Update in Nuclear Imaging of Amyloidosis and Sarcoidosis

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CEDARS-SINAI

Outline

- Amyloidosis
  - General considerations
  - Nuclear imaging methods
  - Role of MRI
  - Diagnostic algorithm
- Sarcoidosis
  - General concepts
  - Nuclear imaging methods
  - Complementary imaging with MRI
  - Diagnostic algorithm

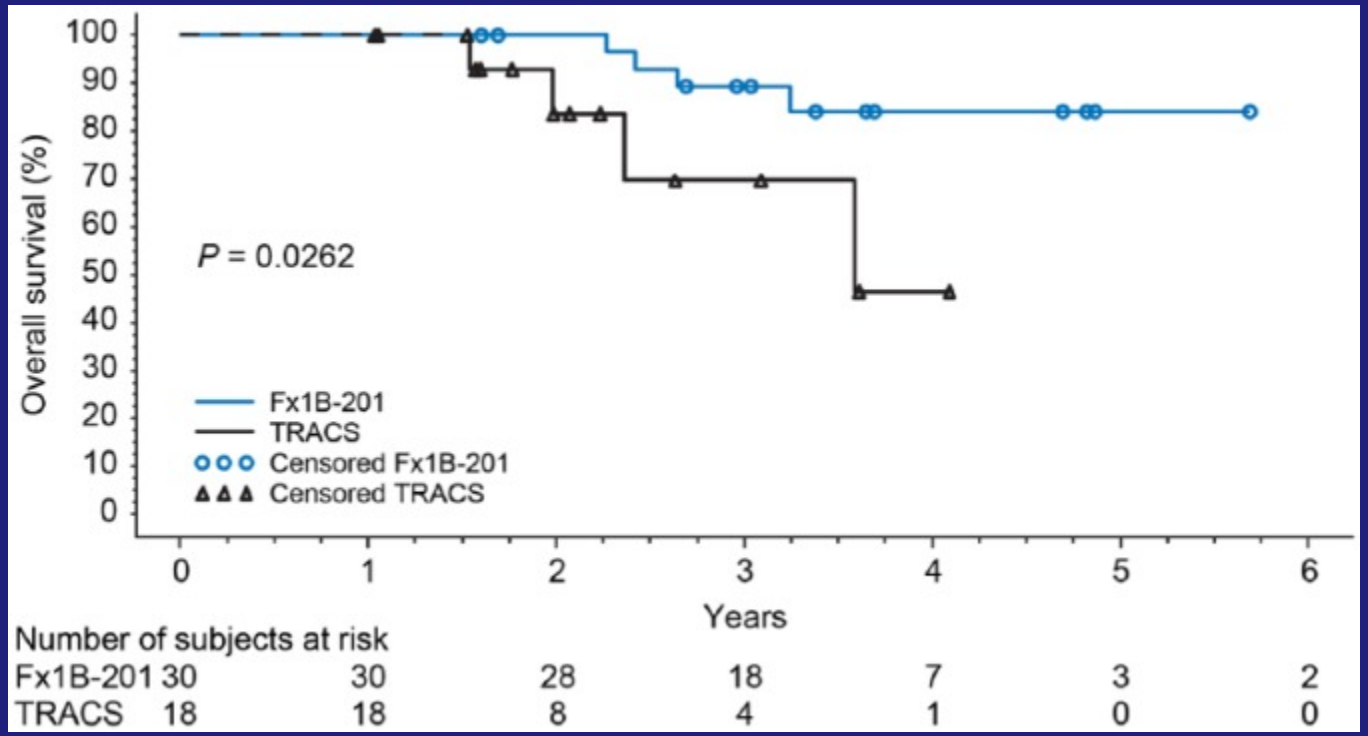
Cardiac Amyloid

- Amyloidosis-major types: ATTR and Light Chain
- How do we distinguish between the subtypes with nuclear imaging?
  - Tc-99m-Pyrophosphate (Tc-99m-PYP) scanning
- Significance of assessment of Tc99m-PYP uptake
- SPECT
  - Improved localization over planar
  - Dual isotope imaging

Cardiac Amyloid

- ATTR
  - ATTR includes senile (“Wild-type”) (95%) and hereditary/familial types (5%)
  - Senile type: tends to be an older male with LVH
  - 25% of men over 85 have it (may include patients with AS-low flow low gradient or patients with HFPEF)
  - Biopsy:
    - Congo red stain positive
    - Immunohistochemistry stain positive for kappa or lambda light chains
  - Medical therapy (tafamidis, Diflunisal, small interfering RNA)

ATTR Amyloidosis: Prognosis and Treatment



Median overall survival for ATTR WT is 3.6y

Tafamidis improves survival compared to non-treatment

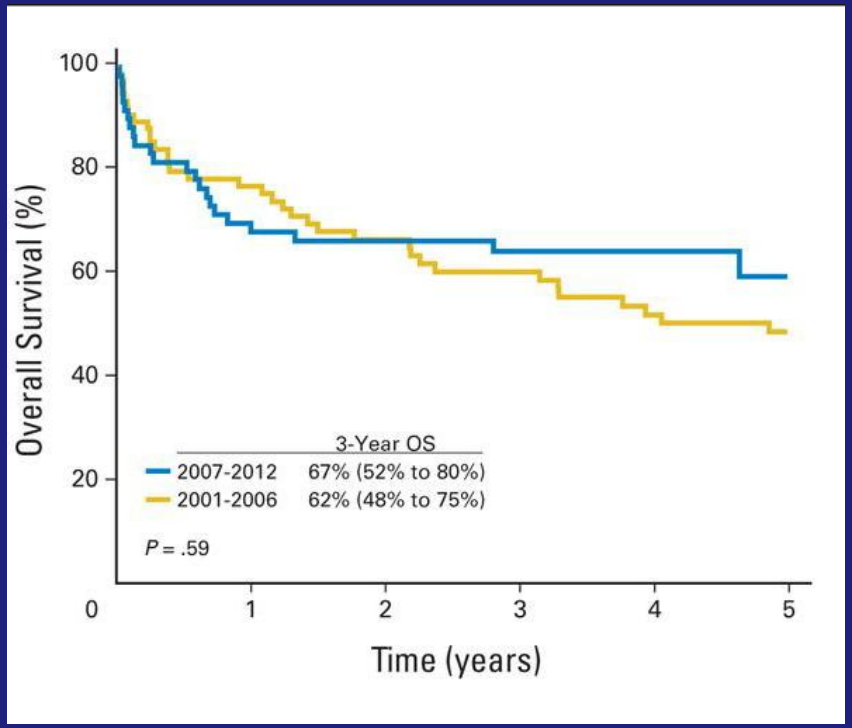
Sultan et al. Clin Med Insights Cardiol. 11:1-4 2017

Cardiac Amyloid

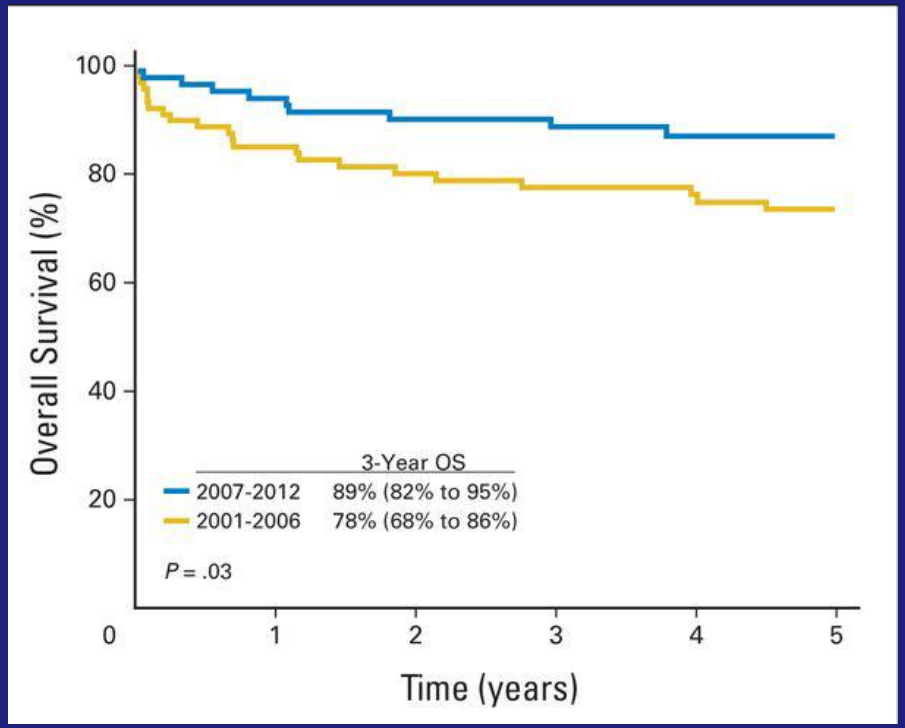
- AL is a systemic disorder
  - Characterized by monoclonal gammopathy
  - Immunoglobulin light chain produced by a clonal cell population
  - Lambda chain predominant
  - Biopsy
    - Congo red staining with infiltration
    - Bone marrow biopsy and presence of circulating light chains
  - Treatment
    - consists of chemotherapy and stem cell transplantation
    - Cardiac transplantation

