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I-124 Evuzamitide PET/CT is More Sensitive than Tc-99m Pyrophosphate for the Diagnosis of Hereditary Transthyretin Cardiac Amyloidosis

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Disclosures

- Received salary support from The Amyloidosis Foundation.
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Introduction

- There is a significant need to improve the early diagnosis of ATTR-CA.
- Although Tc-99m pyrophosphate (PYP) myocardial uptake can non-invasively diagnose ATTR-CA in the correct clinical context, reported sensitivity in a large multi-center study is ~70%.
- We sought to determine if PET/CT scanning using ^{124}I-evuzamitide can detect cardiac TTR amyloidosis in subjects with Tc99-PYP not diagnostic for cardiac amyloidosis (Perugini grade 0 and grade 1 Tc99-PYP scans) but for whom strong suspicion or endomyocardial biopsy evidence of ATTR-CM exists.

Gillmore JD, Maurer MS, Falk RH, et al. Nonbiopsy Diagnosis of Cardiac Transthyretin Amyloidosis. Circulation. 2016;133(24):2404-2412.

Methods

- Prospective pilot cohort study among outpatient subjects seen in our cardiac amyloidosis program.
- 25 subjects were divided into 3 cohorts:
  1. **10 Subjects with negative PYP scans (Perugini grade 0 and grade 1), but positive EMB and/or high suspicion for ATTR-CA (e.g. increased wall thickness, heart failure, etc)**
  2. 5 Subjects who are allele carriers of TTR variants.
  3. 10 Subjects with ATTR-CA with extracardiac symptoms, and/or biopsy proven extra-cardiac amyloidosis.

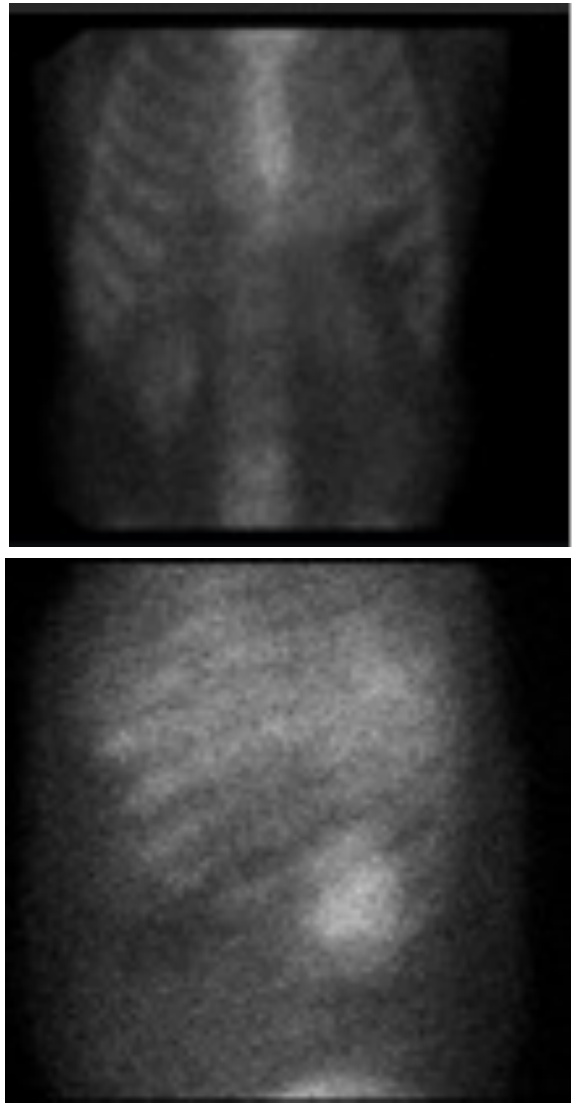
Methods

- For the main (first) cohort, 10 subjects underwent whole-body PET/CT using a Siemens Biograph mCT scanner, 5 hours after injection of ~1 mCi ^{124} I-evuzamitide (Attralus, San Francisco).
- A low dose non-contrast CT scan was acquired first for attenuation correction and co-registration.
- PET emission sequence was then obtained using five minute PET acquisitions per bed position, with an additional 20 minutes of cardiac acquisition in patients 4-10.
- PET images are corrected for attenuation, random coincidences, scatter, decay, and prompt gamma emission, and processed using Siemens IRW image analysis software.

