

Extracardiac uptake of the SPECT/CT imaging agent, ^{99m}Tc-p5+14 (AT-05), in patients with AL or ATTR cardiac amyloidosis

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BACKGROUND

- Systemic amyloidosis is commonly associated with the deposition of misfolded transthyretin (ATTR) or immunoglobulin light chains (AL).
- Cardiac amyloid is an ominous manifestation of the disease with a poor prognosis.
- Early and accurate diagnosis of cardiac amyloidosis is important to ensure optimal benefit from treatment.
- Extracardiac deposits are common in patients with systemic amyloidosis and can involve any organ or tissue and may contribute to the poor quality of life.
- We have developed a pan-amyloid-reactive peptide, p5+14, that when labeled with technetium-99m is capable of detecting amyloid in numerous organs and tissues using planar gamma and SPECT/CT imaging.
- Unlike other cardiac amyloid imaging agents, ^{99m}Tc-p5+14 can stably bind to both amyloid fibrils and hypersulfated glycosaminoglycans in amyloid throughout the body.
- Here we describe additional non-physiological distribution of ^{99m}Tc-p5+14 in patients with AL or ATTR cardiac amyloidosis.

METHODS

- Patients >18 years of age with a diagnosis of cardiac amyloidosis (*n*=30) and healthy volunteers (HV) (*n*=5) will be recruited (NCT05951816).
- The study has recruited *n*=21 subjects, (*n*=5) healthy subjects and (*n*=16) patients with ATTR or AL amyloidosis.
- Subjects were administered a single IV injection of ^{99m}Tc-p5+14 (<22 mCi and <1 mg of peptide).
- SPECT/CT and planar images were acquired at 1 hour and 3 hours post-injection.
- Images were visually evaluated, and the signal-to-background (organ:blood) uptake of tracer in the heart, liver, spleen and kidney was estimated by manual segmentation of the SPECT images.