AL Survival with SCT

Cardiac AL

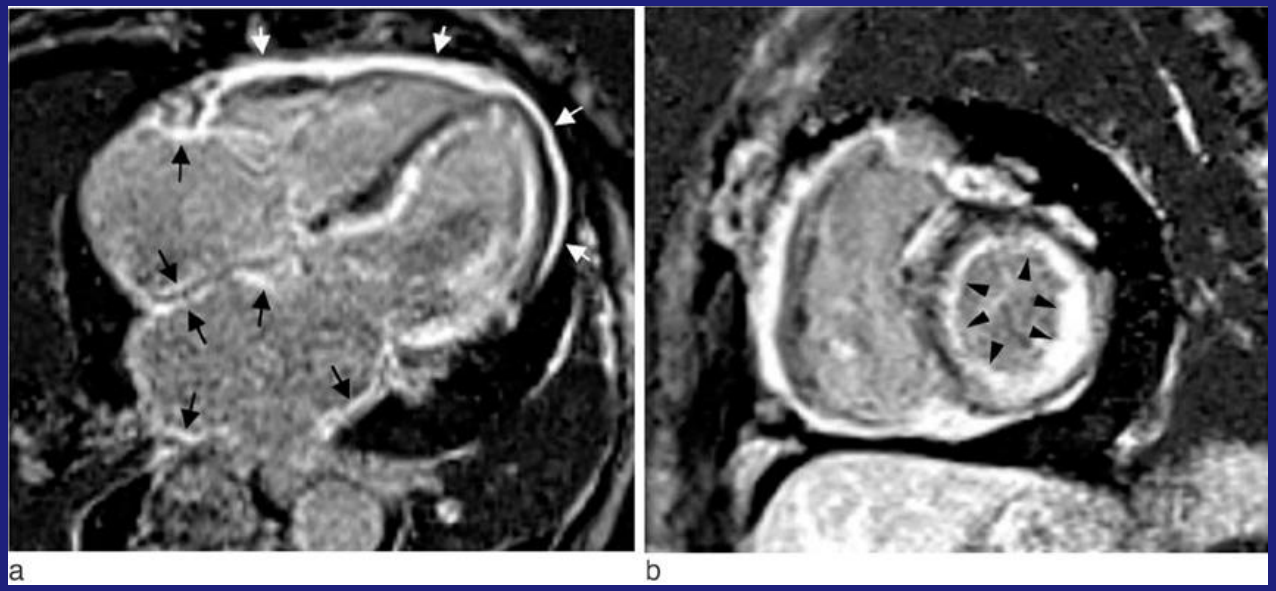


Non-cardiac AL



D' Souza et al. Journal of Clinical Oncology 33, 2015 3741-3749

CMR: Usual initial imaging test



Diffuse late gadolinium enhancement (LGE): high sensitivity

Does not distinguish between ATTR and AL

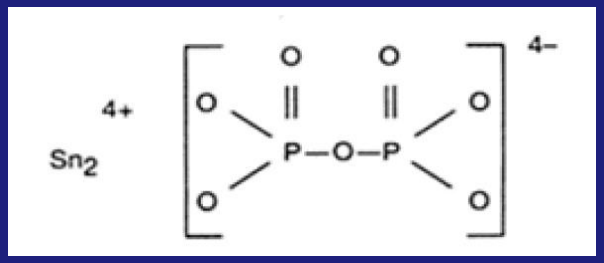
Nuclear Medicine for Cardiac Amyloid

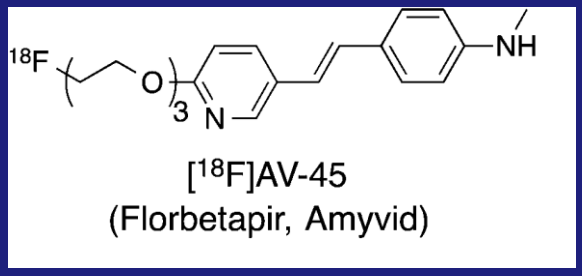
Tc-99m pyrophosphate

- Bone imaging tracer since 1970's
- High specificity for ATTR
- SPECT increasing utilization

F-18 Florbetapir

- FDA approved 2012 (brain)
- Images the amyloid protein itself
- AL>ATTR uptake



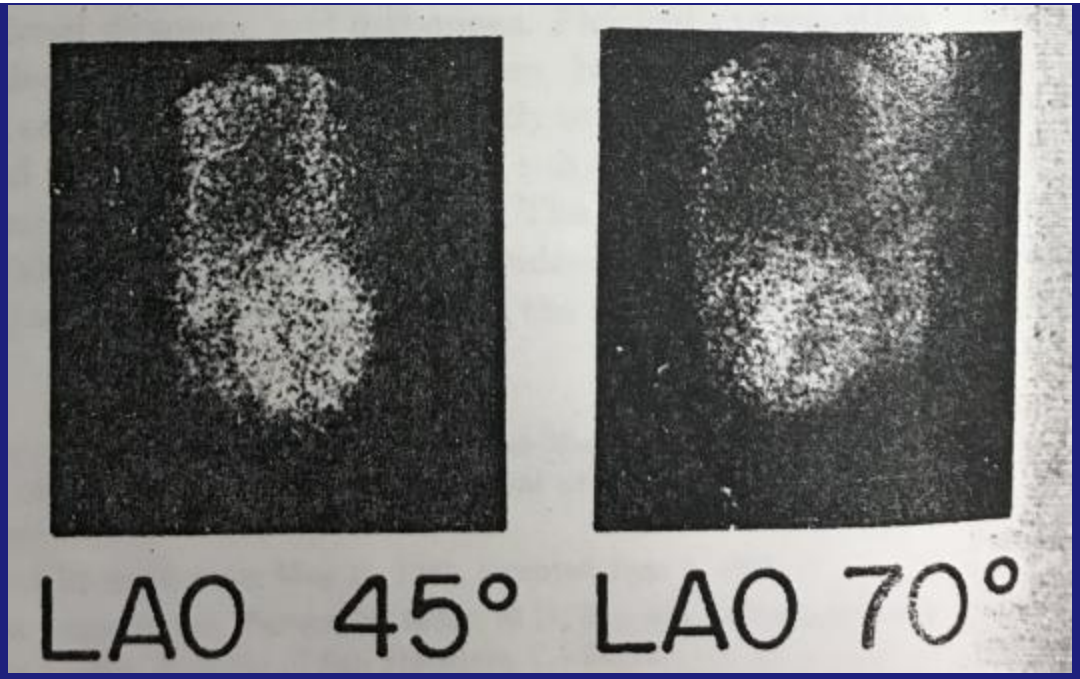


^{99m}Tc-PYP in Cardiac Amyloidosis

Am Heart J. 1982 Apr;103(4 Pt 1):562-3.

Diagnostic considerations in cardiomyopathy: unique scintigraphic pattern of diffuse biventricular technetium-99m-pyrophosphate uptake in amyloid heart disease.

Schiff S, Bateman T, Moffatt R, Davidson R, Berman D.



"We propose that the scintigraphic pattern of intense, diffuse, biventricular uptake of Tc-99m PYP may be highly specific for the diagnosis of amyloid cardiomyopathy."