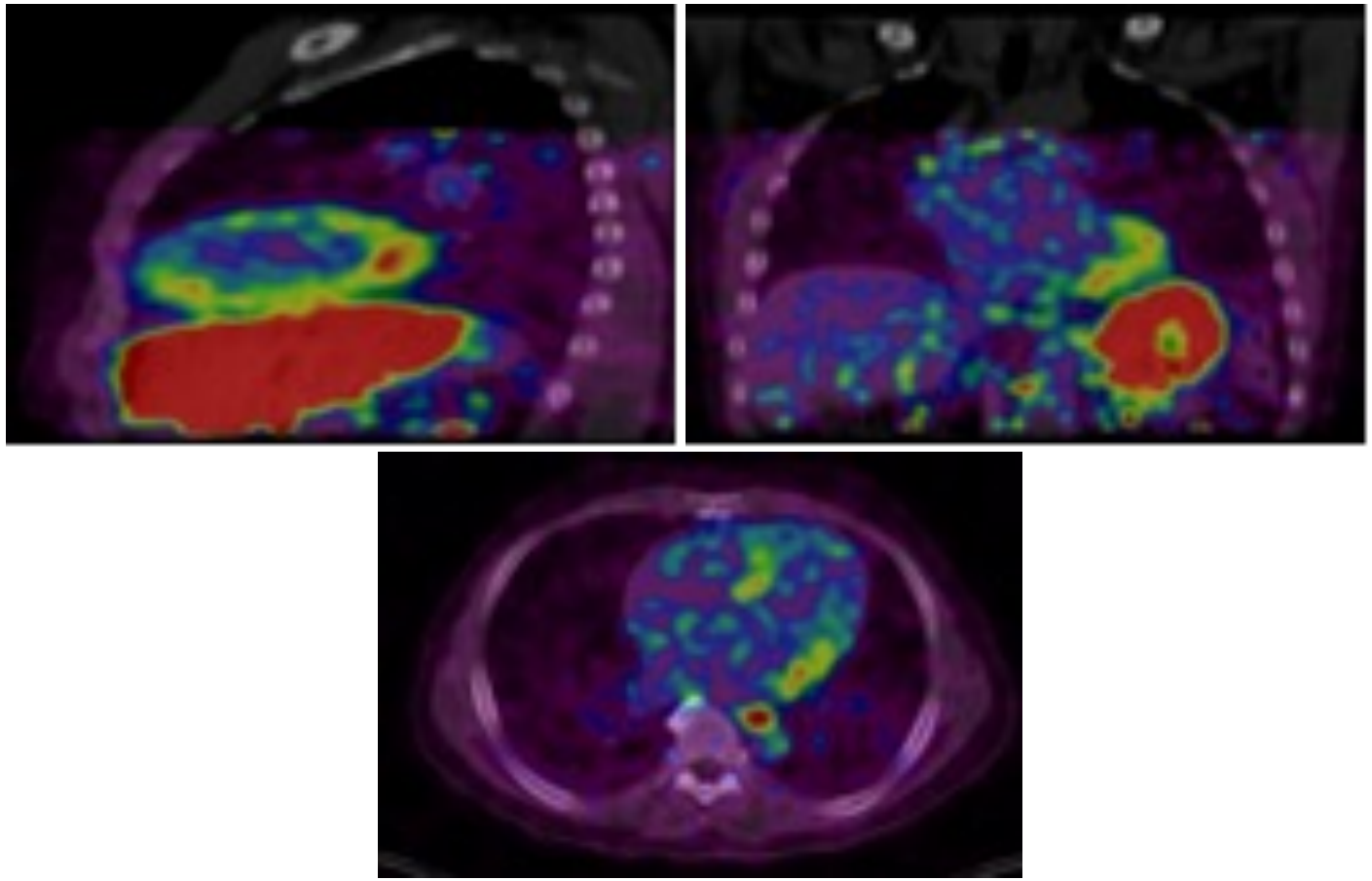
Results

Subject	Age	Gender	Genotype	Perugini grade	SPECT/CT	Endomyocardial biopsy	PET cardiac uptake
1	64	M	Val122Ile	grade 1	Not performed	positive	positive
2	64	M	ALA60	grade 1	Not performed	positive	positive
3	45	M	Glu89Gln	grade 1	No myocardial uptake	Not performed (had previous +PYP)	positive
4	81	M	Val122Ile	grade 0	No myocardial uptake	positive	positive
5	67	M	Thr60Ala	grade 0	Not performed	Not performed (+ neuropathy)	positive
6	65	M	Thr60Ile	grade 1	No myocardial uptake	Not performed (+ neuropathy)	positive
