MAYO CLINIC

ISA
INTERNATIONAL SOCIETY OF AMYLOIDOSIS

XIX INTERNATIONAL SYMPOSIUM ON AMYLOIDOSIS

MAY 26-30, 2024 – ROCHESTER, MN

COURSE DIRECTORS:
Angela Dispenzieri, M.D. – Mayo Clinic
Morie A. Gertz, M.D. – Mayo Clinic
Martha Grogan, M.D. – Mayo Clinic
Dr. Stefan Schönland, Heidelberg University Hospital, Germany,
ISA President 2022-2024




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KNIGHT CARDIOVASCULAR Institute

OHSU

MORRIS KIM, MD

Cardiovascular Disease Fellow

Derrick Gillan, Jessica Cardin, Eva Medvedova, Nadine Mallak, Ahmad Masri

Oregon Health & Science University (OHSU)

Portland, OR

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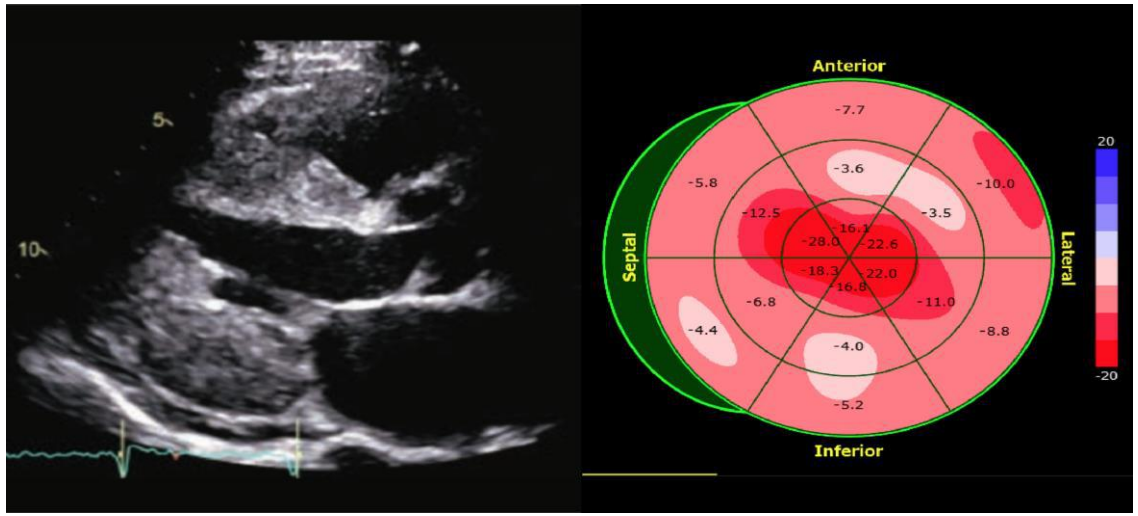
LEARNING OBJECTIVES

- Review the current paradigm of non-invasive diagnosis of cardiac and systemic amyloidosis
- Explore the feasibility of utilizing ^{124}I-evuzamitide (AT-01), a novel pan-amyloid radiotracer, in non-invasive diagnosis of systemic amyloidosis

NON-INVASIVE IMAGING OF AMYLOIDOSIS

REVIEW OF THE CURRENT OPTIONS

- **Echocardiogram with strain imaging**
- **^{99m}Tc-pyrophosphate (PYP) SPECT/CT**
- **Cardiac magnetic resonance imaging (CMR): gold standard imaging modality**