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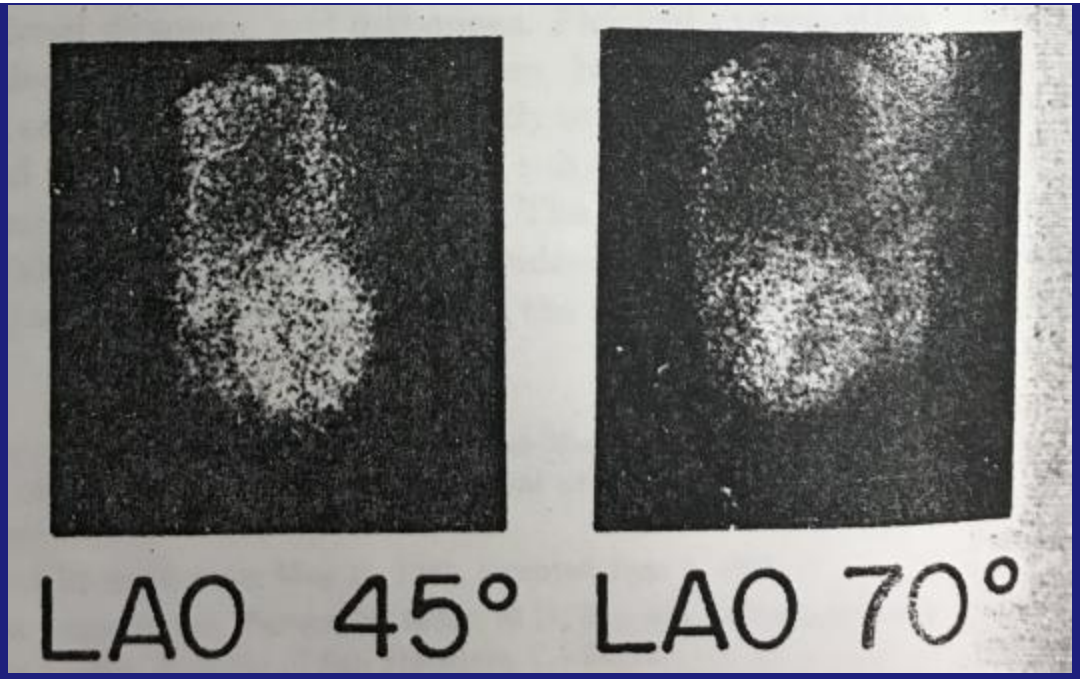
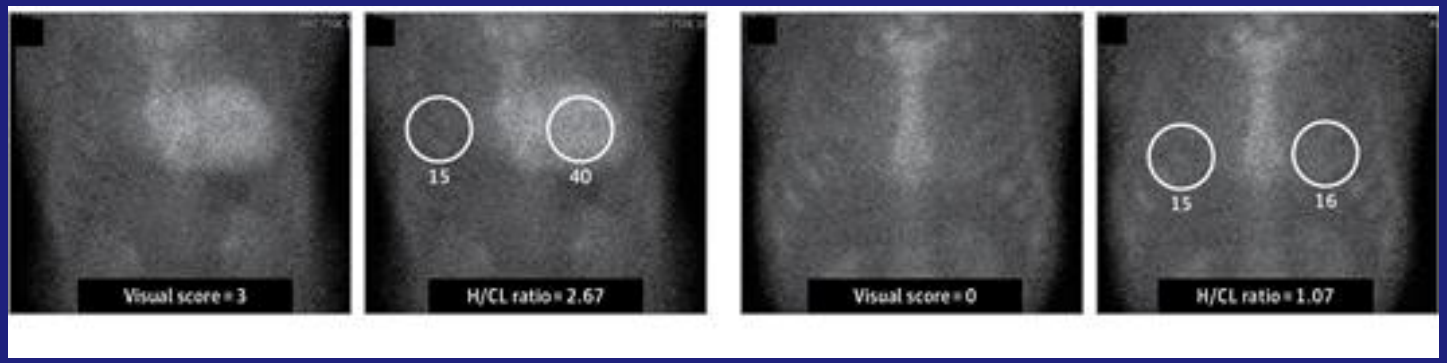


Sporadic use early on due to apparent low sensitivity

"We propose that the scintigraphic pattern of intense, diffuse, biventricular uptake of Tc-99m PYP may be highly specific for the diagnosis of amyloid cardiomyopathy."

Planar Imaging



^{99m}Tc-PYP 20mci

Planar and SPECT acquisition (30min)

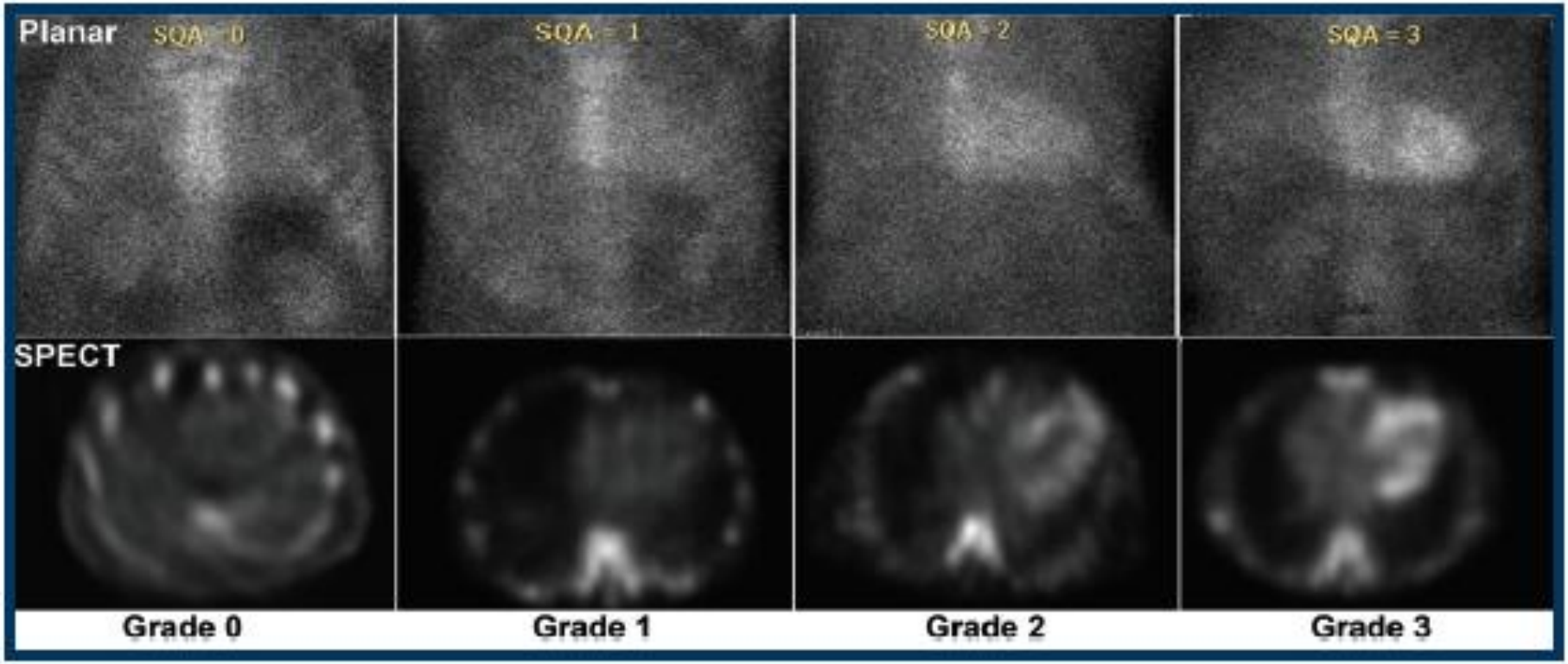
0

3h

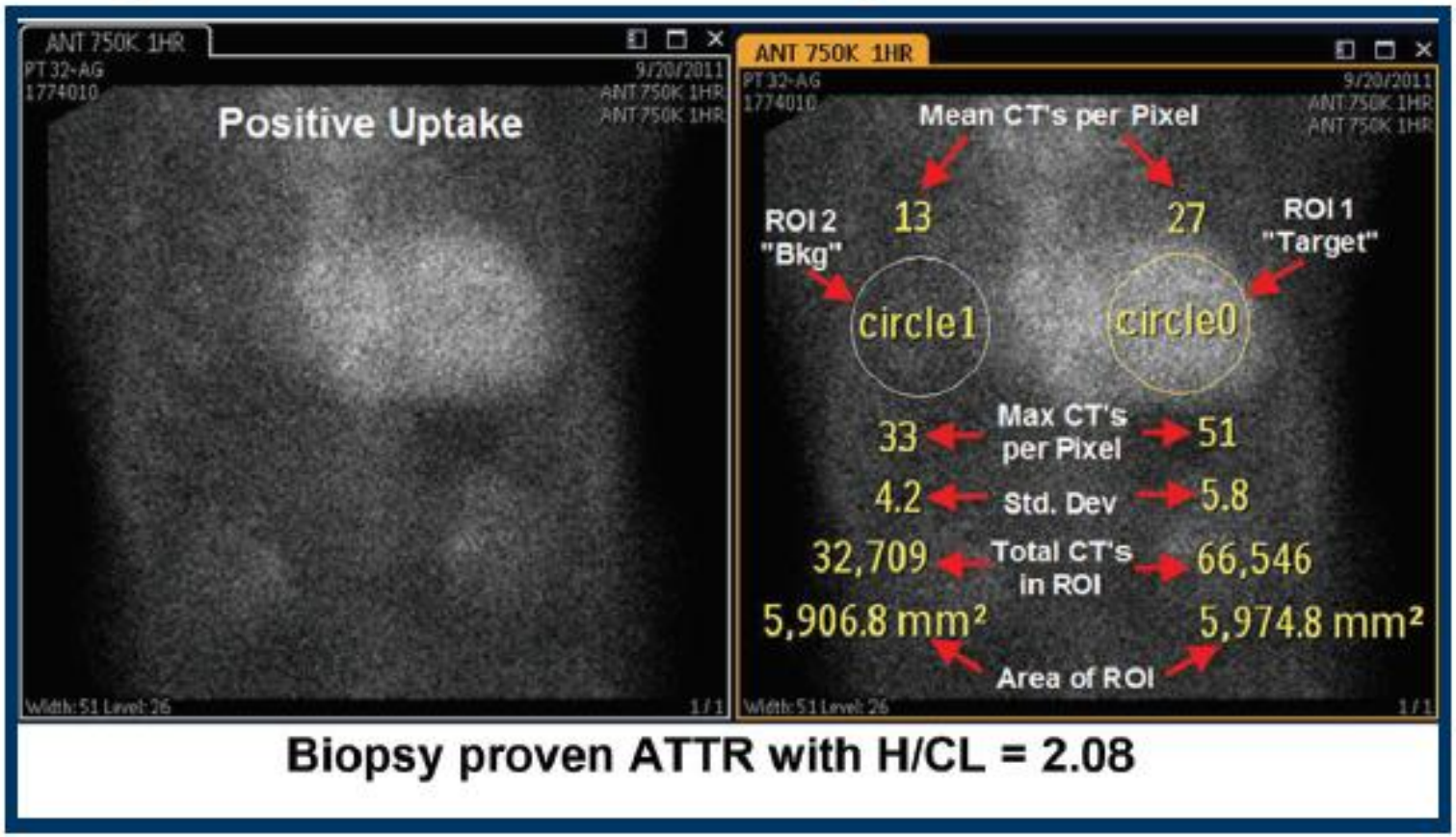
Standard approach:
Recommended by ASNC guidelines
Can distinguish patients with strong uptake and absence of uptake