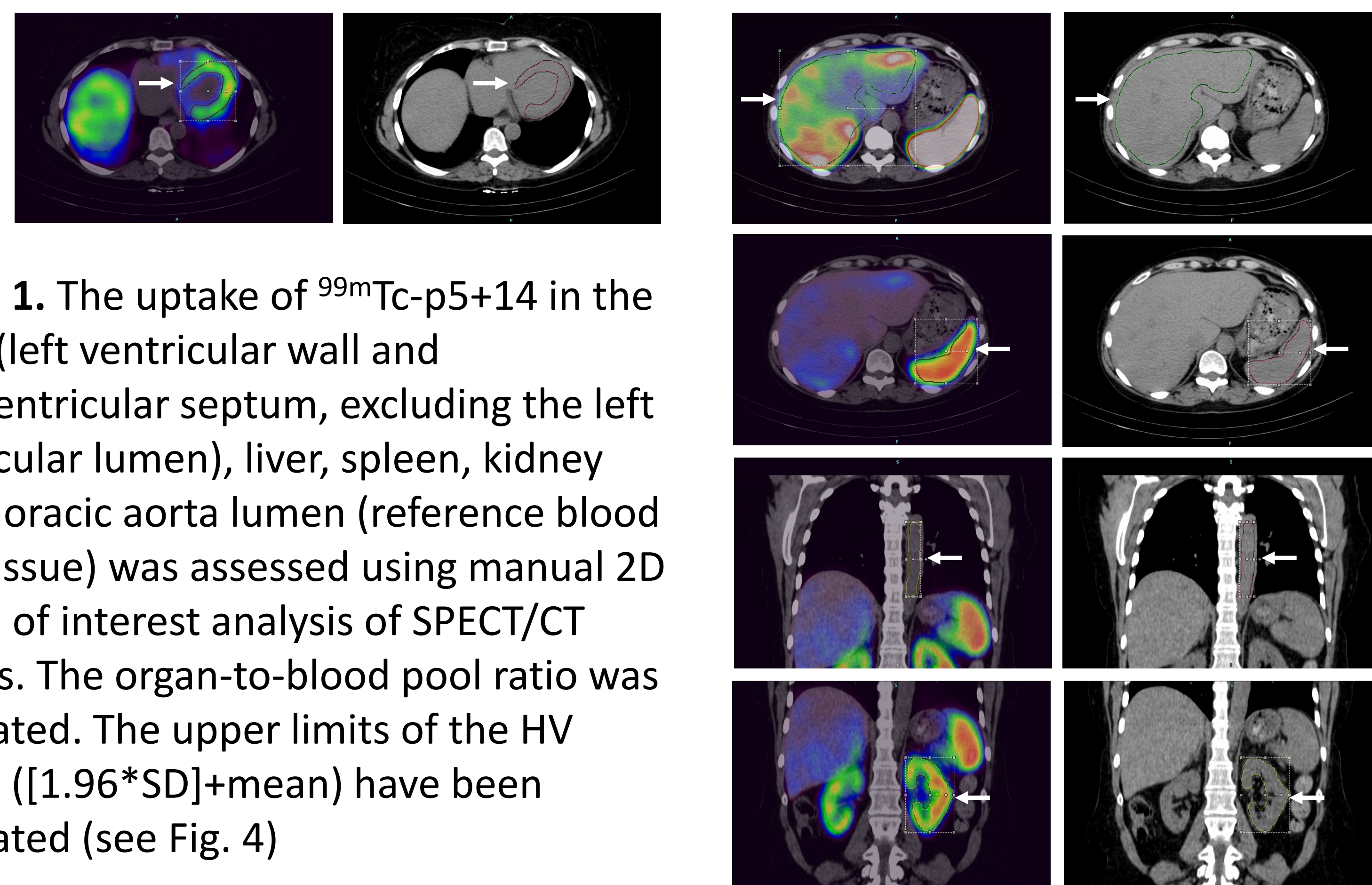


Figure 1. The uptake of ^{99m}Tc-p5+14 in the heart (left ventricular wall and interventricular septum, excluding the left ventricular lumen), liver, spleen, kidney and thoracic aorta lumen (reference blood pool tissue) was assessed using manual 2D region of interest analysis of SPECT/CT images. The organ-to-blood pool ratio was calculated. The upper limits of the HV values ([1.96*SD]+mean) have been calculated (see Fig. 4)

Patient	Patient ID	Amyloid	^{99m} Tc-p5+14 date	^{99m} Tc-PYP date	Mutation or isotype	Male/Female	Race
1	AT05-001	ATTRwt	9/18/2023	9/21/2023	wt	M	White
2	AT05-002	HV	9/27/2023	na	na	F	White
3	AT05-003	HV	10/8/2023	na	na	M	White
4	AT05-004	ATTRv	10/23/2023	10/26/2023	wt	M	White
5	AT05-005	HV	11/29/2023	na	na	M	White
6	AT05-006	HV	12/6/2023	na	na	F	White
7	AT05-007	ATTRv	12/18/2023	12/21/2023	T60A	M	White
8	AT05-008	ATTRwt	1/29/2023	2/1/2024	wt	M	Black
9	AT05-009	ATTRv	2/5/2024	2/8/2024	V122I	M	Black
10	AT05-010	HV	2/21/2024	na	na	M	White
11	AT05-011	AL	3/18/2024	3/21/2024	kappa	M	Black
12	AT05-012	ATTRv	4/22/2024	4/25/2022	T60A	F	White
13	AT05-013	AL	5/20/2024	5/23/2024	lambda	M	White
14	AT05-014	ATTRv	6/17/2024	6/20/2024	V122I	M	Black
15	AT05-015	ATTRwt	7/8/2024	7/11/1934	wt	M	Black
16	AT05-016	AL	7/22/2024	7/25/2024	lambda	F	White
17	AT05-017	ATTRwt	9/30/2024	10/3/24 HDP	wt	M	White
18	AT05-018	ATTRwt	10/14/2024	10/17/2024	wt	M	White
19	AT05-019	ATTRwt	2/17/2025	2/20/2025	wt	M	White
20	AT05-020	AL	2/24/2025	2/27/2025	lambda	F	White
21	AT05-021	AL	3/10/2025	3/13/2025	lambda	M	White

Figure 2. Summary of subjects and patient amyloid types with demographics for the first 21 subjects enrolled in the ^{99m}Tc-p5+14 Phase 1 study evaluating safety and biodistribution.

