardiac amyloidosis is important to ensure optimal benefit from treatment.
- Nuclear gamma imaging has transformed the diagnosis of cardiac ATTR amyloidosis, and this technique can provide an excellent tool for the detection of cardiac amyloid of any type.
- We have developed a pan-amyloid reactive peptide, p5+14, labeled with technetium-99m, for detecting all types of amyloid using planar gamma and SPECT/CT imaging.
- ^{99m}Tc -p5+14 can stably bind both amyloid fibrils and the hypersulfated glycosaminoglycans found in amyloid deposits.
- Here we update the characteristics of ^{99m}Tc -p5+14 binding in the heart of patients with ATTR and AL cardiac amyloidosis.

METHODS

- ^{99m}Tc -p5+14 is being evaluated in a pilot Phase 1 single-center, open-label study (NCT05951816).
- Twenty-one subjects completed the study, which includes five ($n=5$) healthy volunteers (HV), five ($n=5$) patients with AL, and 11 ($n=11$) patients with ATTR amyloidosis.
- ^{99m}Tc -p5+14 was synthesized using chelator-free chemistry at the UT Graduate School of Medicine radiopharmacy.
- Subjects were administered ≤ 22 mCi of radiotracer IV. Whole body planar and SPECT/CT imaging was performed at 1 h and 3 h post-injection (pi).
- ^{99m}Tc -pyrophosphate (PYP) images were acquired on patients 72 h after ^{99m}Tc -p5+14 imaging.
- Images were visually evaluated, and the uptake of tracer in the heart and the signal-to-background was estimated by manual image segmentation of the planar and SPECT images using the lung and blood pool as background, respectively.