Tc-99m-PYP SPECT

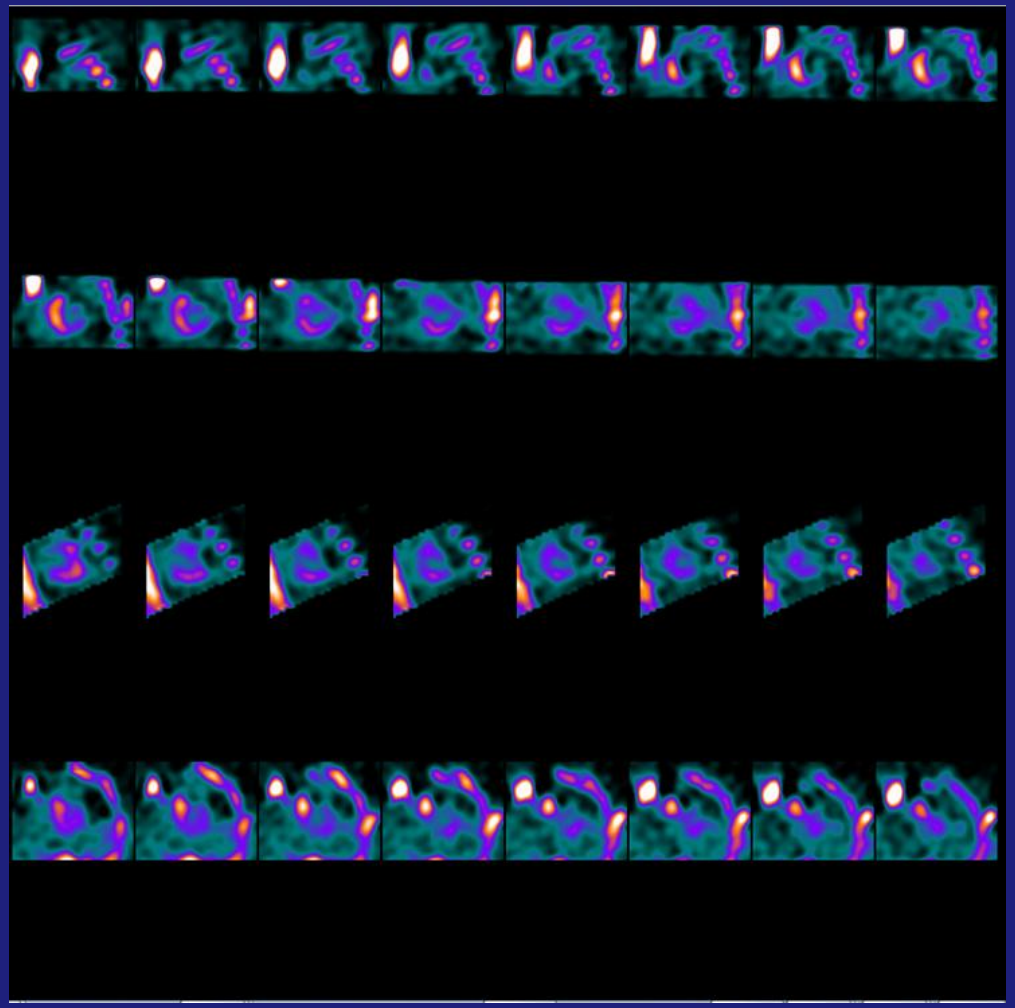
Semiquantitative Assessment of PYP Uptake