7	60	M	Val122Ile	grade 1	Not performed	positive	positive
8	53	F	Val30Met	grade 1	No myocardial uptake	positive	positive
9	54	M	Val30Met	grade 0	No myocardial uptake	Not performed (+genotype)	negative
10	64	F	Val30Met	grade 0	No myocardial uptake	Not Performed (+genotype)	negative

Subject 1-Negative PYP, positive EMB, Positive 124I-Evuzamitide

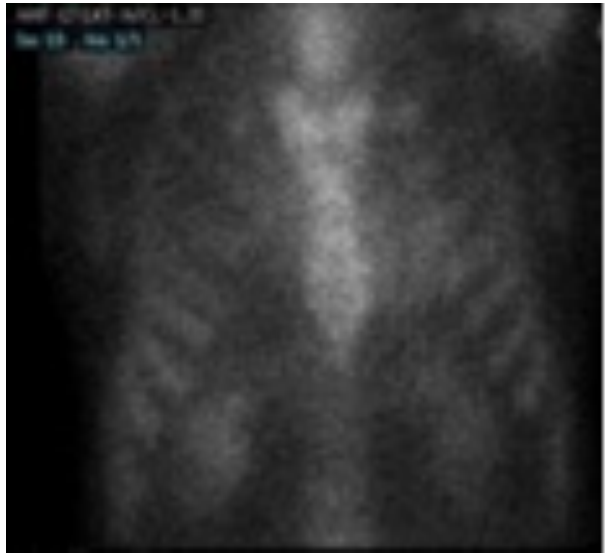


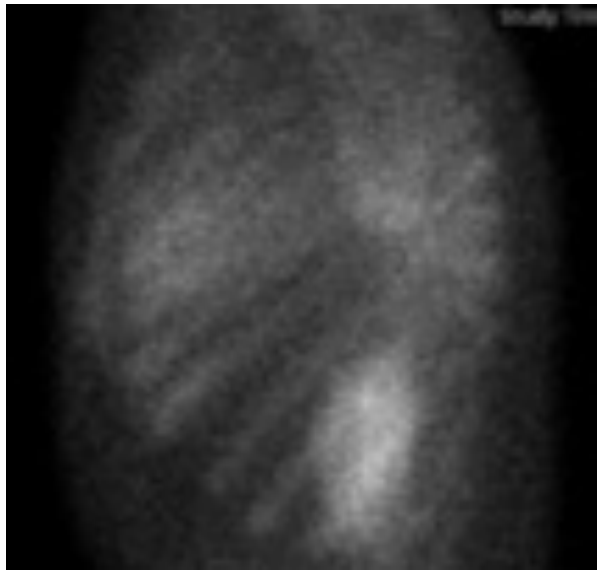
A. Anterior and Lateral Tc99-PYP scan after three hours of incubation showing no significant myocardial retention of the isotope (Perugini grade 1 scan).