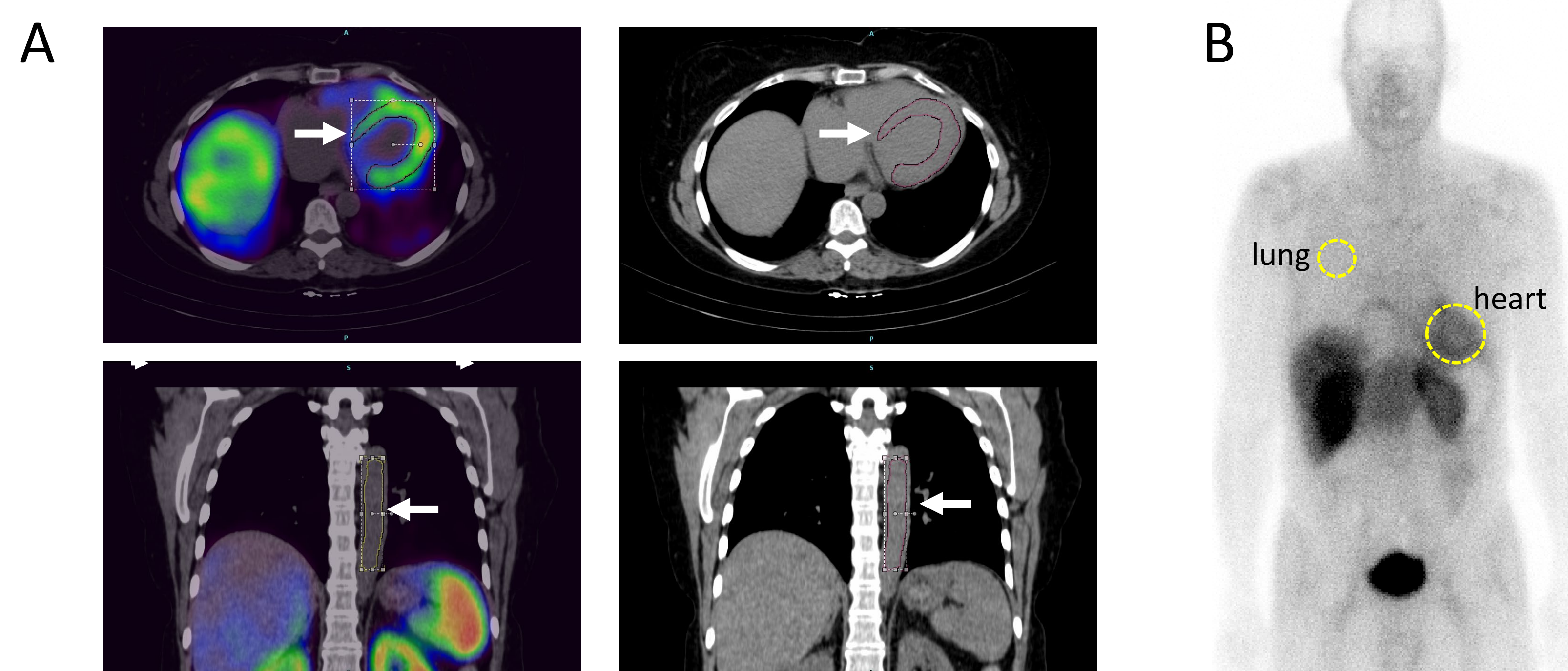


Figure 1. For semi-quantitative analyses, the uptake of ^{99m}Tc -p5+14 and ^{99m}Tc -PYP in the heart and blood (in SPECT/CT images) and heart and lung (in planar images) were assessed using manual 2D region of interest analysis of the images.

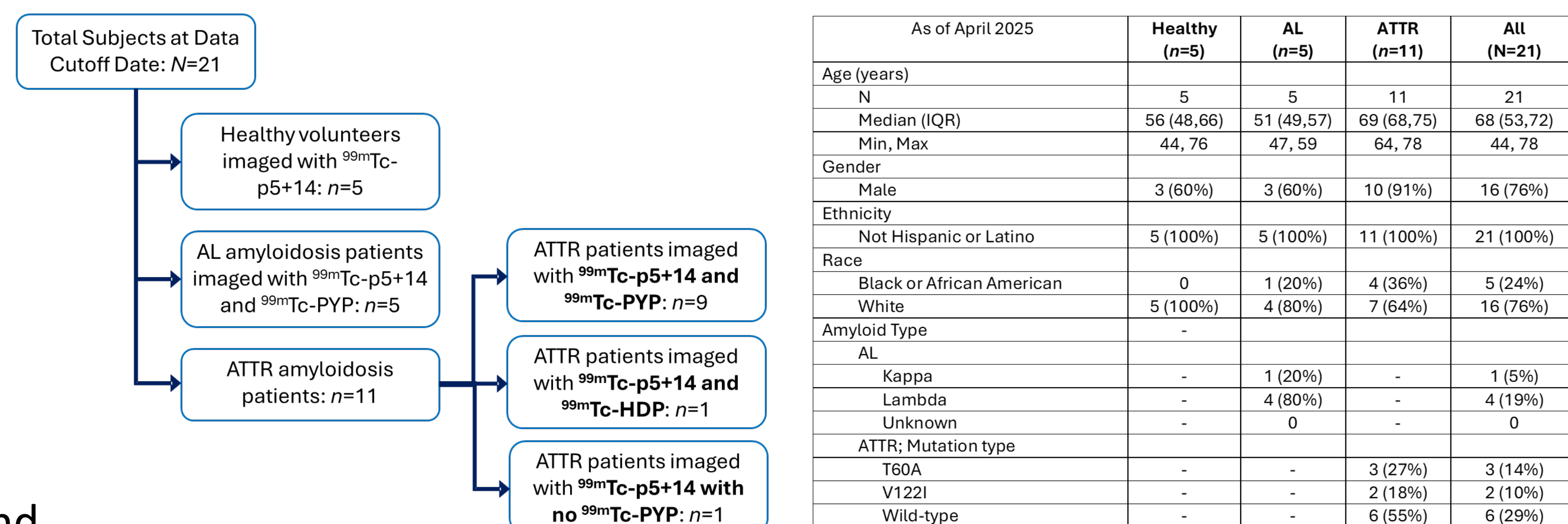


Figure 2. Study design for the Phase 1 safety and biodistribution evaluation of ^{99m}Tc -p5+14 and patient demographics for the first 21 subjects enrolled.

