

Exploring cardiac uptake of the SPECT radiotracer, ^{99m}Tc-p5+14 (AT-05), in patients with amyloidosis – Significant correlations exist between structural or functional parameters and signal-to-background measurements

R. Eric Heidel¹, Emily B. Martin¹, Alan Stuckey¹, Bryan Whittle², Hannah Watson², Anne Kassira¹, Rebecca Hung³, Stephen J. Kennel¹, Jonathan S. Wall¹

¹University of Tennessee Graduate School of Medicine, TN, USA. ²University of Tennessee Medical Center. ³Vanderbilt University Medical Center

BACKGROUND

- Systemic amyloidosis is an infiltrative cardiomyopathy often associated with the deposition of misfolded transthyretin (ATTR) or monoclonal immunoglobulin light chains (AL) as amyloid fibrils.
- Peptide p5+14 binds all types of amyloid and can be labeled with technetium-99m for planar gamma scintigraphy (PGS) or SPECT/CT imaging.
- ^{99m}Tc-p5+14 can stably bind two ubiquitous components of amyloid deposits – the amyloid fibril and the hypersulfated glycosaminoglycans - affording direct imaging of cardiac amyloid.
- PGS and SPECT/CT images are generally not considered quantitative; however, a simple signal-to-background ratio can be measured.
- Here, we perform exploratory correlation analyses of ^{99m}Tc-p5+14 uptake in the heart in PGS and SPECT/CT images with structural or functional measures of cardiac amyloidosis.
- Despite the small sample sizes in this pilot study, significant moderate/strong correlations were observed.

METHODS

- Data were collected as part of an ongoing Phase 1 study (NCT05951816). We present data on $n=16$ patients diagnosed with cardiac amyloidosis ($n=11$ with ATTR and $n=5$ with AL) and $n=5$ healthy volunteers (HV).
- ^{99m}Tc-p5+14 was synthesized onsite and subjects received ≤ 22 mCi of radiotracer IV, with whole body PGS followed by SPECT/CT imaging performed at 1 h and 3 h post injection.
- Blood was collected, and a transthoracic echocardiogram was performed.
- ^{99m}Tc-pyrophosphate (PYP) imaging was performed on $n=14$ patients 72 h after ^{99m}Tc-p5+14 imaging.
- Uptake of tracer in the interventricular septum (IVS) and left ventricular (LV) wall was measured by manual image segmentation of the PGS and SPECT images using the lung or blood for background measurements.
- Pearson (r) correlations were performed to test for associations between the uptake of ^{99m}Tc-p5+14 and metrics of interest.