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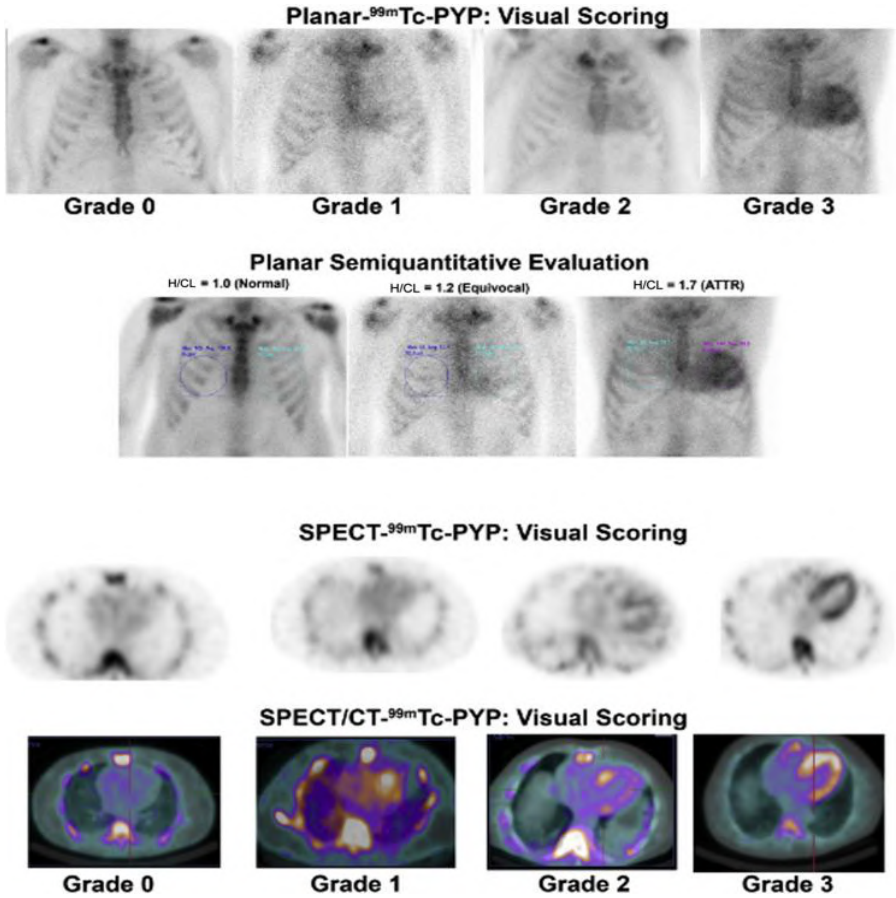