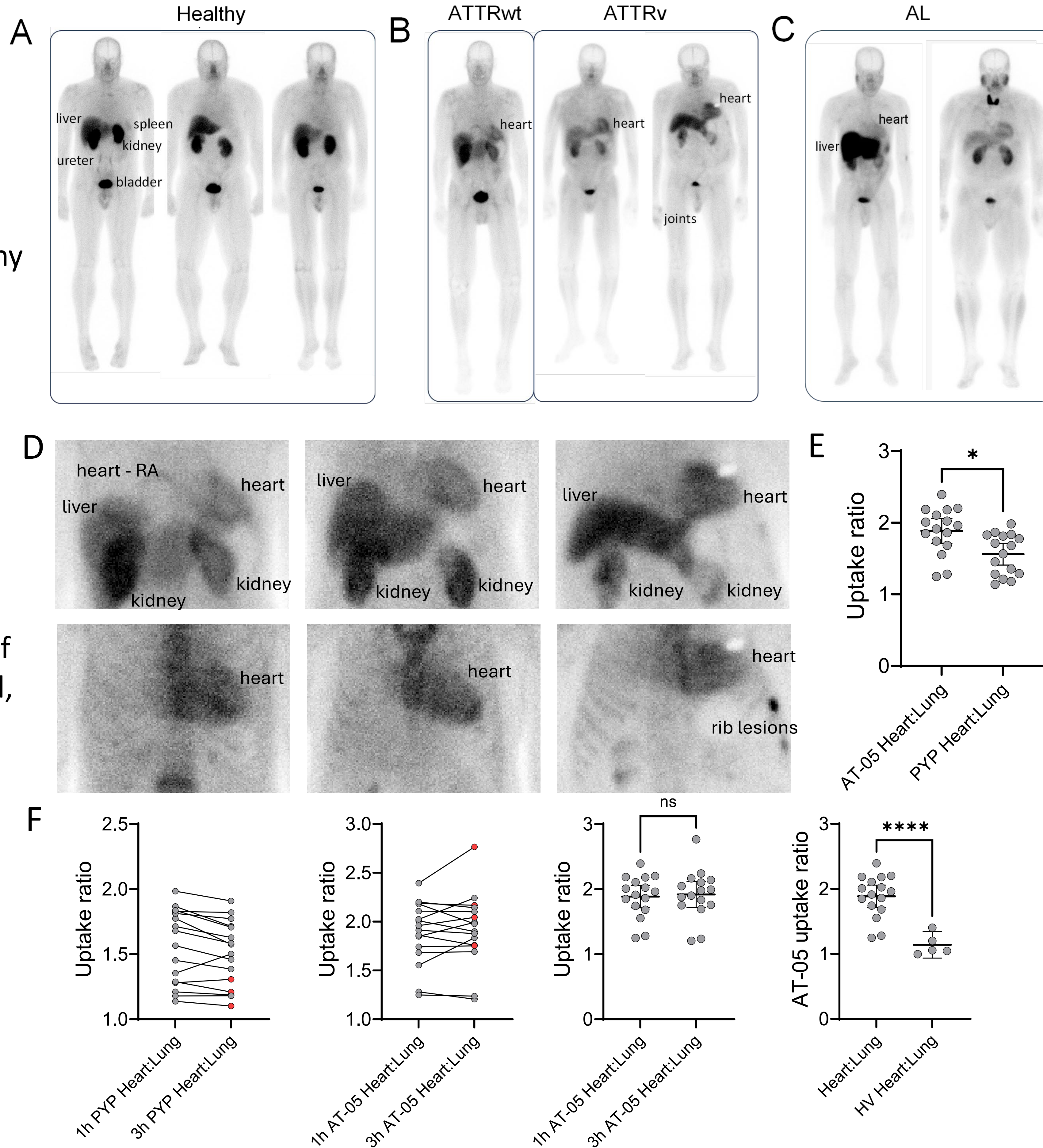


Figure 3. Analysis of planar images. (A-C) Cardiac uptake of ^{99m}Tc -p5+14 was visible in patients only. (D) Cardiac uptake of ^{99m}Tc -p5+14 at 1 h (upper) differed from ^{99m}Tc -PYP (lower). (E) The H:L for p5+14 was modestly but significantly higher than PYP. (F) Both ^{99m}Tc -PYP and ^{99m}Tc -p5+14 were stably bound over 3 h pi (red=AL). The peptide H:L was significantly higher in patients than HV.