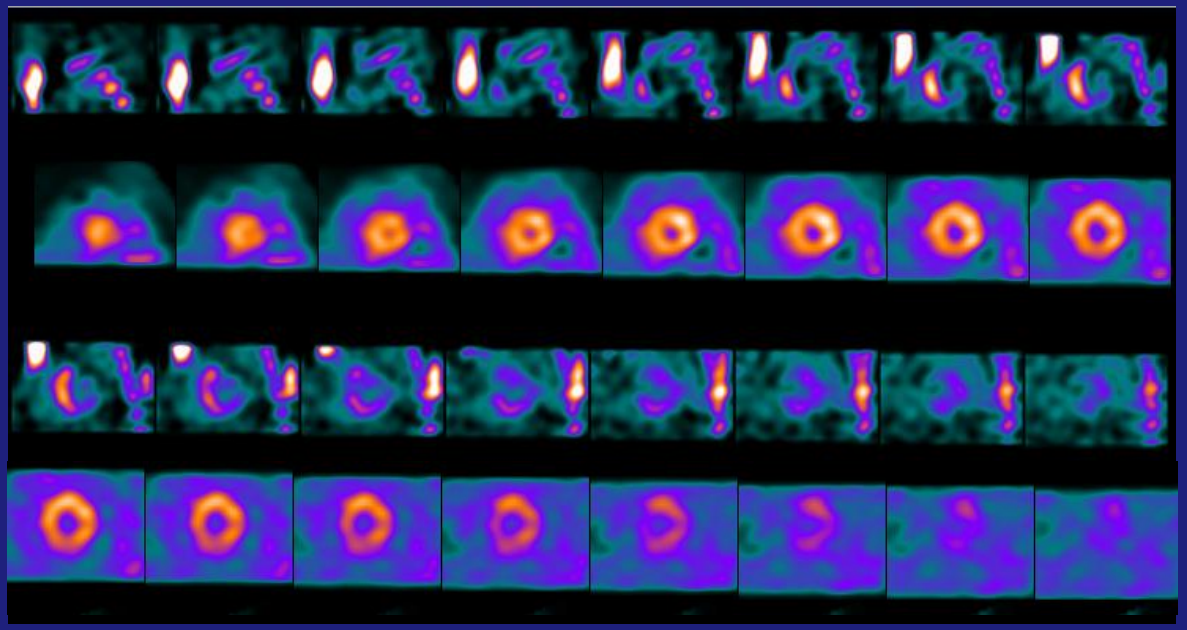
Quantification of Tc99m PYP Uptake



Limitation of Planar Imaging

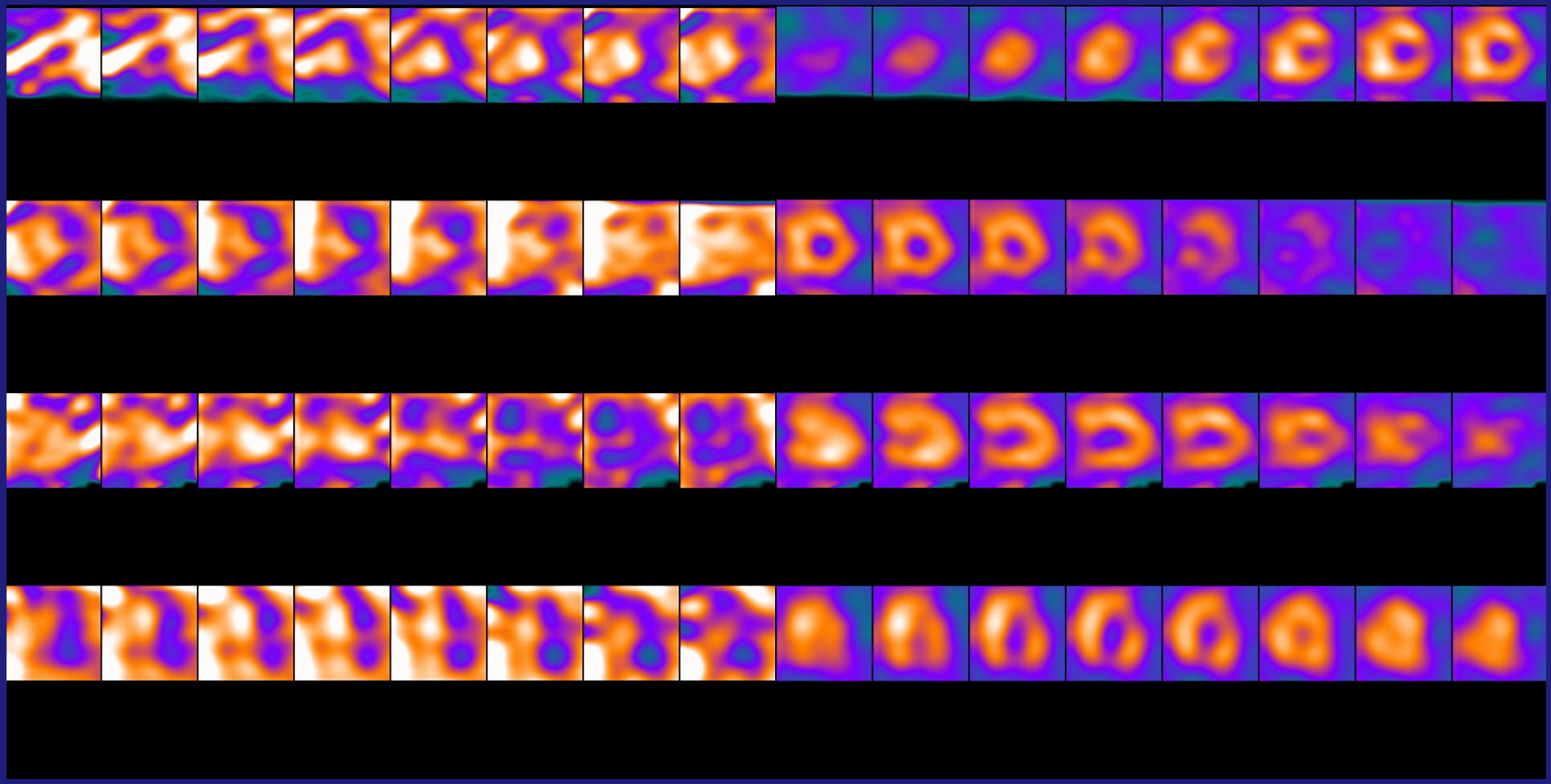


Simultaneous Dual Isotope Imaging with Tl-201/Tc99m-PYP SPECT



Tc-99m-PYP SPECT

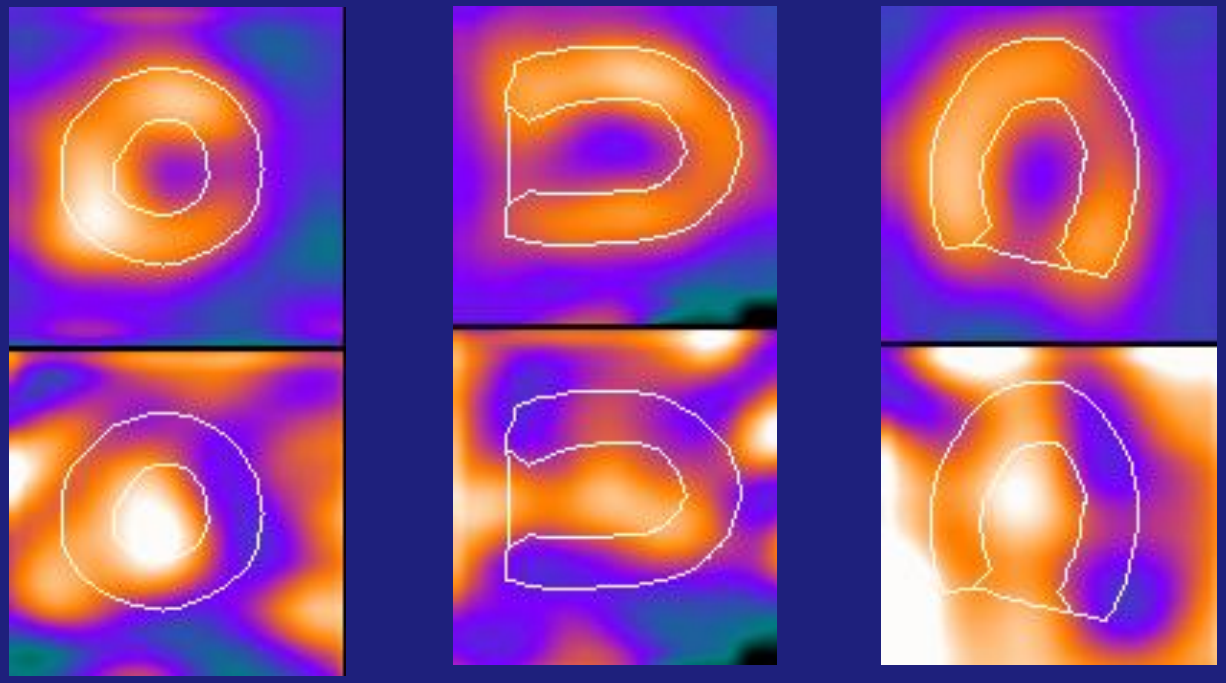
Tl-201 SPECT



Simultaneous Dual Isotope Imaging with Tl-201/Tc99m-PYP SPECT

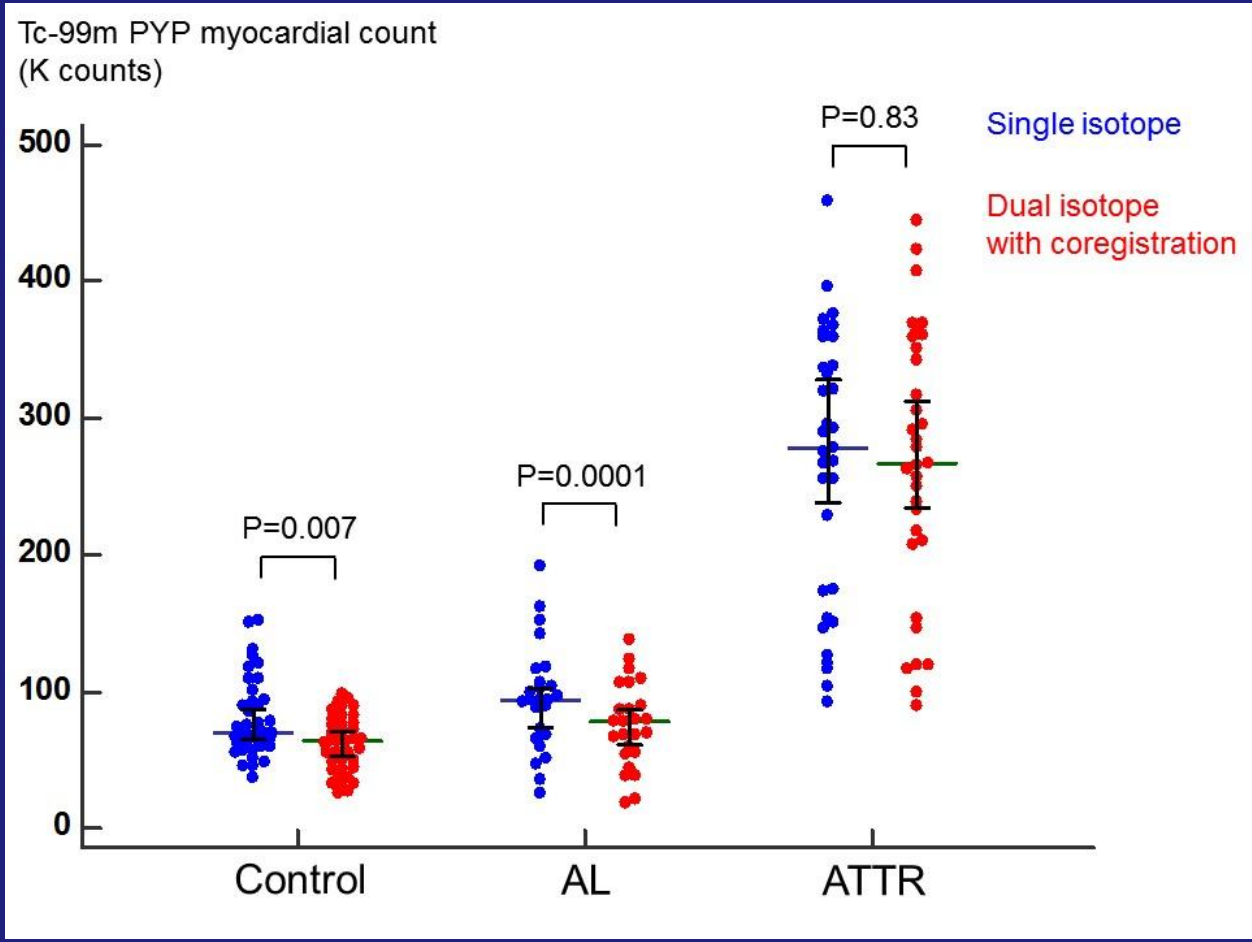
^{201}Tl

^{99m}Tc -PYP

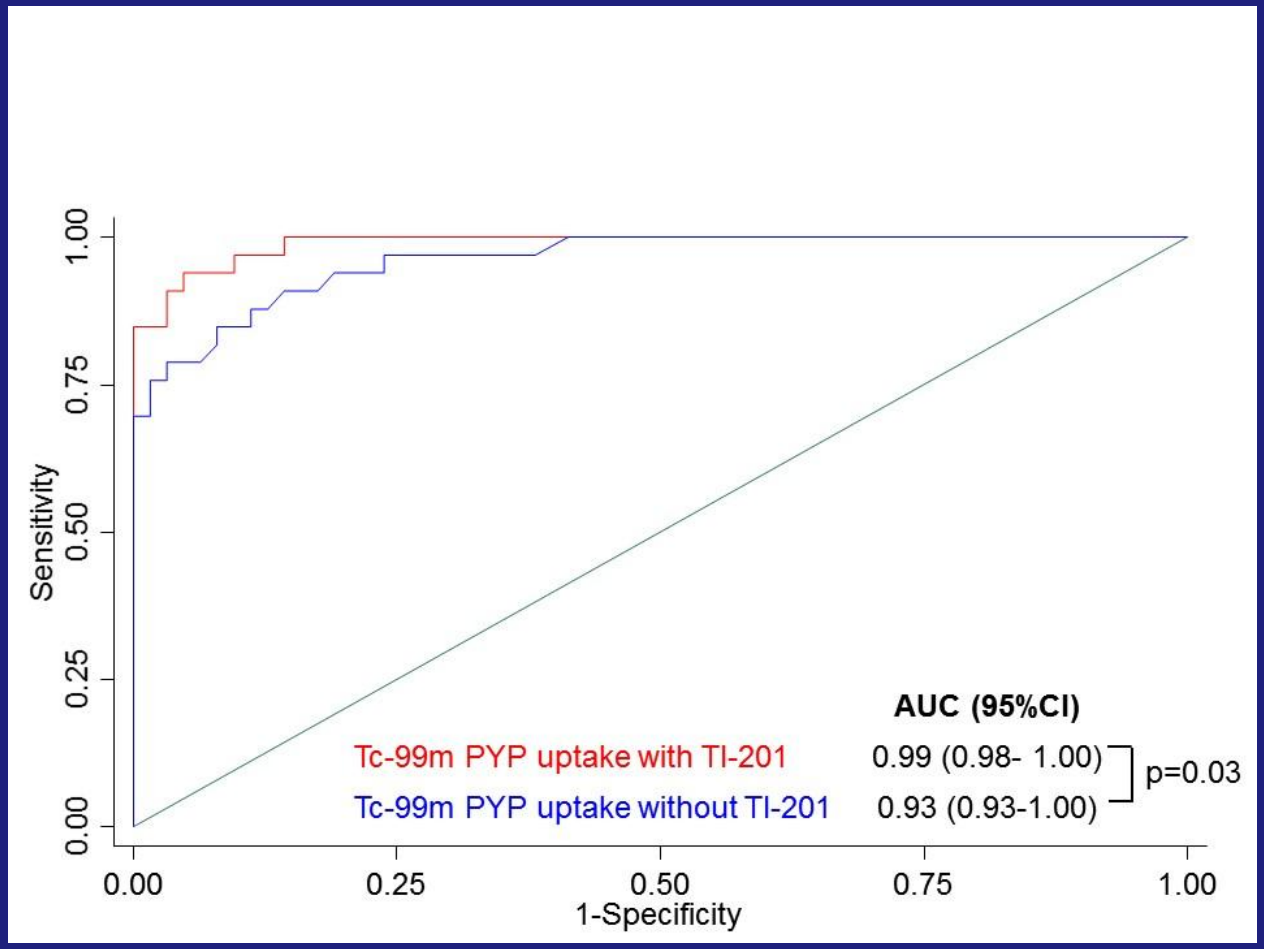


Tl-201 allows unequivocal demonstration of the absence of myocardial Tc99m-PYP uptake

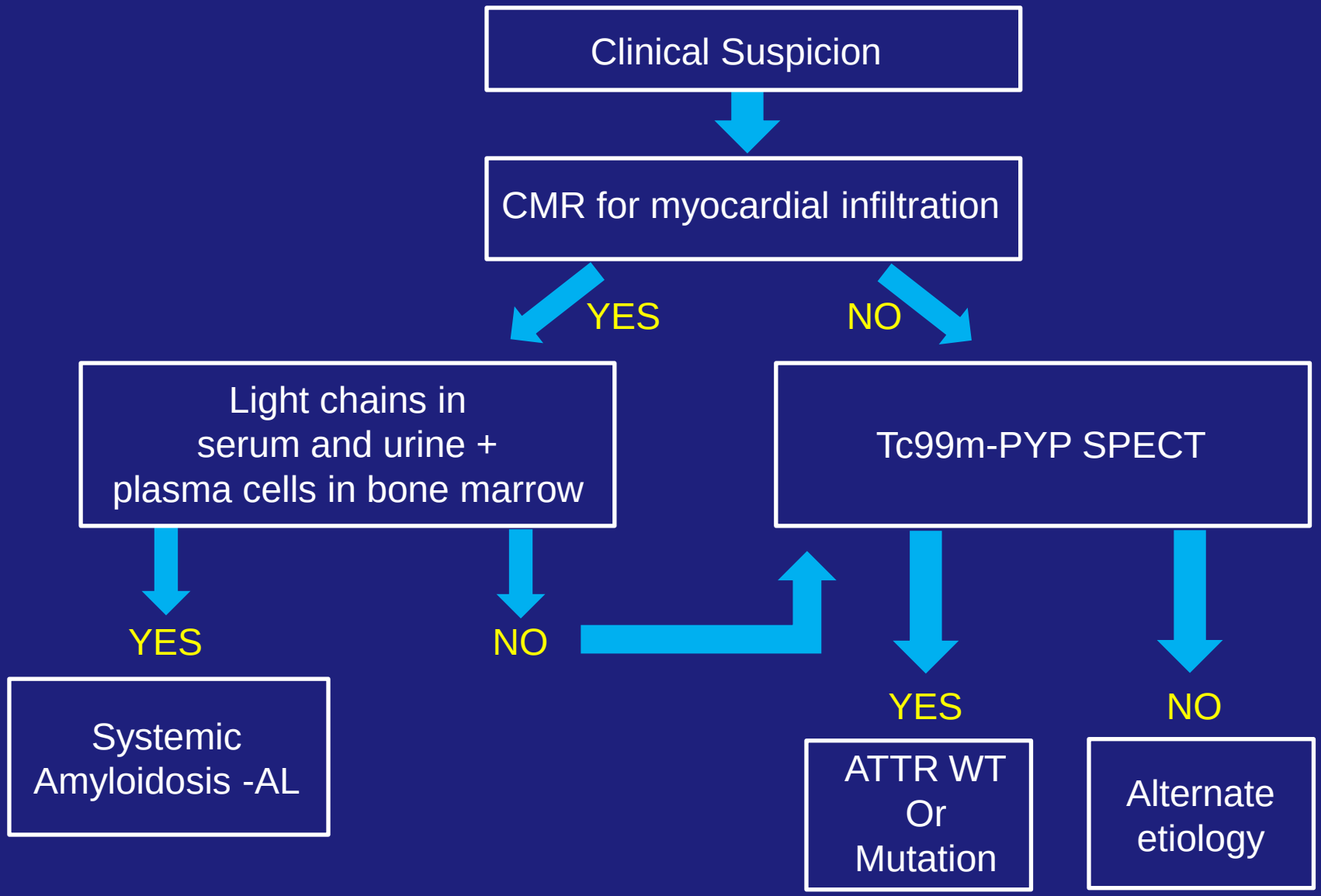
Myocardial Tc99m-PYP counts with and without the use of Tl-201 for processing of raw images and for quantification



Prediction of ATTR by Tc-99m PYP SPECT with and without the use of Tl-201



Clinical Approach to the Use of Imaging in Diagnosis of Cardiac Amyloidosis