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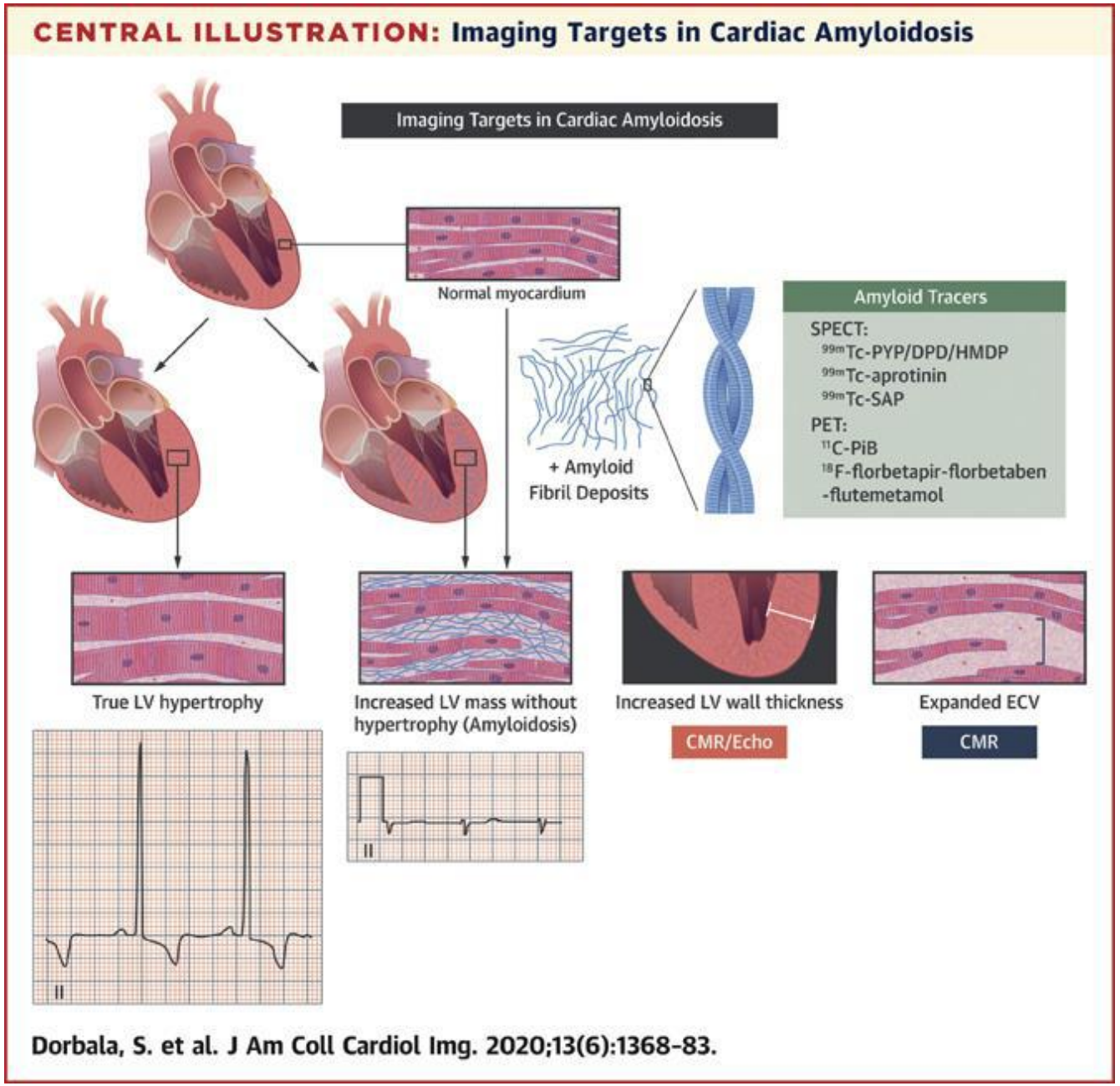
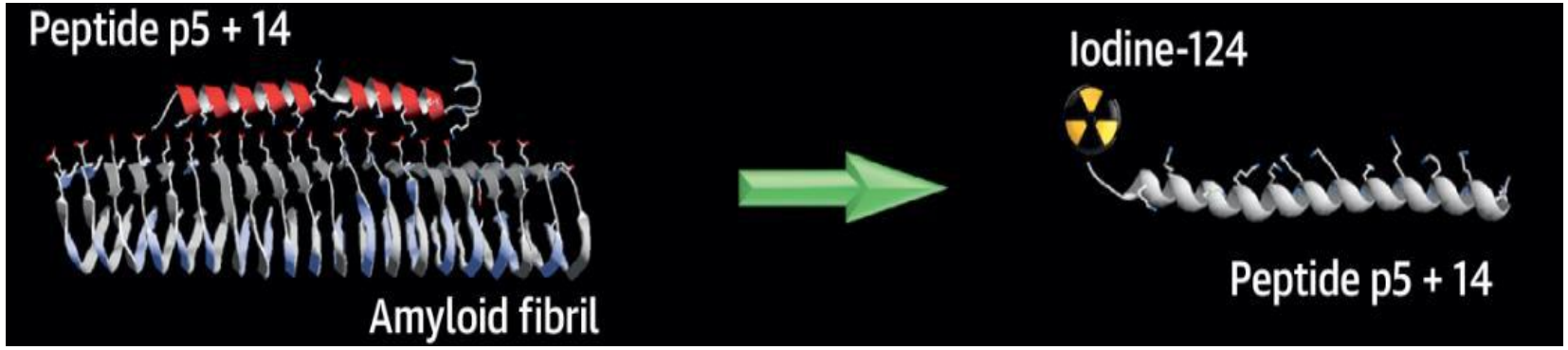


