

# DETECTION OF CARDIAC AMYLOIDOSIS, AND MORE, USING SPECT/CT IMAGING OF TECHNETIUM-99m-LABELED PEPTIDE p5+14 (AT-05)



Wall, J.S.<sup>1</sup>, Martin, E.B.<sup>1</sup>, Heidel, R.E.<sup>1</sup>, Stuckey, A.<sup>1</sup>, Whittle, B.<sup>2</sup>, Jackson, J.W.<sup>1</sup>, Williams, A.<sup>1</sup>, Hancock, T.<sup>1</sup>, Kassira, A.<sup>3</sup>, Hung, R.R.<sup>4</sup>, and Kennel, S.J.<sup>1</sup>

<sup>1</sup>University of Tennessee Graduate School of Medicine, Knoxville TN, 37920. <sup>2</sup>University of Tennessee Medical Center, Knoxville TN, 37920. <sup>3</sup>University Cardiology, University of Tennessee Medical Center, Knoxville TN, 37920. <sup>4</sup>Vanderbilt Heart, Vanderbilt University Medical Center, Nashville, TN, 37232.

## BACKGROUND

The prevalence of cardiac amyloidosis is increasing due to enhanced clinical vigilance and increased awareness; however, early and accurate diagnosis of patients remains challenging. Cardiac amyloid is the major cause of mortality in patients with AL and ATTR amyloidosis. The pan-amyloid reactive peptide, p5+14, labeled with iodine-124 (<sup>124</sup>I-evuzamitide) has enabled sensitive detection of whole-body amyloid using PET/CT imaging. Therefore, a p5+14-peptide labeled with technetium-99m for gamma imaging of cardiac amyloid of any type could be invaluable for timely diagnosis. We present data from a single site Phase 1 study of <sup>99m</sup>Tc-p5+14 (AT-05) showing detection of amyloid deposits in the heart as well as observations on extracardiac uptake (NCT05951816).

## METHODS

Patients >18 years of age with a diagnosis of cardiac amyloidosis (*n*=30) and healthy subjects (*n*=5) are recruited. Subjects are administered a single IV injection of <sup>99m</sup>Tc- p5+14 (<22 mCi and <1 mg of peptide). SPECT/CT and planar images are acquired at 1 h and 3 h post injection. Patient images are compared with those of healthy subjects, both visually and by region of interest analyses, to assess differential cardiac uptake. Contemporaneous <sup>99m</sup>Tc-PYP imaging is performed in patients for comparative purposes.