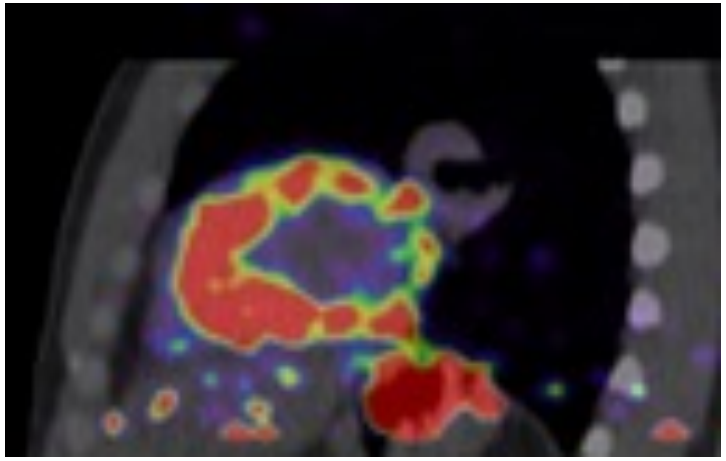
B. Transaxial, Coronal, and sagittal PET/CT images showing I-124 Evuzamitide uptake in the left ventricle and right ventricle, left and right atrial uptake, most prominently in the basal lateral wall and septum.

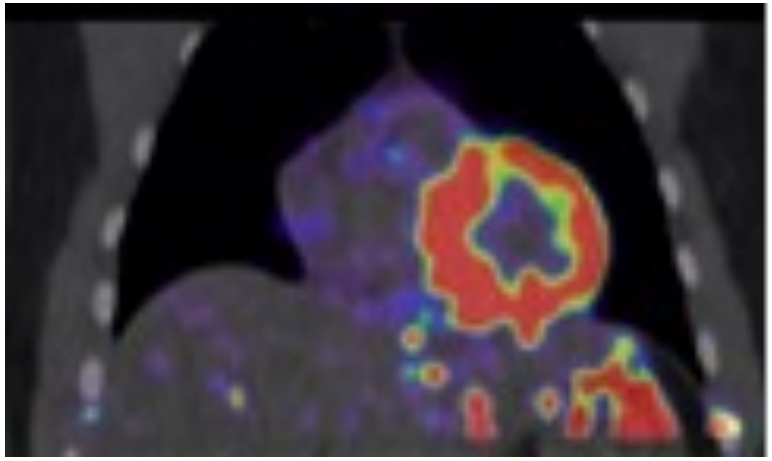
Subject 3-Negative PYP after silencer Tx, Positive 124I-Evuzamitide

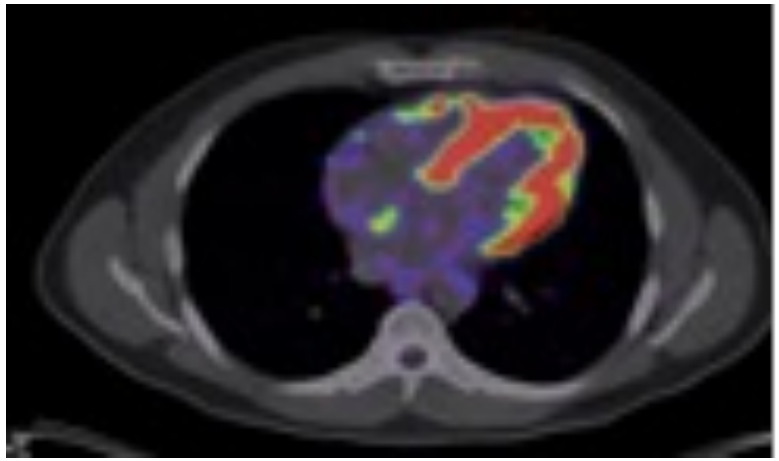




A. Anterior and Lateral Tc99-PYP scan after three hours of incubation showing no significant myocardial retention of the isotope (Perugini grade 1 scan).