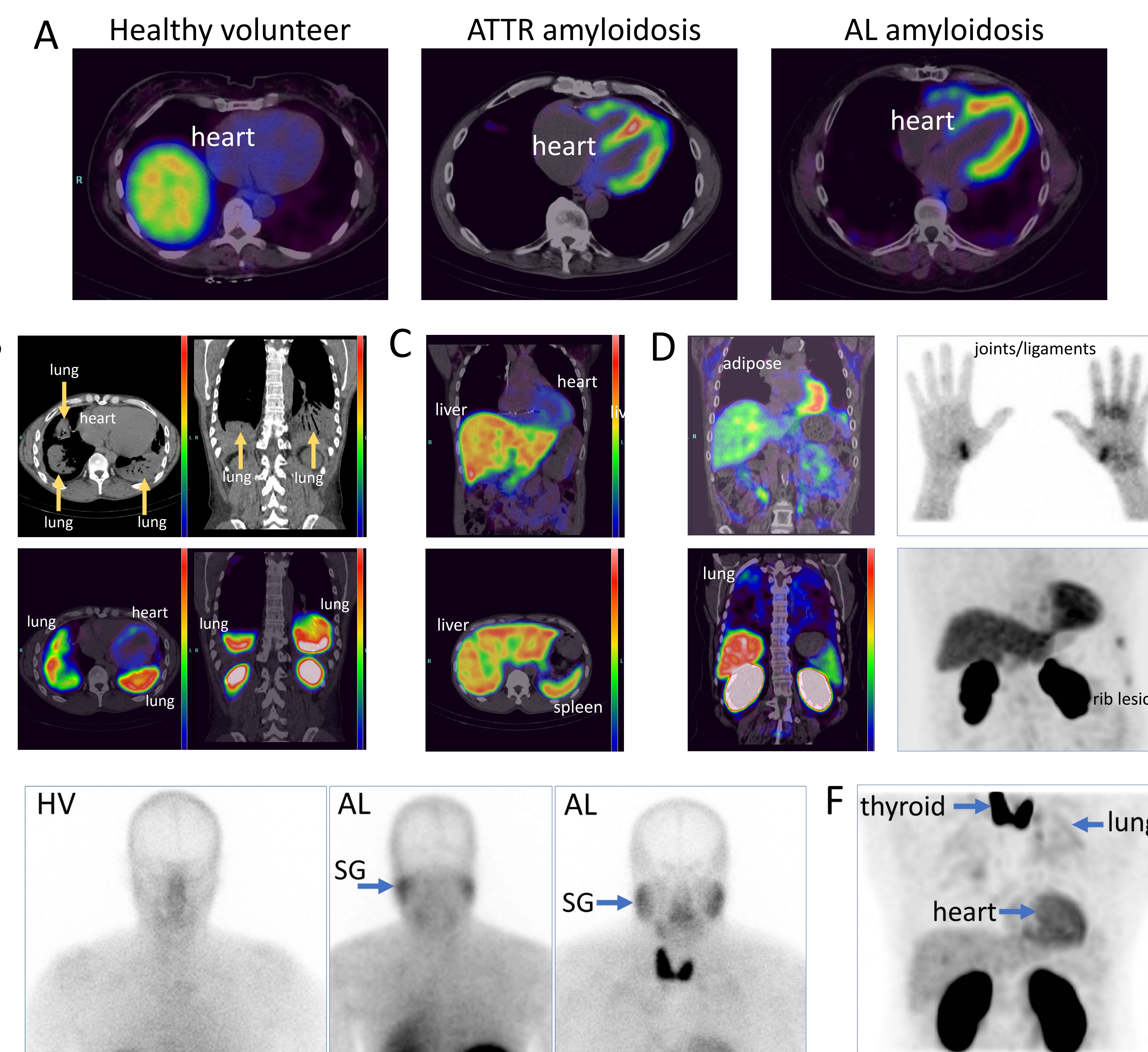


Figure 3. Biodistribution of ^{99m}Tc-p5+14. (A) Binding the AL and ATTR cardiac amyloid in patients with no uptake in healthy heart. (B and C) Pulmonary, hepatic and splenic uptake in AL patients (D) Tracer uptake in adipose tissue, joints/ligaments, lung and rib lesions of patients with ATTR amyloidosis. (E) Salivary gland (SG) uptake in AL patients not seen in HV. (F) Thyroid gland and pulmonary uptake in AL patient.