^{124}I-EVUZAMITIDE (AT-01)

NOVEL PAN-AMYLOID RADIOTRACER

- First-in-human study of ^{124}I-evuzamitide cardiac and whole-body PET/MRI
- Assess feasibility and tracer distribution in patients suspected to have or diagnosed with systemic amyloidosis



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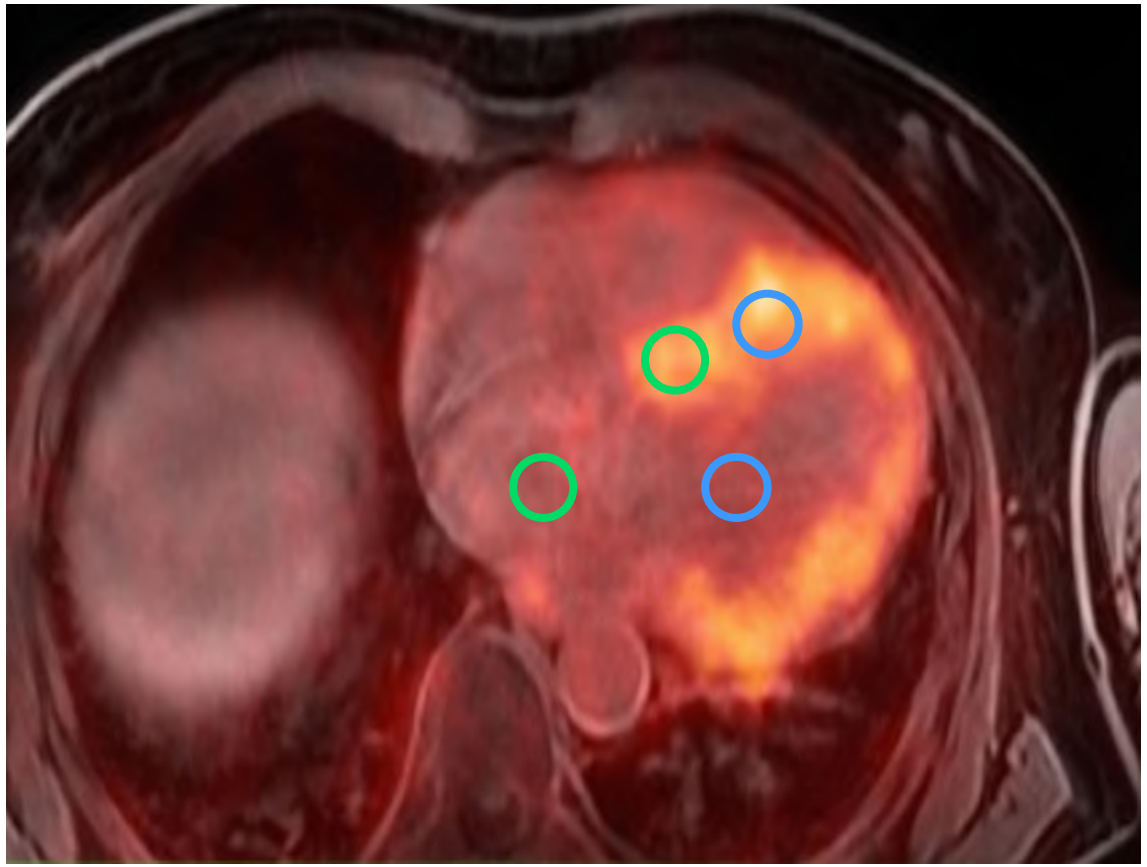
PATIENT SELECTION

- **50 patients** (27 ATTR, 7 AL, 16 controls)
- Cardiac amyloidosis was suspected or diagnosed in all patients prior to enrollment.
- Designed to test the performance of hybrid PET/MRI using ^{124}I-evuzamitide in high-risk/known amyloid patients vs controls
- Hybrid ^{124}I-evuzamitide cardiac PET/MRI → whole-body (WB) PET/MRI
- Mean administered activity 1.04±0.02 mCi (average 5-6 minutes per bed)
- All patients received potassium iodide 130 mg for 3 days, first dose at least 30 minutes prior to ^{124}I-evuzamitide administration