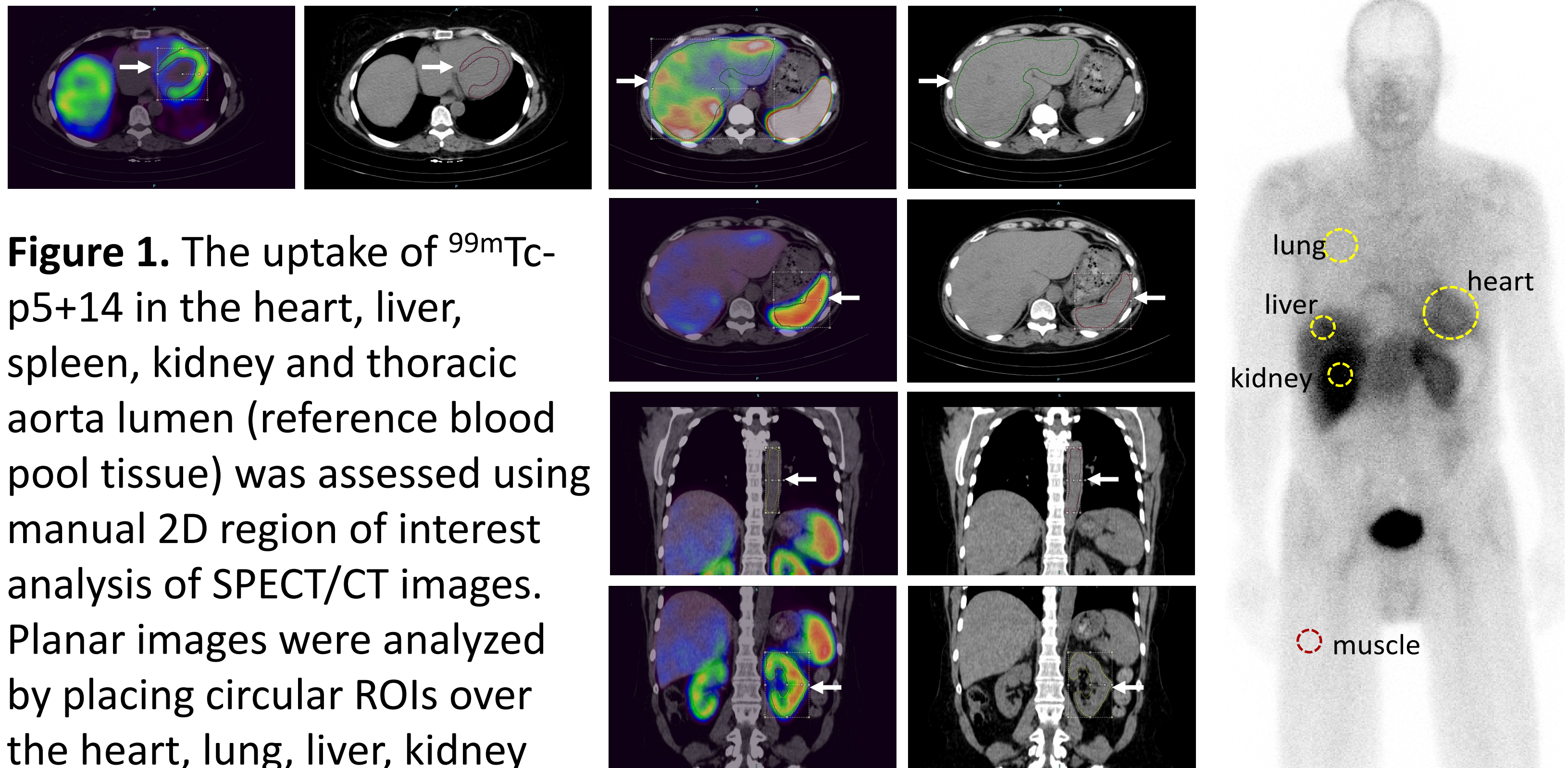


Figure 1. The uptake of ^{99m}Tc-p5+14 in the heart, liver, spleen, kidney and thoracic aorta lumen (reference blood pool tissue) was assessed using manual 2D region of interest analysis of SPECT/CT images. Planar images were analyzed by placing circular ROIs over the heart, lung, liver, kidney and muscle.