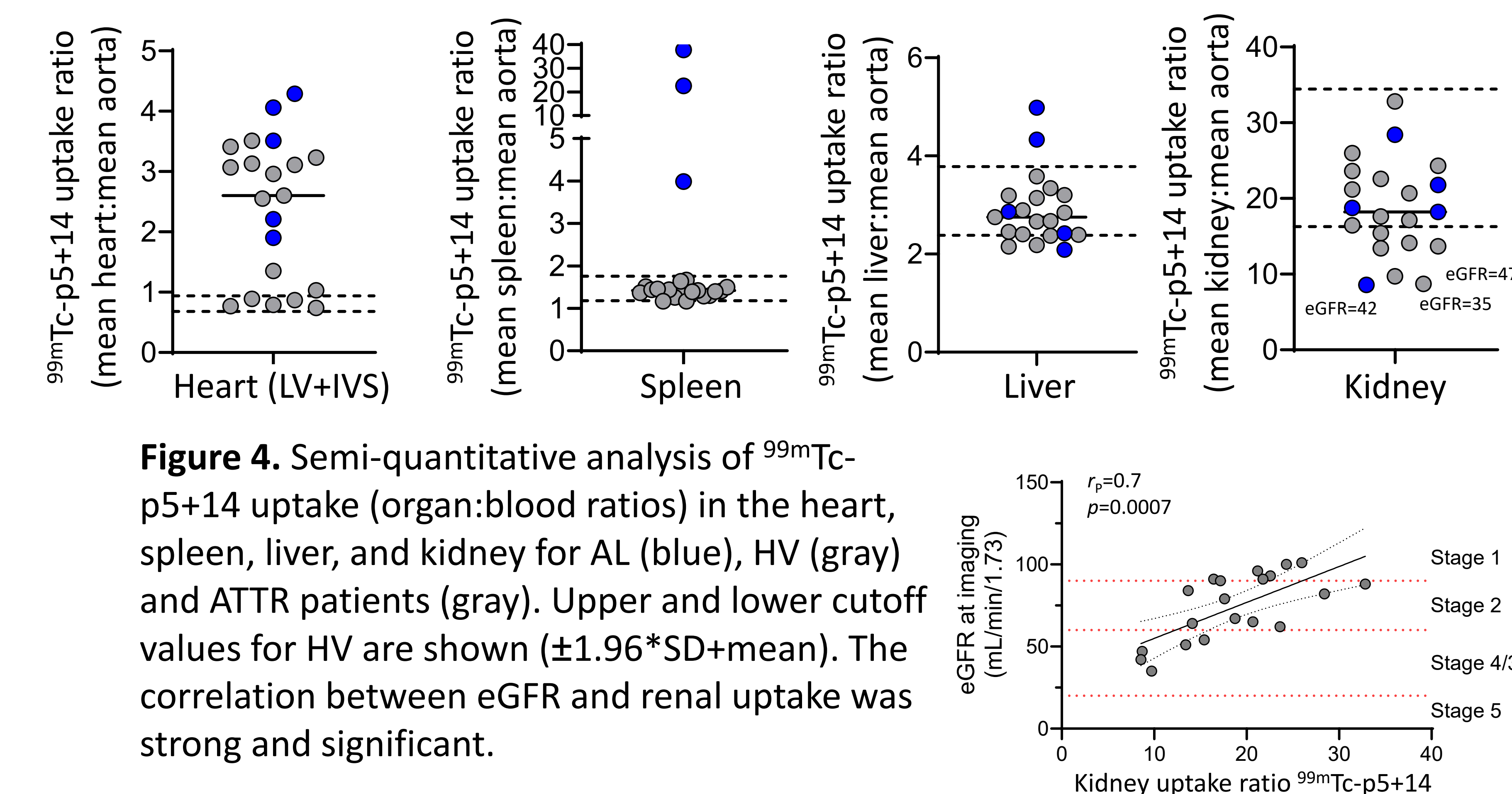


Figure 4. Semi-quantitative analysis of ^{99m}Tc-p5+14 uptake (organ:blood ratios) in the heart, spleen, liver, and kidney for AL (blue), HV (gray) and ATTR patients (gray). Upper and lower cutoff values for HV are shown ($\pm 1.96 \times \text{SD} + \text{mean}$). The correlation between eGFR and renal uptake was strong and significant.

RESULTS:

- No cardiac ^{99m}Tc- p5+14 uptake was seen in healthy subjects (100% negative percent agreement; 5/5).
- Cardiac amyloid was readily imaged in patients with AL or ATTR amyloidosis (94% positive percent agreement; 15/16).
- Extracardiac, non-physiological uptake of radiotracer has also been observed in both planar and SPECT/CT images.
- In ATTR patients, ^{99m}Tc-p5+14 was observed in focal lesions and pleura of the lungs as well as joints.
- In patients with cardiac AL amyloidosis, tracer uptake was observed in the lung, liver, spleen, salivary glands, thyroid gland, and tongue.
- The 95% confidence interval of signal-to-background values in HV (*n*=5) identified significant uptake in the liver and spleen of patients with AL but not ATTR amyloidosis.

CONCLUSION:

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

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