QUANTIFYING ^{124}I-EVUZAMITIDE UPTAKE

- LV septum standardized uptake value (SUV)/mean LV blood pool SUV

- LV septum SUV – mean LA SUV



BASELINE CHARACTERISTICS

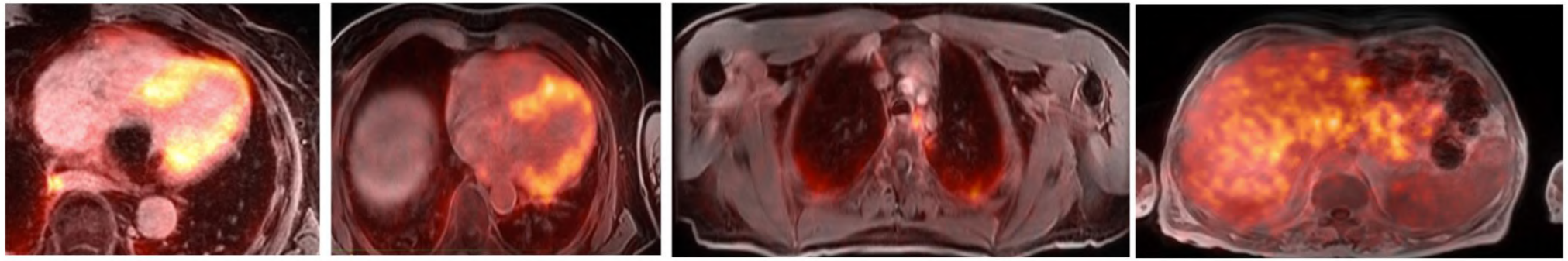
Variable	Cardiac Amyloidosis (N=34)	Controls (N=16)	p-value
Age (years)	74.7±8	66.44±9	0.002
Male sex	31 (91%)	6 (37.5%)	<0.001
Cardiac Amyloidosis subtype			—
Light chain	7 (20.6%)	-	
Transthyretin	27 (79.4%)	-	
Controls Underlying Phenotype:			
LVH/HCM		4 (25%)	
Extracardiac AL amyloidosis		5 (31%)	
Transthyretin variant carrier		5 (31%)	
Orthopedic amyloid deposit		2 (13%)	
Systemic amyloidosis without cardiac involvement	0%	7 (43.8%)	—
Pathogenic transthyretin variant	4 (11.8%)	5 (31.3%)	0.250
Left ventricular hypertrophy (basal LV septum ≥12 mm)	33 (97%)	10 (62.5%)	0.366