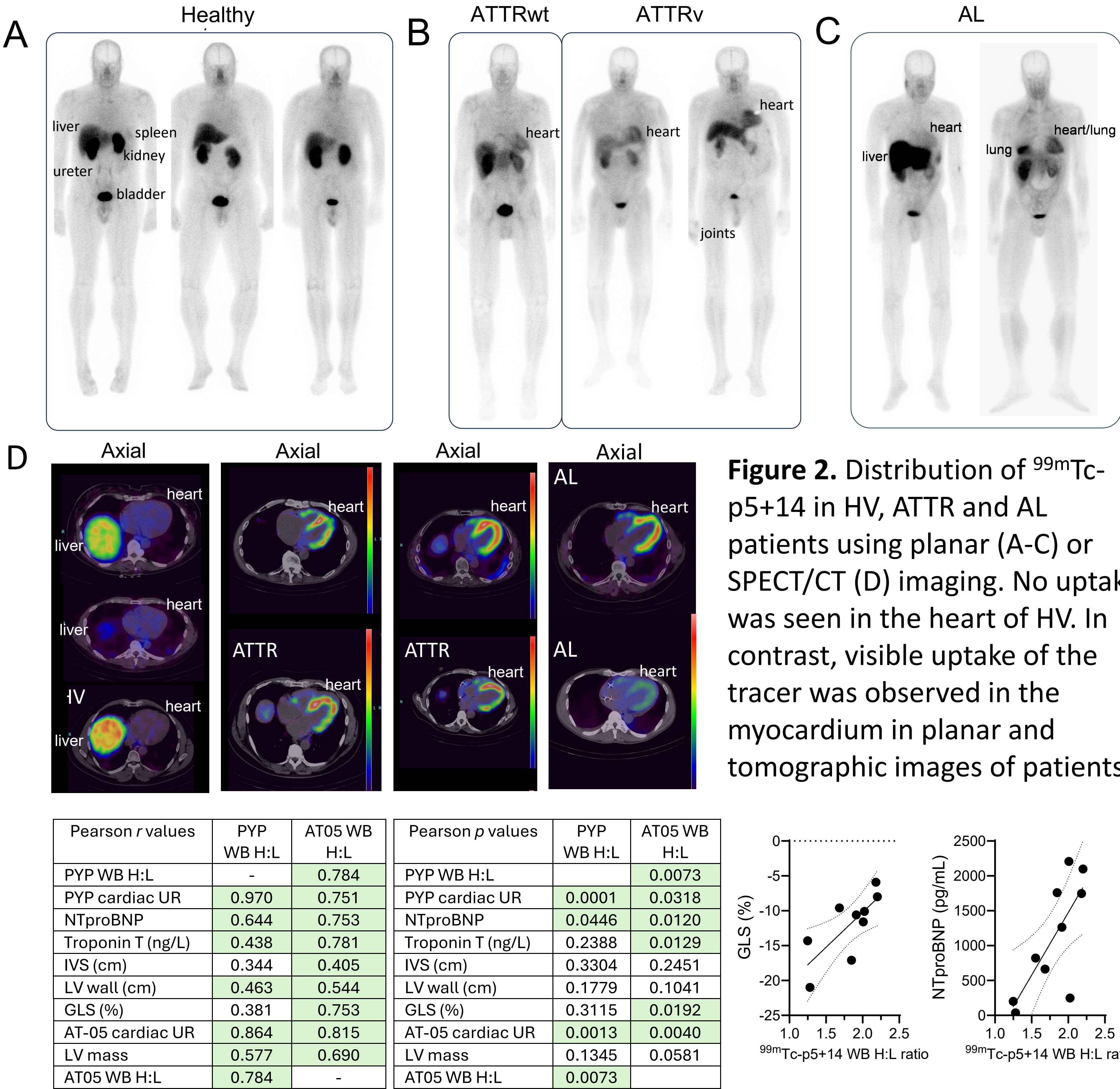


Figure 2. Distribution of ^{99m}Tc-p5+14 in HV, ATTR and AL patients using planar (A-C) or SPECT/CT (D) imaging. No uptake was seen in the heart of HV. In contrast, visible uptake of the tracer was observed in the myocardium in planar and tomographic images of patients.