Summary

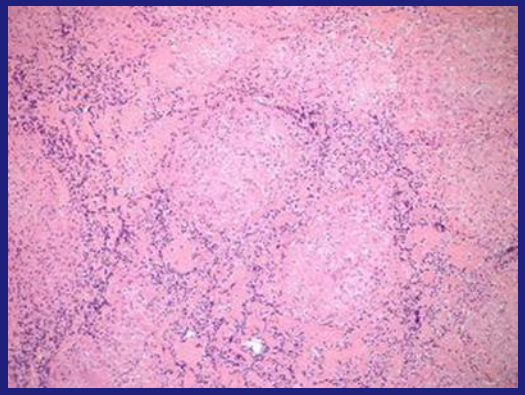
- ATTR best diagnosed by Tc-99m-PYP SPECT
- Myocardial Tc-99m-PYP uptake is usually absent in AL
- Quantification may be important for assessment of progression/effects of therapy
- Quantification is improved by simultaneous dual isotope imaging with Tl-201

Sarcoidosis

- Clinical features
- Nuclear imaging for inflammation (F18-FDG)
- Quantification of FDG uptake
- Potential benefits of quantitative assessment

Sarcoidosis

- Systemic disease of unknown cause
  - Pulmonary> skin > eye > bone
  - Cardiac involvement recognized in only a small % of cases
  - Nearly 25% of patients with extracardiac sarcoid have cardiac involvement (autopsy findings)
- Cardiac sarcoid
  - Heart block
  - VT
  - Heart failure
  - Atrial arrhythmias