RESULTS

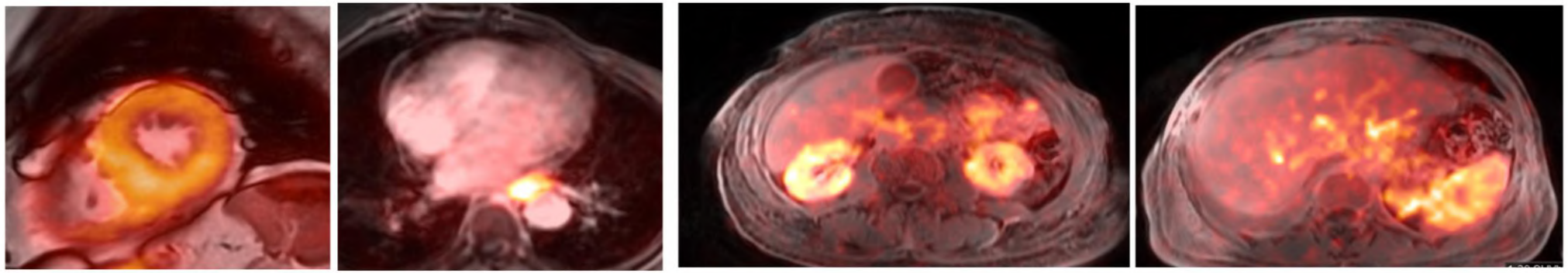
Variable	Cardiac Amyloidosis (N=34)	Controls (N=16)	p-value
^{124}I-evuzamitide administered activity (mCi)	1.05 (0.02)	1.04 (0.01)	0.124
Mean time from ^{124}I-evuzamitide to start of cardiac PET (hours)	3.15	3.05	0.571
Mean time from ^{124}I-evuzamitide to start of Whole-body PET (hours)	4.00	3.85	0.405
Mean myocardial SUV	7.58 (2.12)	3.43 (0.75)	<0.001
Mean LV blood pool SUV	4.28 (1.20)	3.39 (0.63)	0.001
SUVR (myocardium over LV blood)	1.76 (1.67, 1.93)	0.94 (0.87, 1.06)	<0.001
Mean LA blood pool SUV	3.67 (0.95)	3.52 (0.85)	0.602
Mean Myocardium SUV – LA SUV	3.4 (2.58, 3.36)	0 (0, 0.55)	<0.001
^{124}I-evuzamitide distribution			—
Cardiac	34 (100%)	0 (0%)	
Spleen	5 (14.7%)	2 (12.5%)	
Liver	4 (11.8%)	2 (12.5%)	
Renal	3 (8.8%)	6 (37.5%)	
Lungs	4 (11.8%)	1 (6.3%)	
Orthopedic	12 (35.3%)	5 (31.3%)	

EXAMPLES OF ^{124}I-EVUZAMITIDE UPTAKE

WT ATTR-CM | Variant ATTR-CM | Variant ATTR in Lungs | Liver involvement in WT-ATTR