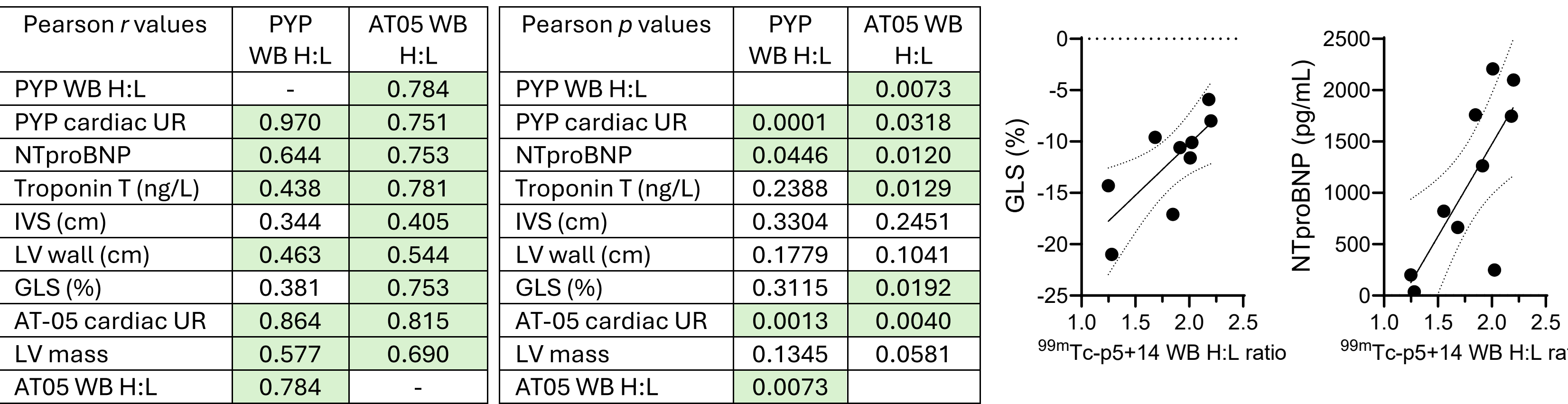


Figure 3. Strong correlations were observed for PGS ^{99m}Tc-p5+14 heart:lung (H:L) ratios and serum biomarkers and echo parameters in ATTR patients ($n=10$) patients. Significant linear correlations between PGS ^{99m}Tc-p5+14 H:L ratios and GLS ($p=0.0192$) as well as NTproBNP ($p=0.0120$) were also observed.