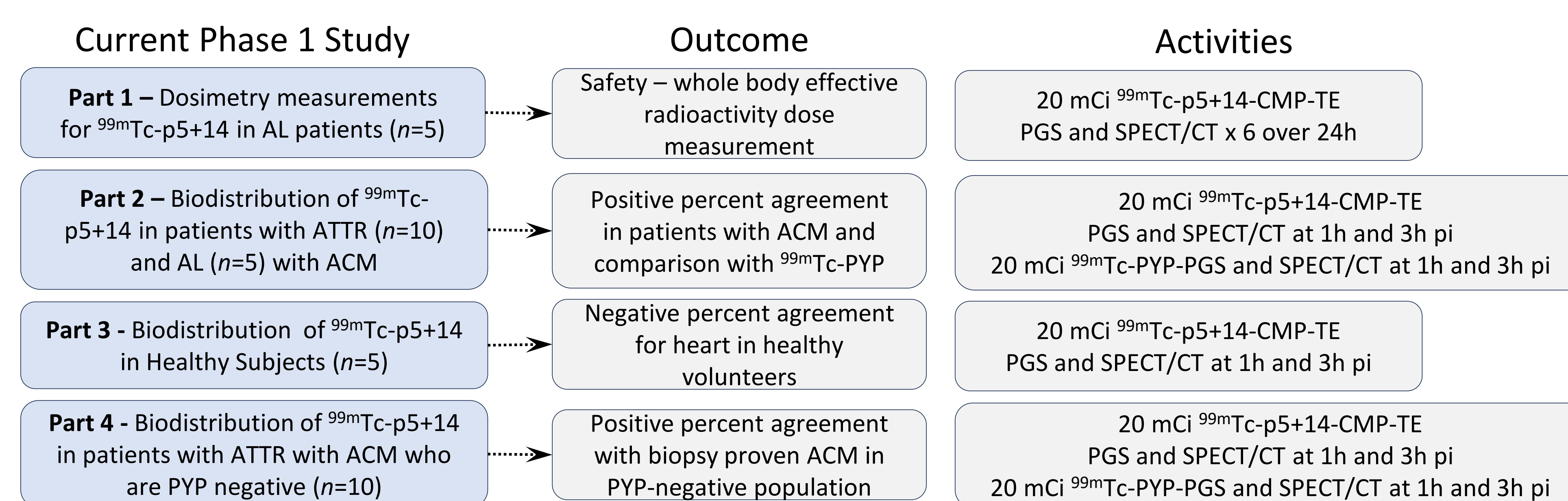
## RESULTS

At present, five (*n*=5) healthy subjects and eighteen (*n*=18) patients have been recruited. No cardiac uptake of <sup>99m</sup>Tc- p5+14 was seen in healthy subjects (100% specificity; *n*=5). In contrast, cardiac amyloid was readily imaged in patients. This was observed in both planar and SPECT/CT images acquired at 1 h and 3 h post injection. Comparison of <sup>99m</sup>Tc-p5+14 and <sup>99m</sup>Tc-PYP in the same patient suggests that the myocardium uptake-to-blood pool ratio is 3-fold higher for the peptide at 1 h post injection. Extracardiac uptake of radiotracer has also been observed in the lungs of patients with ATTR and the liver, spleen, salivary glands, lung, and tongue in AL patients.

## DISCUSSION

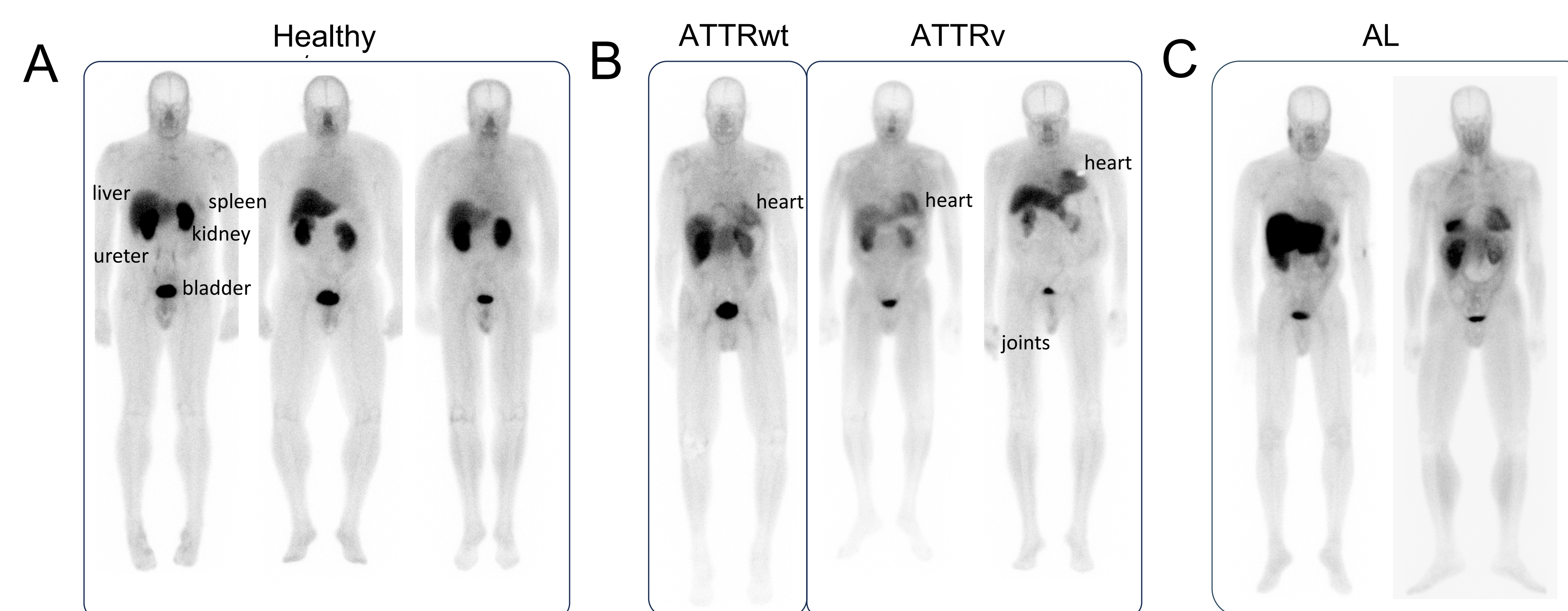
Nuclear imaging using <sup>99m</sup>Tc-p5+14 could provide a facile and accurate method for the detection of all types of cardiac amyloidosis as well as non-invasive data on extracardiac sites of amyloid involvement that may be clinically impactful.