Diagnosis of Cardiac Sarcoid
HRS Criteria

Cardiac biopsy positive
OR
Extracardiac biopsy positive
AND

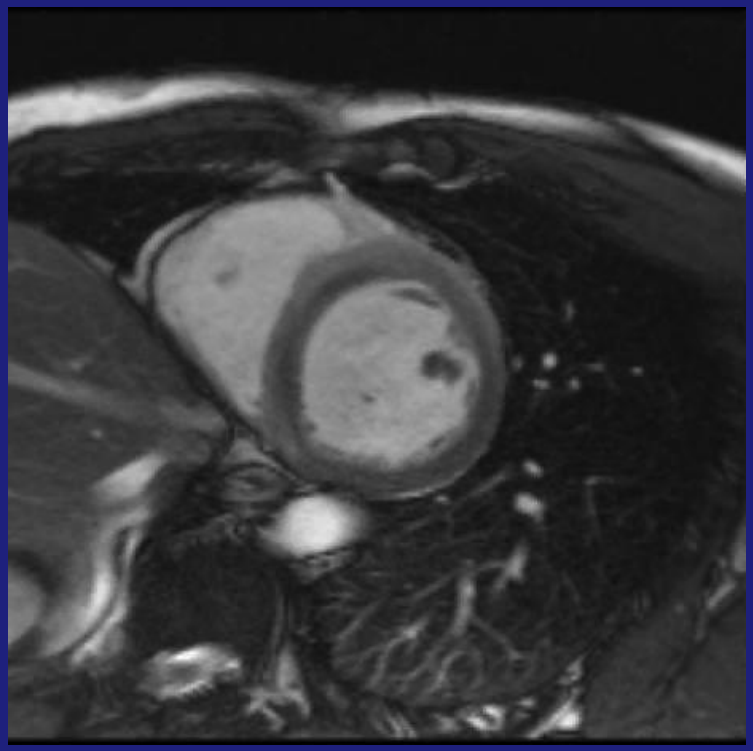
- Steroid +/- immunosuppressant responsive cardiomyopathy or heart block
- Unexplained reduced LVEF (<40%)
- Unexplained sustained (spontaneous or induced) VT
- Mobitz type II 2nd degree heart block or 3rd degree heart block
- Patchy uptake on dedicated cardiac PET (in a pattern consistent with CS)
- Late Gadolinium Enhancement on CMR (in a pattern consistent with CS)
- Positive gallium uptake (in a pattern consistent with CS)

Diagnostic and Therapeutic Strategy in Cardiac Sarcoidosis

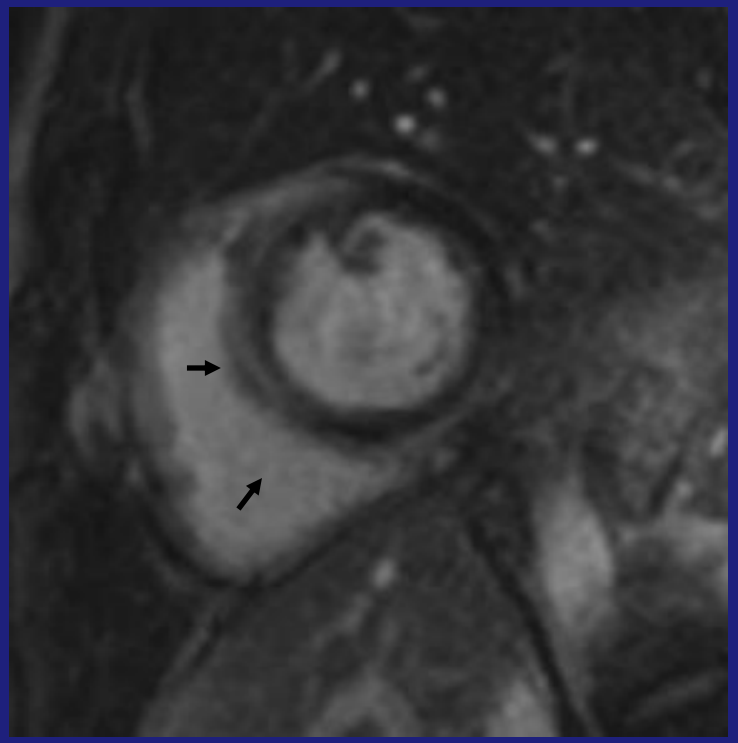
- Indications for screening
  - Diagnosed extracardiac sarcoidosis
  - Unexplained 2° or 3° AV block age <55 y
  - Unexplained monomorphic VT
  - Non ischemic dilated cardiomyopathy
- Routine screening
  - Physical, ECG, Echo, Holter
- Advanced screening
  - CMR
  - PET (F18-FDG has replaced Ga67)
  - Invasive EP study

J Nucl Med 2014; 55: 99-106

CMR for Sarcoid Imaging



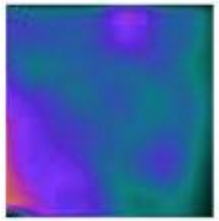
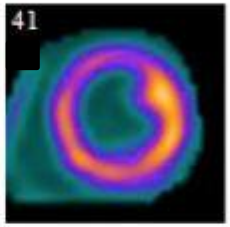
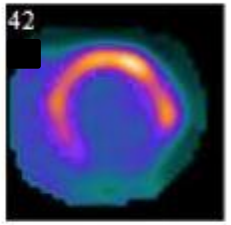
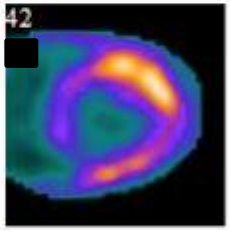
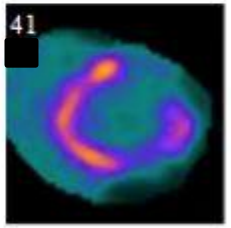
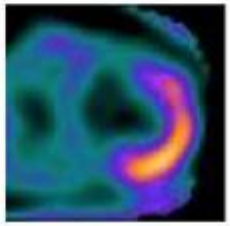
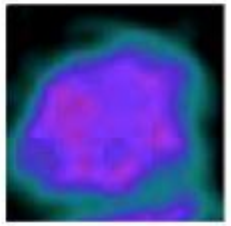
Post-contrast cine image
shows difference in signal intensity



Delayed gadolinium image
dark myocardium (without fibrosis)
and enhancement (in regions of fibrosis)

Assessment of inflammation for treatment decisions is made with PET imaging

F18-FDG PET Imaging for Inflammation

Disease Category	Uptake Pattern	Perfusion	Metabolism
Normal	Perfusion: Normal Metabolism: No FDG Uptake		
Mild or Early Disease	"Focal Mismatch Pattern" Perfusion: No or mild defect Metabolism: FDG uptake in area of defect		
Moderate or Progressive Disease	"Focal Mismatch Pattern" Perfusion: Moderate defect Metabolism: FDG uptake in area of defect		
Severe or Fibrous Disease	Perfusion: Severe defect Metabolism: No or minimal FDG uptake		

Bokhari et al., FDG-PET is a Superior Tool in the Diagnosis and Management of Cardiac Sarcoidosis, ACC Expert analysis Apr 10, 2017

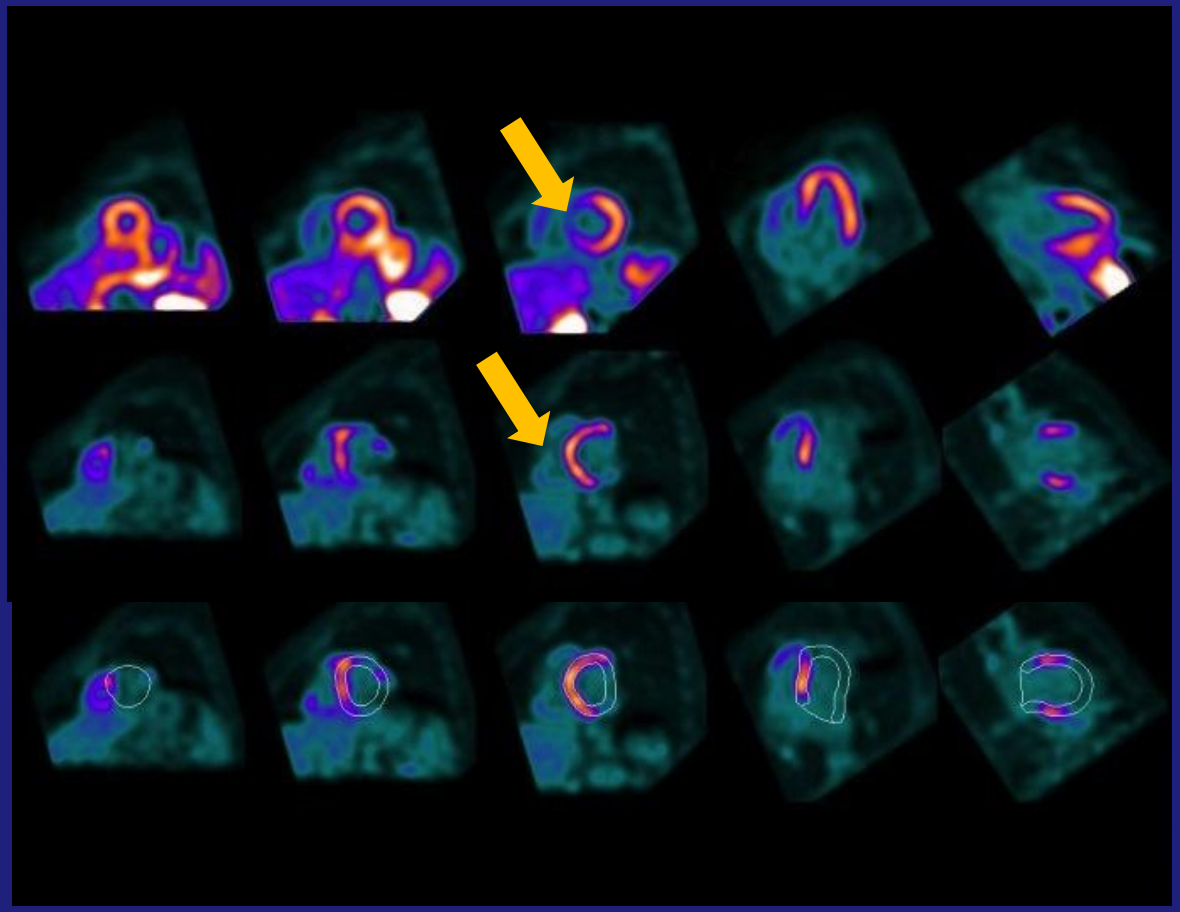
Practical Concerns

F18-FDG for detection of myocardial inflammation

- Myocardial glucose uptake suppression is the goal
  - F18-FDG uptake indicates inflammation
- CSMC pre- test preparation protocol:
  - HFLC dietary preparation 24-48hr
  - Prolonged fast 12-16 hours
  - Heparin iv at 45 min and 15 min pre F18-FDG*
- Diabetic patients
  - Early morning zero carbohydrate meal

* There is evolving consensus regarding the use of heparin.