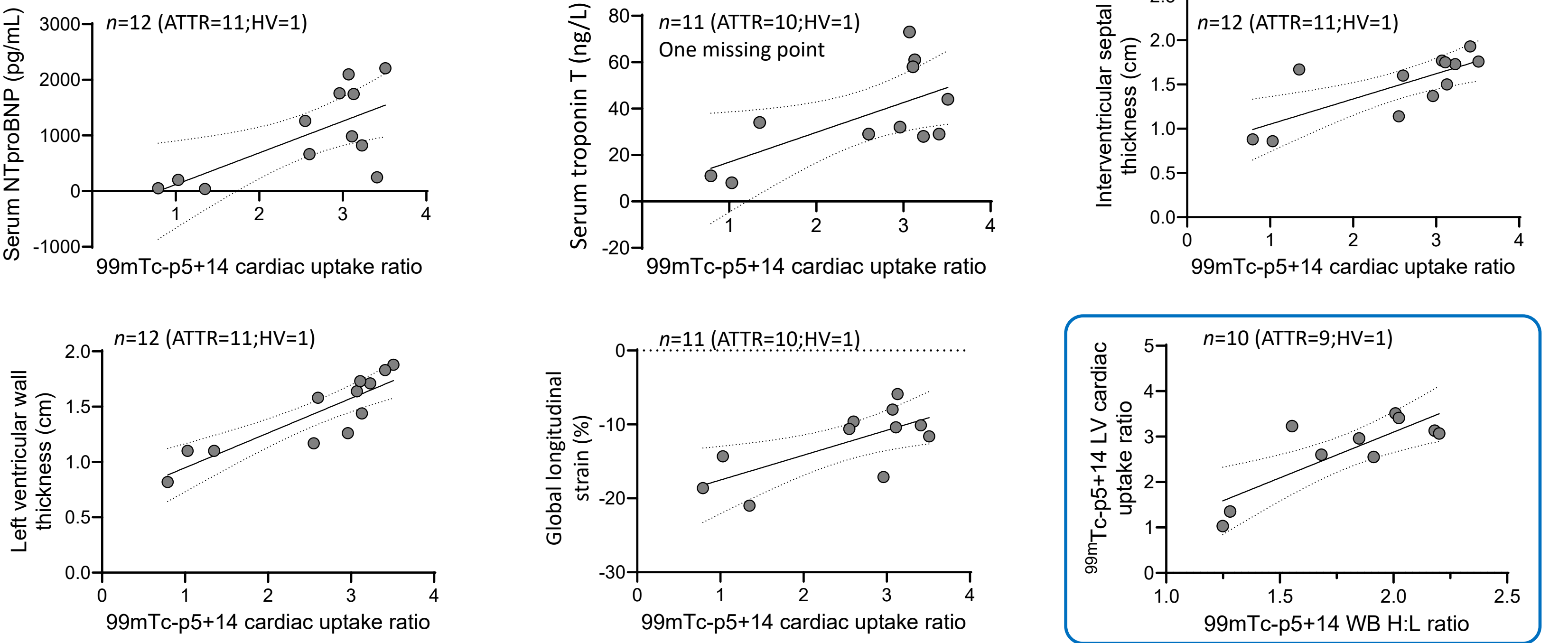


Figure 4. Strong correlations of high significance were observed between SPECT ^{99m}Tc-p5+14 left ventricular cardiac:blood uptake ratio and metrics of cardiac function (NTproBNP, troponin T, and global longitudinal strain) and structure (IVS or LV wall thickness). The SPECT/CT cardiac uptake ratio correlated also with the H:L ratio from planar images (blue).

A

	ATTR patients imaged with ^{99m} Tc-PYP and one Healthy Subject			
Measurement	AT-05 (^{99m} Tc-p5+14) Cardiac uptake		^{99m} Tc-PYP Cardiac uptake	
	Pearson r	p value	Pearson r	p value
^{99m} Tc-PYP uptake	0.951	0.0003	1.000	-
Serum NTproBNP	0.693	0.0182	0.842	0.0087
Troponin T	0.619	0.0563	0.508	0.1983
IVS thickness	0.749	0.0079	0.524	0.1821
LV wall thickness ²	0.876	0.0004	0.689	0.0589
GLS ²	0.693	0.0263	0.398	0.3763
AT-05 uptake	1.000	-	0.951	0.0003
LV mass	0.888	0.0014	0.906	0.0128

B

	ATTR and AL patients and one Healthy Subject			
Measurement	AT-05 (^{99m} Tc-p5+14) Cardiac uptake		^{99m} Tc-PYP Cardiac uptake	
	Pearson r	p value	Pearson r	p value
^{99m} Tc-PYP uptake	0.339	0.2816	1.000	-
Serum NTproBNP	0.496	0.0428	0.307	0.3317
Troponin T	0.435	0.0920	0.583	0.0465
IVS thickness	0.557	0.0203	0.322	0.3067
LV wall thickness	0.683	0.0025	0.391	0.2082
GLS	0.726	0.0015	0.005	0.9877
AT-05 uptake	1.000	-	0.339	0.2816
LV mass	0.720	0.0025	0.645	0.0439

Figure 5. Summary of correlations for ATTR patients and all patients. Cardiac uptake is ratio of LV wall and IVS ($n=3$ axial slices) to blood pool ($n=3$ coronal slices of thoracic aorta). (A) Population evaluated = all ATTR patients who received ^{99m}Tc-PYP ($n=10$) and one healthy subject ($n=1$). (B) Population evaluated = ATTR patients imaged with PYP ($n=10$), AL patients ($n=5$) and one healthy subject ($n=1$).

RESULTS:

- The ^{99m}Tc-p5+14 PGS uptake ratio in ATTR patients correlated significantly with NTproBNP ($r=0.75$, $p=0.012$) and global longitudinal strain [GLS, ($r=0.75$, $p=0.019$)].
- Significant positive linear correlations included SPECT/CT uptake ratio and the IVS ($r=0.75$, $p=0.008$), LV wall thickness ($r=0.88$, $p=0.0004$), GLS ($r=0.69$, $p=0.026$), and NTproBNP ($r=0.69$, $p=0.018$).
- Notably, for ^{99m}Tc-p5+14, the PGS uptake ratio correlated with the SPECT/CT uptake ratio ($r=0.82$, $p=0.004$) in patients with ATTR. Correlations were also noted in ATTR patients with the LV mass (although not significant, $p=0.058$).

CONCLUSION:

- These preliminary data support further evaluation of ^{99m}Tc-p5+14 imaging for detecting cardiac amyloid and its relationship with other measures of amyloid-associated cardiac dysfunction.
- This novel tracer could serve as an effective tool for the screening of cardiac amyloid and may assist with staging and monitoring disease.

DISCLOSURE

EBM, SJK, and AS: Founding shareholder in Attralus Inc. REH, EBM, AS, 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 Inc.