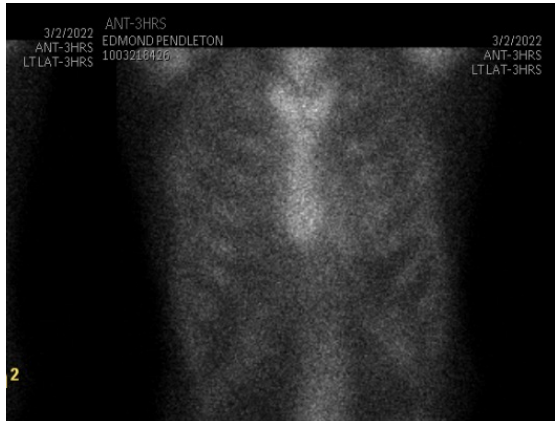


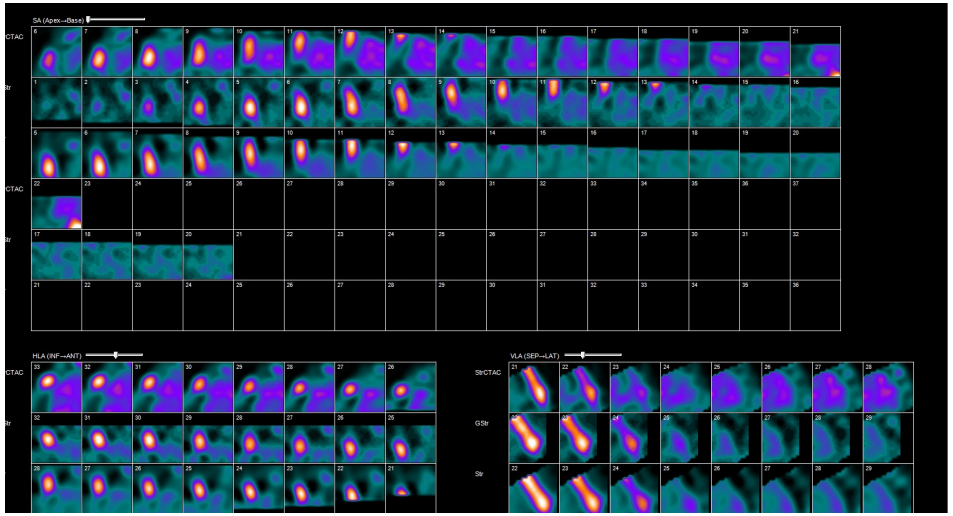


B. Transaxial, Coronal, and sagittal PET/CT images showing I-124 Evuzamitide uptake in the left ventricle and right ventricle, left and right atrial uptake, most prominently in the basal lateral wall and septum.

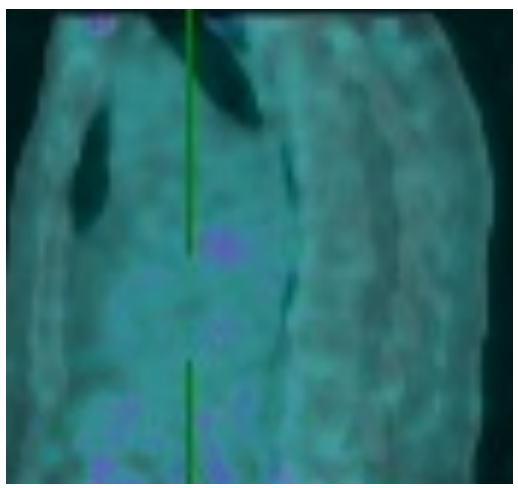
Subject 4-negative PYP x2, positive EMB, Positive 124I-Evuzamitide.