### FIGURE 3



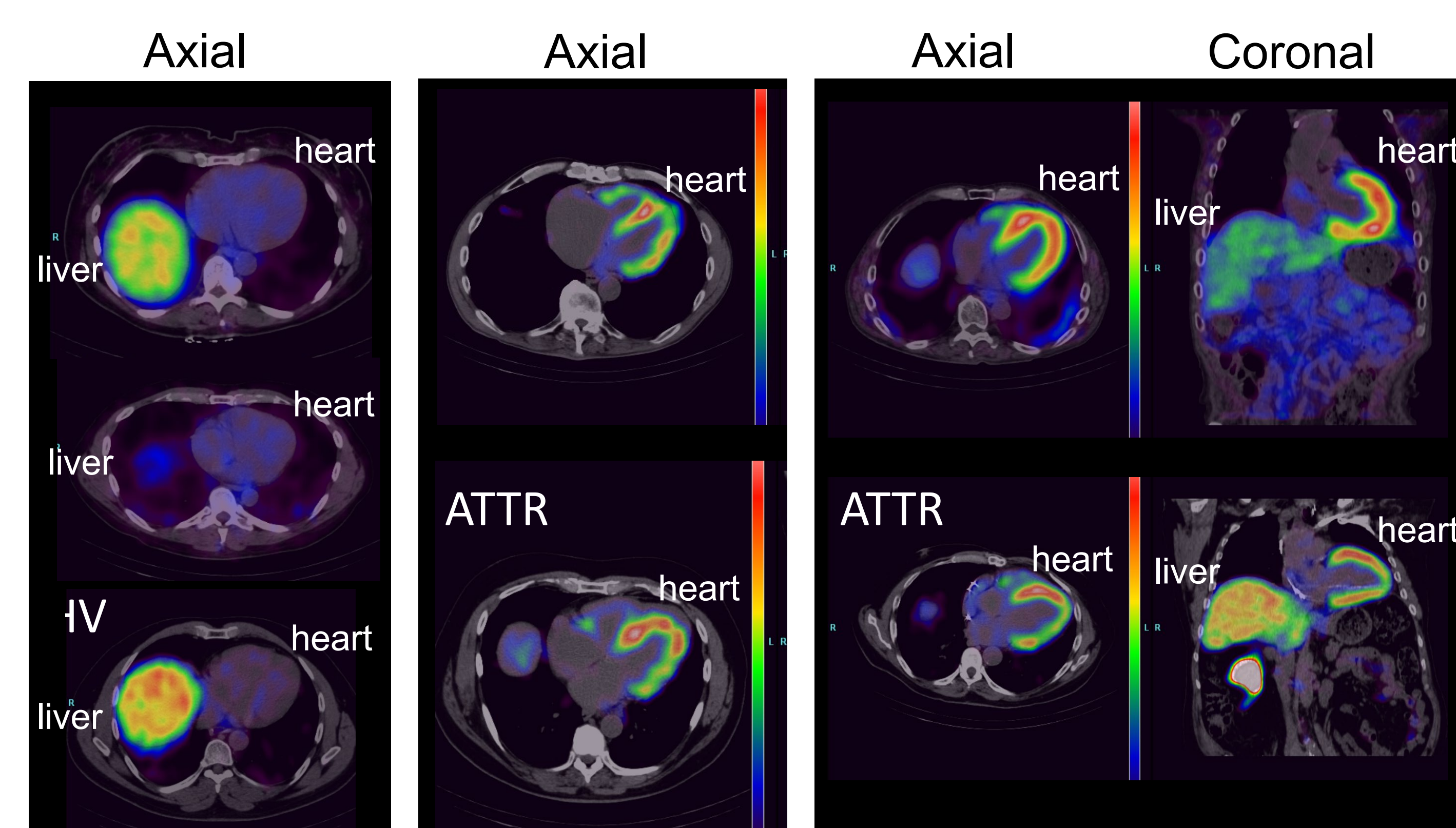
This is a four-part, open-label, single-site Phase 1 study with the assessment of dosimetry as the primary outcome. All parts are recruiting simultaneously. ACM, amyloid cardiomyopathy; TE, transthoracic echo; PGS, planar gamma scintigraphy; CMP, complete metabolic panel.