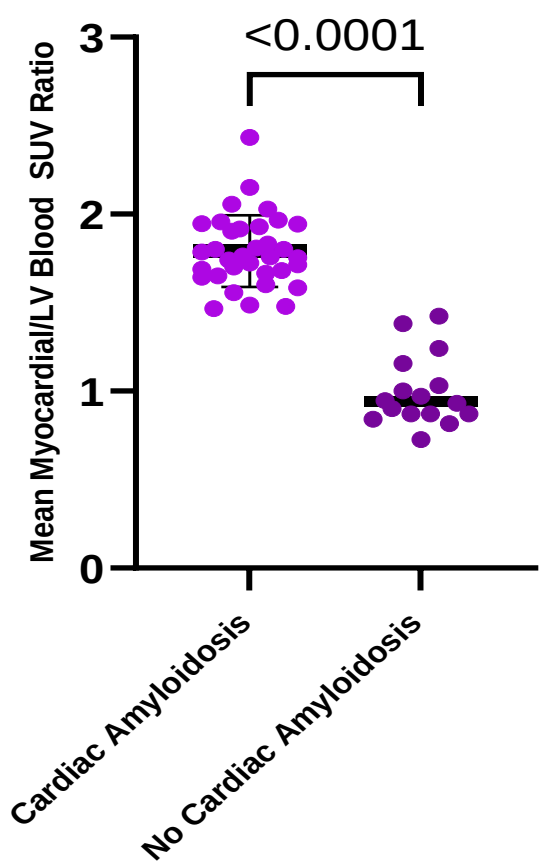


WT ATTR-CM | Variant TTR carrier | Renal AL | Spleen (& Liver) in AL



DIAGNOSTIC PERFORMANCE

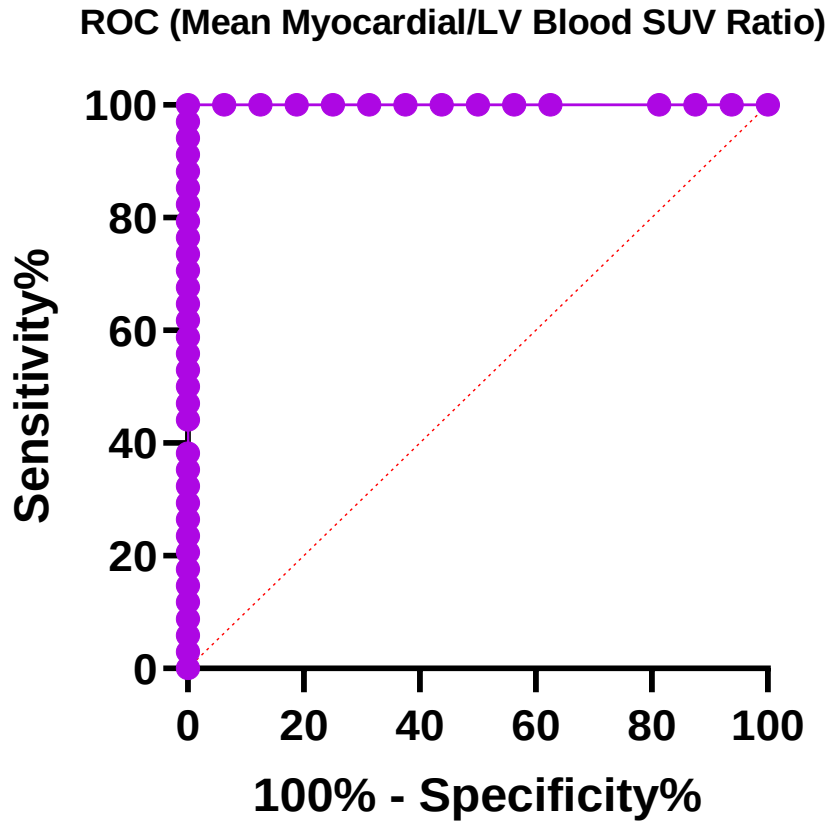
^{124}I-EVUZAMITIDE UPTAKE QUANTIFICATION



Mean myocardial/LV blood SUV ratio cut-off of 1.45 yielded:

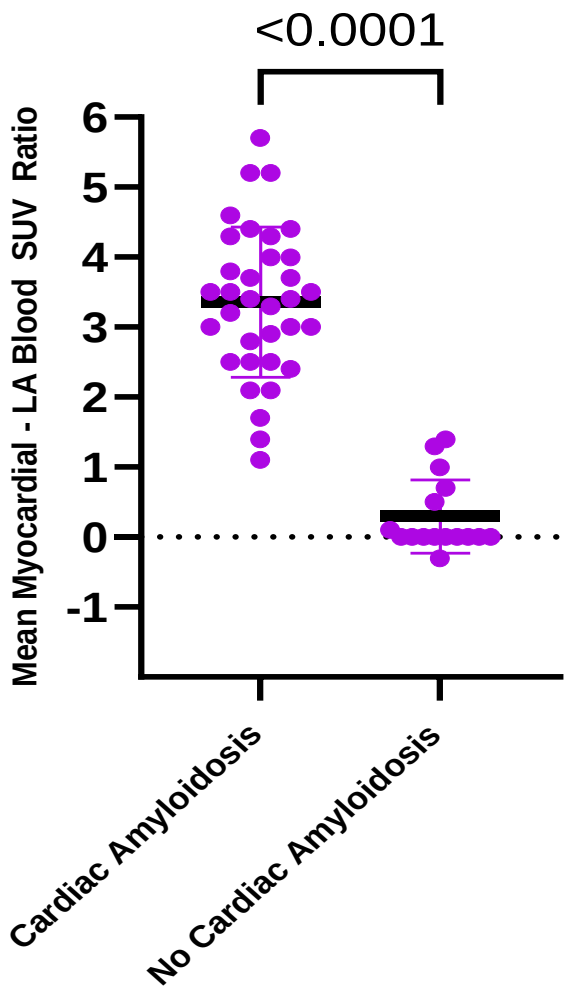
Sensitivity of 100% (95% CI: 90%, 100%)

Specificity of 100% (95% CI: 81%, 100%)