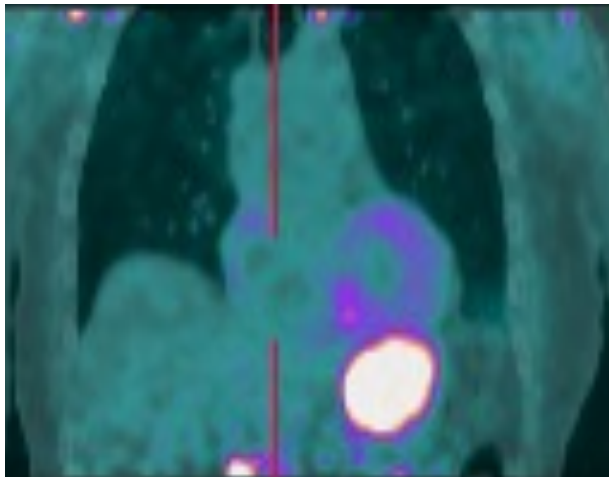
A. Anterior and Lateral Tc99-PYP scan after three hours of incubation showing no significant myocardial retention of the isotope (Perugini grade 0 scan).

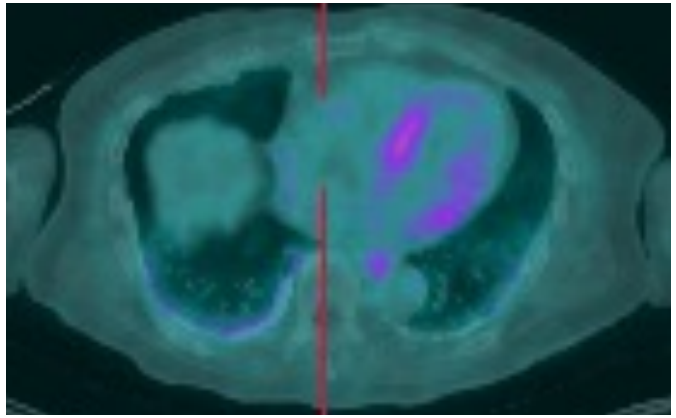




B. Anterior and Lateral Tc99-PYP scan after three hours of incubation showing no significant myocardial retention of the isotope (Perugini grade 1 scan).