### FIGURE 2



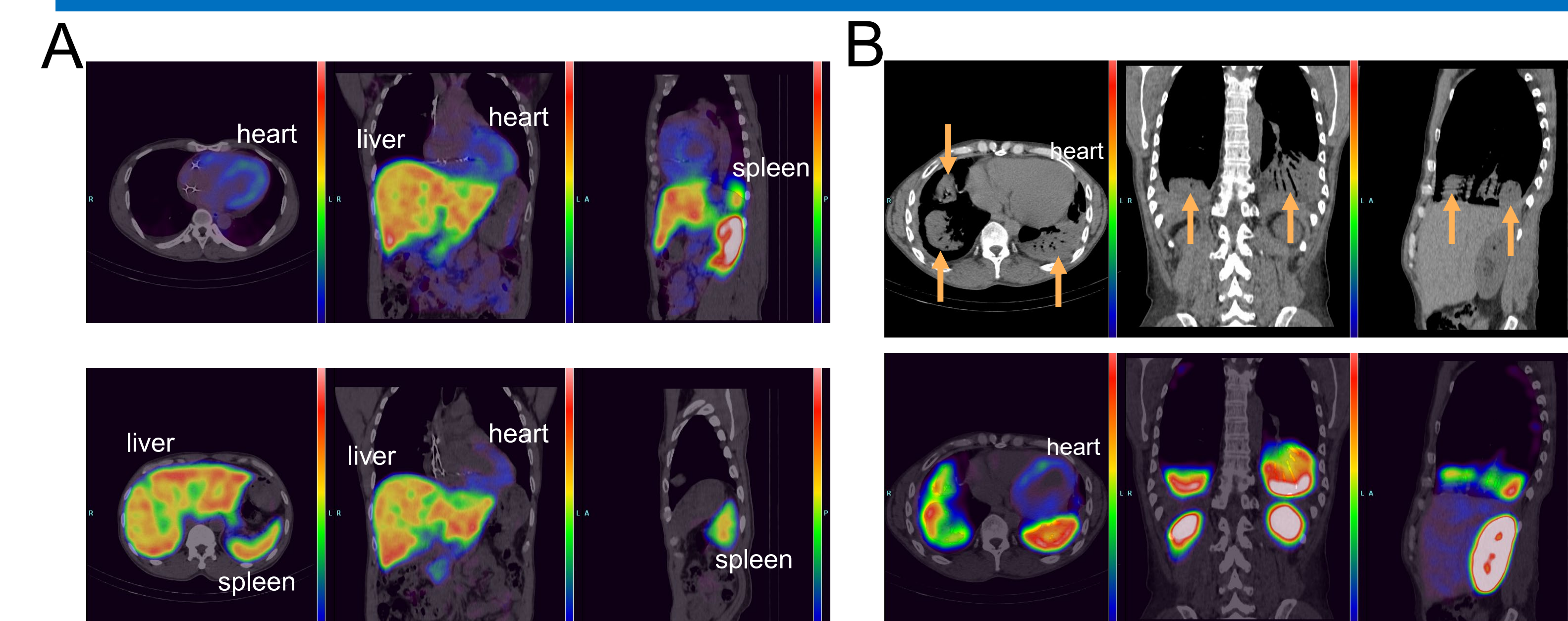
(A) In healthy subjects, physiologic uptake of <sup>99m</sup>Tc-p5+14 was seen in planar images in the kidneys, bladder, and liver with no cardiac uptake. (B) In patients with ATTR, cardiac uptake was observed. (C) In the patients with AL, radiotracer uptake was seen in the heart, liver, spleen as well as lesions in the lung.