DIAGNOSTIC PERFORMANCE

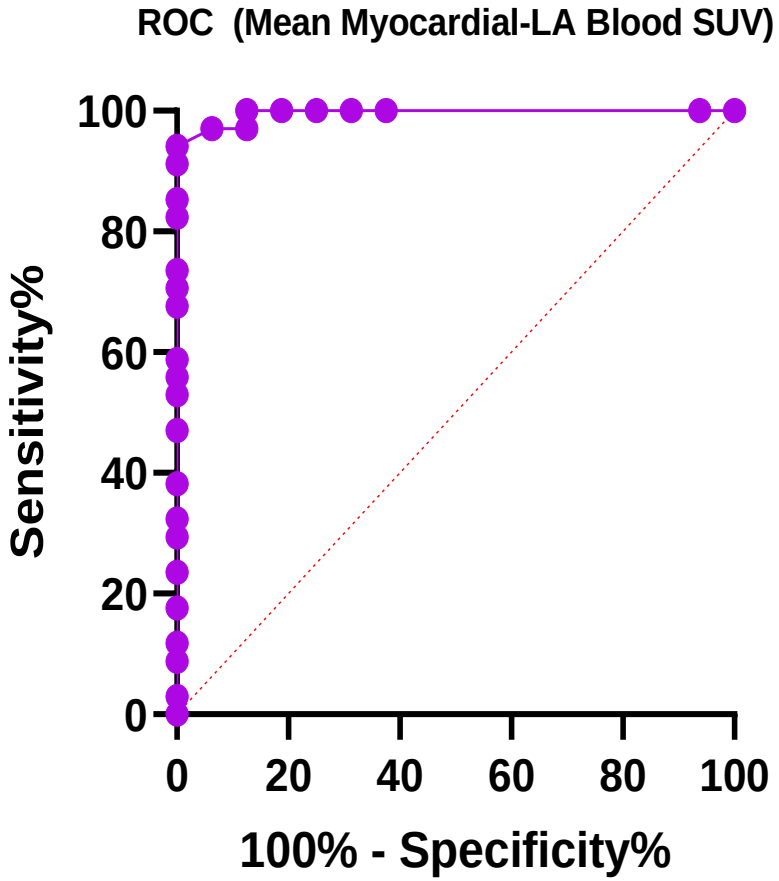
^{124}I-EVUZAMITIDE UPTAKE QUANTIFICATION



Mean myocardial-LA blood SUV ratio cut-off of 1.55 yielded:

Sensitivity of 94%
(95% CI: 81%, 99%)

Specificity of 100%
(95% CI: 81%, 100%)



CONCLUSIONS

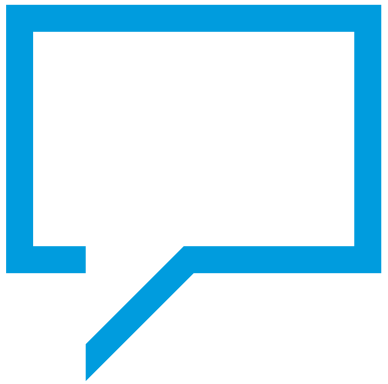
1. ^{124}I-evuzamitide PET/MRI is feasible and provides comprehensive diagnostic evaluation and organ survey of patients suspected to have or diagnosed with systemic amyloidosis.

2. In this population of patients diagnosed with or suspected to have cardiac amyloidosis, ^{124}I-evuzamitide PET/MRI had a 100% sensitivity and specificity for the diagnosis of cardiac amyloidosis.

3. A simple measure of mean myocardial to LV blood pool SUV ratio ≥1.45 yielded a 100% sensitivity and specificity for the diagnosis of cardiac amyloidosis.

4. Our participants were a highly selected group of patients, and as such, an intention-to-diagnose phase III multicenter trial of ^{24}I-evuzamitide in patients suspected to have cardiac amyloidosis is needed to confirm our findings.

QUESTIONS & ANSWERS



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THANK YOU FOR JOINING US IN THIS COURSE

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