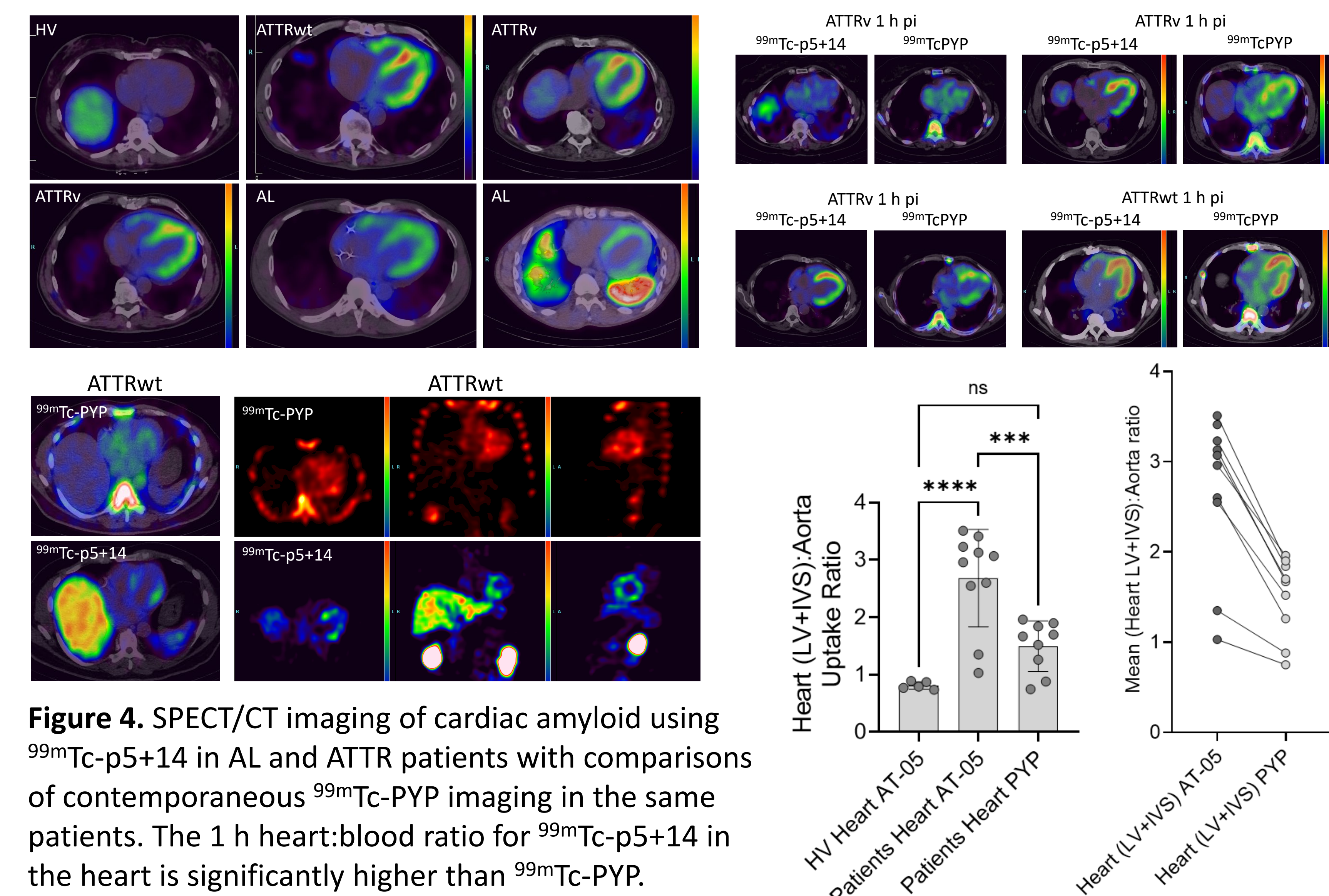


Figure 4. SPECT/CT imaging of cardiac amyloid using ^{99m}Tc -p5+14 in AL and ATTR patients with comparisons of contemporaneous ^{99m}Tc -PYP imaging in the same patients. The 1 h heart:blood ratio for ^{99m}Tc -p5+14 in the heart is significantly higher than ^{99m}Tc -PYP.

RESULTS:

- Patients with cardiac amyloidosis had significant uptake of ^{99m}Tc -p5+14 in the heart, evidenced in planar and SPECT/CT images acquired at 1 h pi.
- No cardiac uptake of ^{99m}Tc -p5+14 was observed in healthy subjects.
- In planar images at 1 h pi, the heart:lung ratio for ^{99m}Tc -p5+14 was greater in patients versus healthy subjects ($p<0.0001$) and patient ^{99m}Tc -PYP images ($p=0.0303$).
- Cardiac uptake of ^{99m}Tc -p5+14 assessed from SPECT/CT images was significantly higher than that of ^{99m}Tc -PYP in ATTR patients ($p=0.0009$) and of ^{99m}Tc -p5+14 in healthy subjects ($p<0.0001$).
- In this small cohort, the positive percent agreement for ^{99m}Tc -p5+14 in patients was 94% (15/16) with a negative percent agreement of 100% (5/5).

CONCLUSION:

- ^{99m}Tc -p5+14 is a promising new radiotracer for the detection of cardiac amyloidosis of any type using planar gamma and SPECT/CT imaging at 1 h post injection. This novel tracer may be a useful screening tool for the early detection of cardiac amyloidosis.

DISCLOSURE

EBM, SJK and AS: Founding shareholder in Attralus Inc.
EBM, AS, REH, TJH, SJK and JSW: Patent rights in peptides used for amyloid imaging, licensed to Attralus. JSW: Co-founder, interim CSO, and shareholder in Attralus Inc. Research funding from Attralus