### FIGURE 3



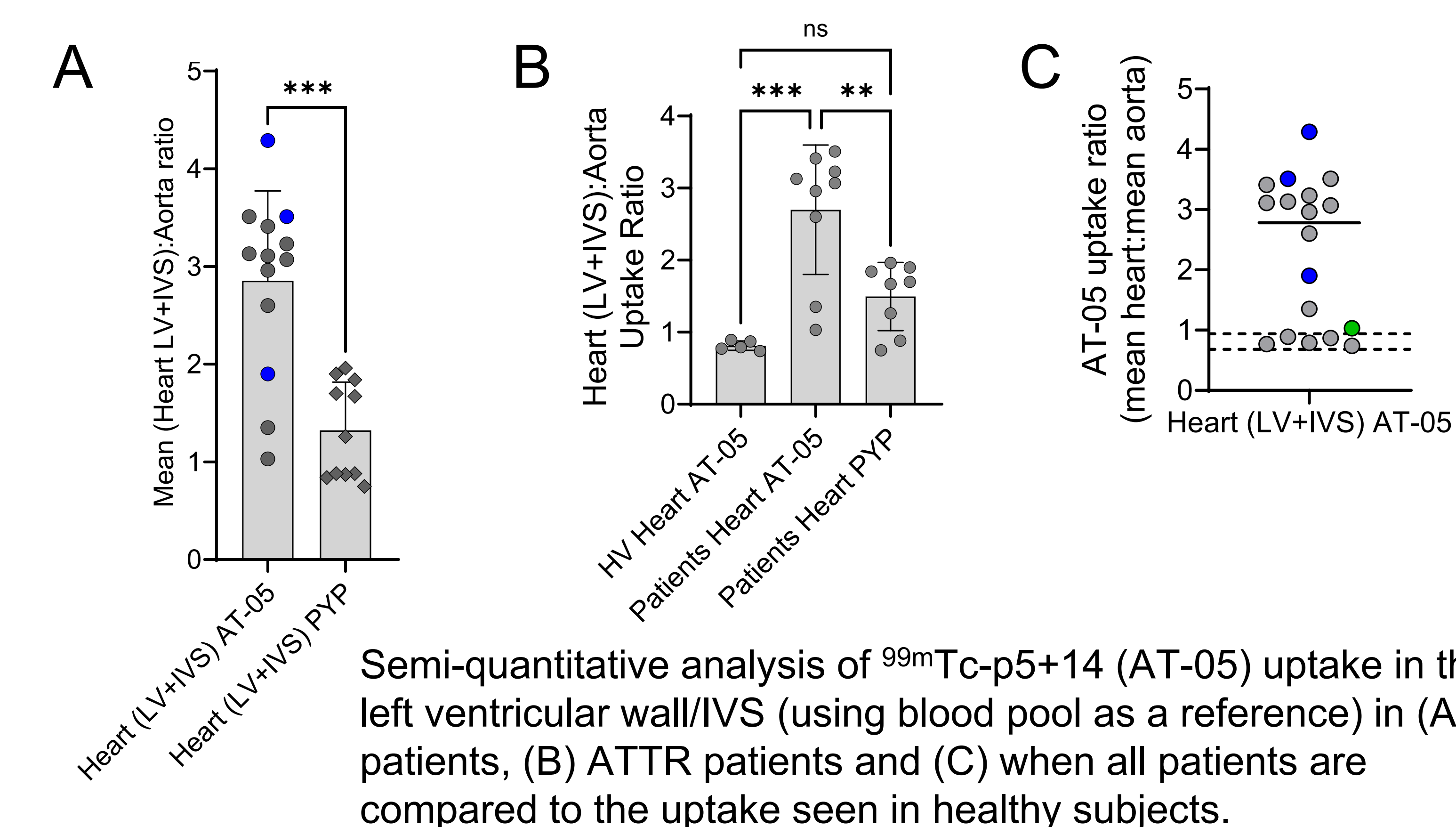
<sup>99m</sup>Tc-p5+14 is taken up in the heart of patients with ATTR cardiac amyloidosis but not healthy volunteers (HV). In SPECT/CT images of patients with ATTR, radiotracer was observed in the left ventricular wall, interventricular septum and right ventricular wall. No <sup>99m</sup>Tc-p5+14 was seen in the heart of healthy subjects in SPECT/CT images.