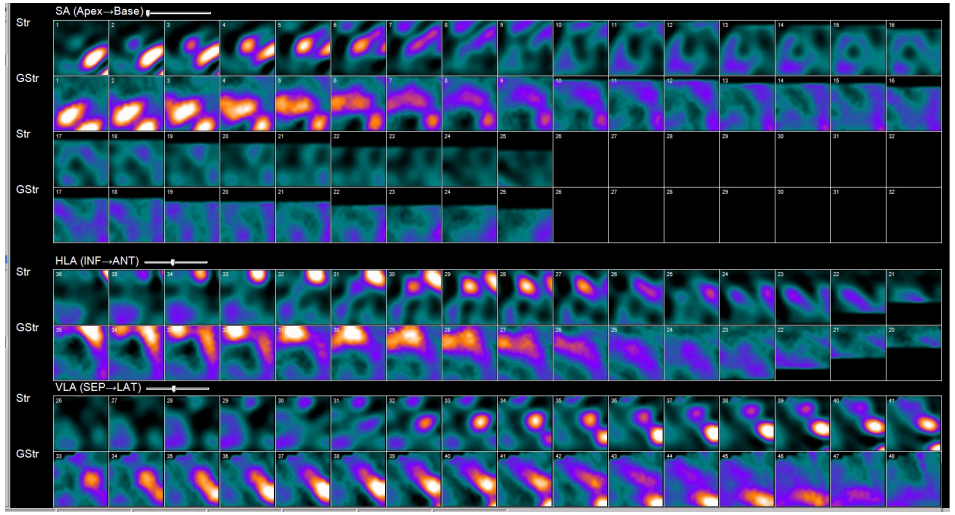


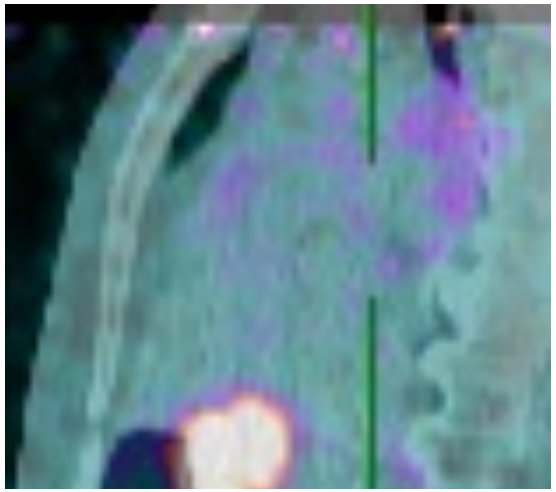
C. Transaxial, Coronal, and sagittal PET/CT images showing I-124 Evuzamitide uptake in the left ventricle and right ventricle, left and right atrial uptake, most prominently in the basal lateral wall and septum.

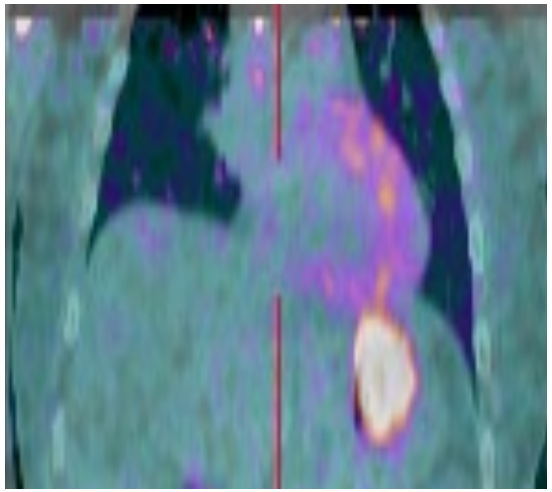
Subject 6-Negative PYP, positive EMB, Positive 124I-Evuzamitide

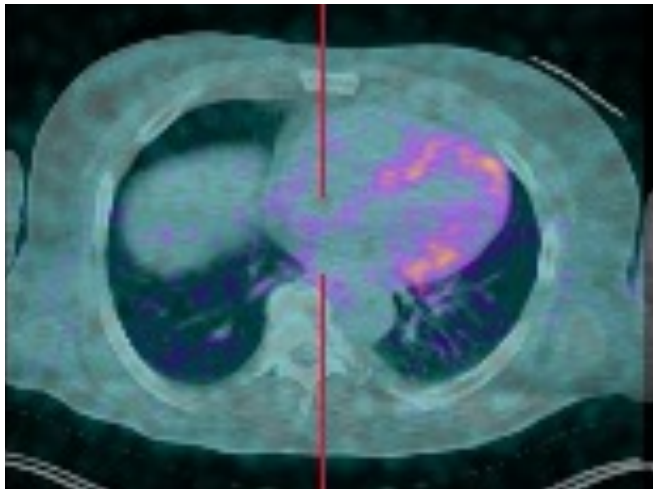
A. Anterior and Lateral Tc99-PYP scan after three hours of incubation showing no significant myocardial retention of the isotope (Perugini grade 1 scan).

B. SPECT showing no myocardial retention of the isotope.









C. Transaxial, Coronal, and sagittal PET/CT images showing I-124 Evuzamitide uptake in the left ventricle and right ventricle, left and right atrial uptake, most prominently in the basal lateral wall and septum.

Summary

- There remains a need to improve the early diagnosis of ATTR-CA, especially in patients with hereditary (variant) ATTR-CA.
- PET-CT scanning with 124I-Evuzamitide was positive for cardiac uptake in 8/10 patients with a negative PYP.
- PET-CT scanning with 124I-evuzamitide is more sensitive than Tc99M-PYP for detecting transthyretin cardiac amyloidosis in patients with hereditary ATTR-CA.
- PET-CT scanning with 124I-evuzamitide has the potential to quantify amyloid load and objectively monitor response to therapy, as quantitative studies are currently underway.
- Limitations of this study include:
  - Some subjects did not get SPECT/CT and thus could have had some myocardial uptake not seen on planar imaging.
  - Data shows a semiquantitative approach currently (+ or -) and quantification is underway.
  - Subjects with ATTRwt-CA not studied.