### FIGURE 4

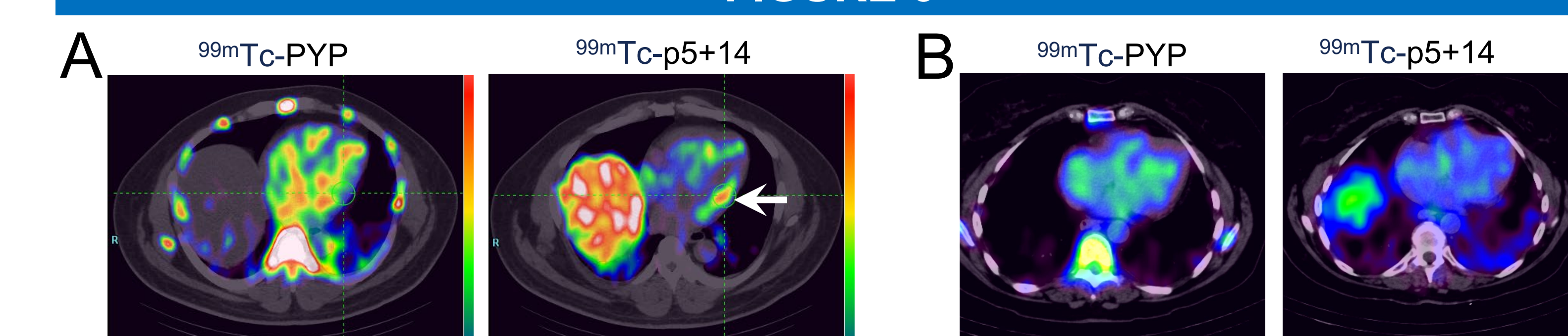


In patients with AL amyloidosis, <sup>99m</sup>Tc-p5+14 uptake was seen in the heart. (A) In addition, non-physiological retention was observed in the liver and spleen in two patients. (B) In one patient, pulmonary lesions that were readily evident in the CT images retained significant radiotracer, suggestive of amyloid.

### FIGURE 5



### FIGURE 6



In two patients with ATTR amyloidosis, contemporaneous <sup>99m</sup>Tc-PYP imaging of the heart was negative. (A) In one patient, focal uptake of <sup>99m</sup>Tc-p5+14 was seen in the LV wall consistent with amyloid seen in the endomyocardial biopsy. (B) In the second patient, with a positive <sup>99m</sup>Tc-PYP scan at diagnosis, <sup>99m</sup>Tc-p5+14 uptake in the heart was also deemed to be negative, suggesting resolution of the amyloid.

## DISCLOSURE INFORMATION

JSW: Co-founder, interim CSO, and shareholder in Attralus Inc. Research funding from Attralus Inc. Patent rights in peptides used for amyloid imaging, licensed to Attralus. EBM and AS: Founding shareholder in Attralus Inc. SJK: Founding shareholder in Attralus Inc. Patent rights in peptides used for amyloid imaging, licensed to Attralus. REH, BW, JWJ, AW, AK, RRRH, TH: Nothing to declare relating to this study.