Perfusion and FDG PET



Rest Rb82 and F18-FDG cardiac PET

Key concept:
FDG uptake in inflamed myocardium but suppressed in healthy tissue which utilizes free fatty acid

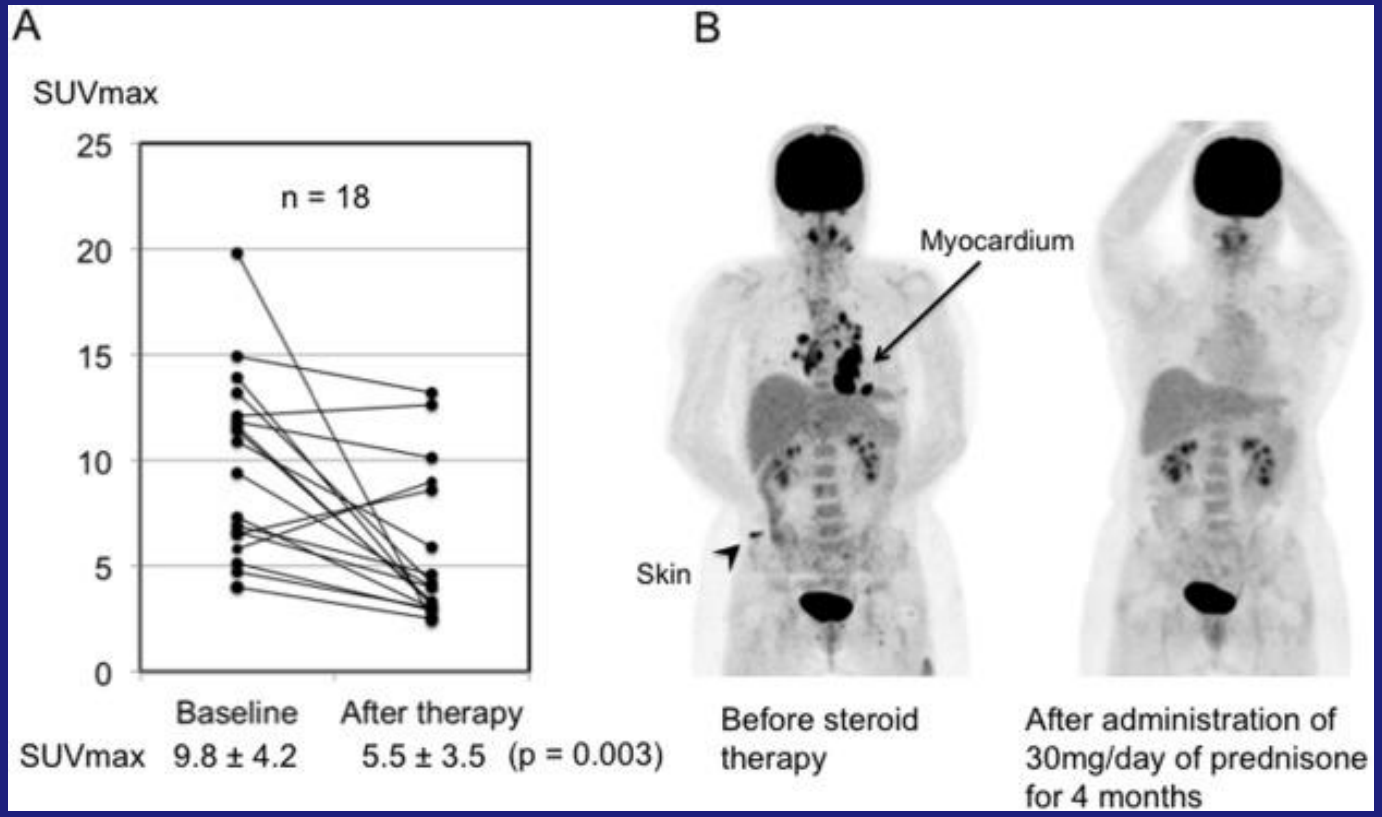
How do you measure disease burden?

Is There a Need to Measure FDG Uptake and How to Quantify?

SUV (standard uptake value): Uptake of FDG activity in a lesion normalized on the basis of a distribution volume.

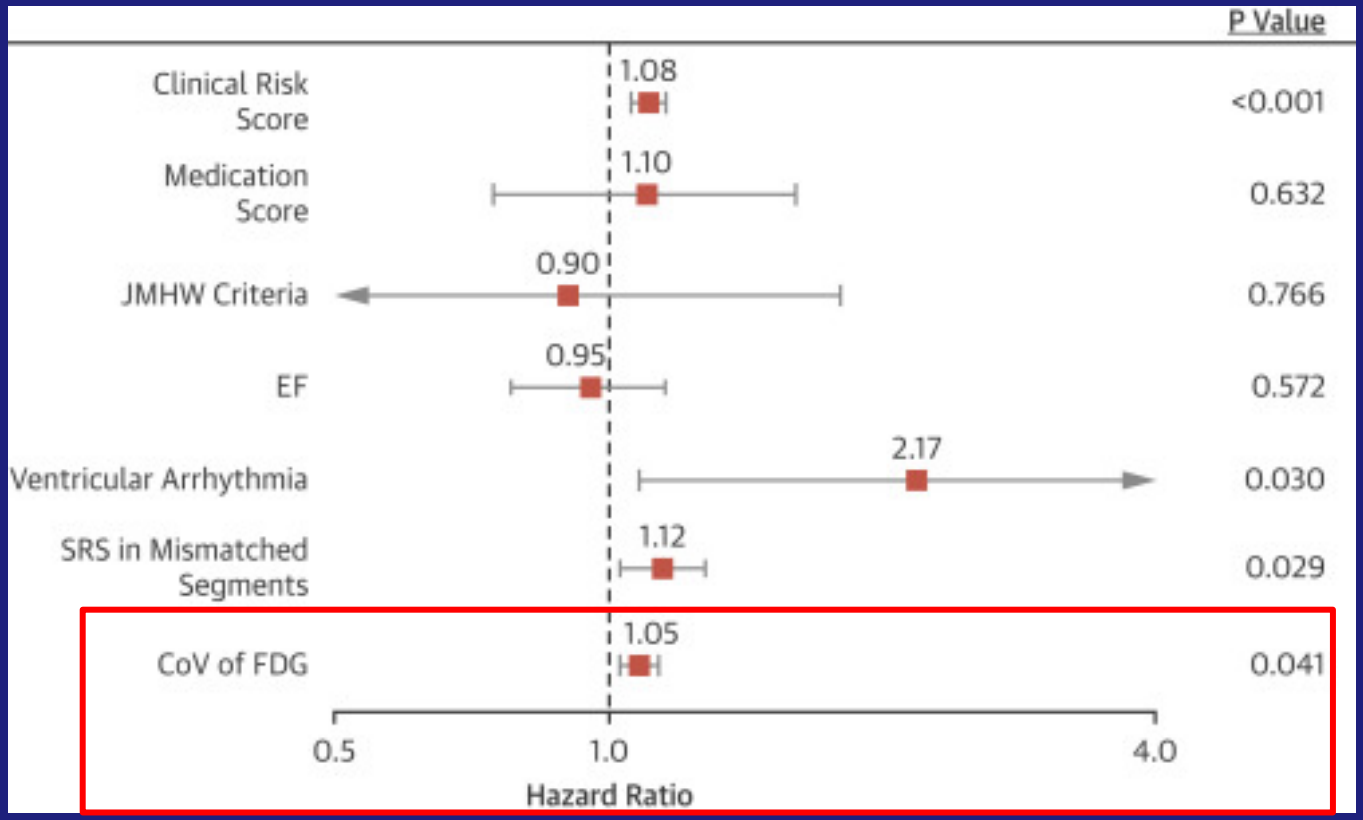
Useful to measure disease activity and monitor treatment

FDG Uptake and Response to Treatment



Yokoyama et al., Quantitative analysis of myocardial 18F-fluorodeoxyglucose uptake by PET/CT for detection of cardiac sarcoidosis International Journal of Cardiology, Volume 195, 2015, 180–187

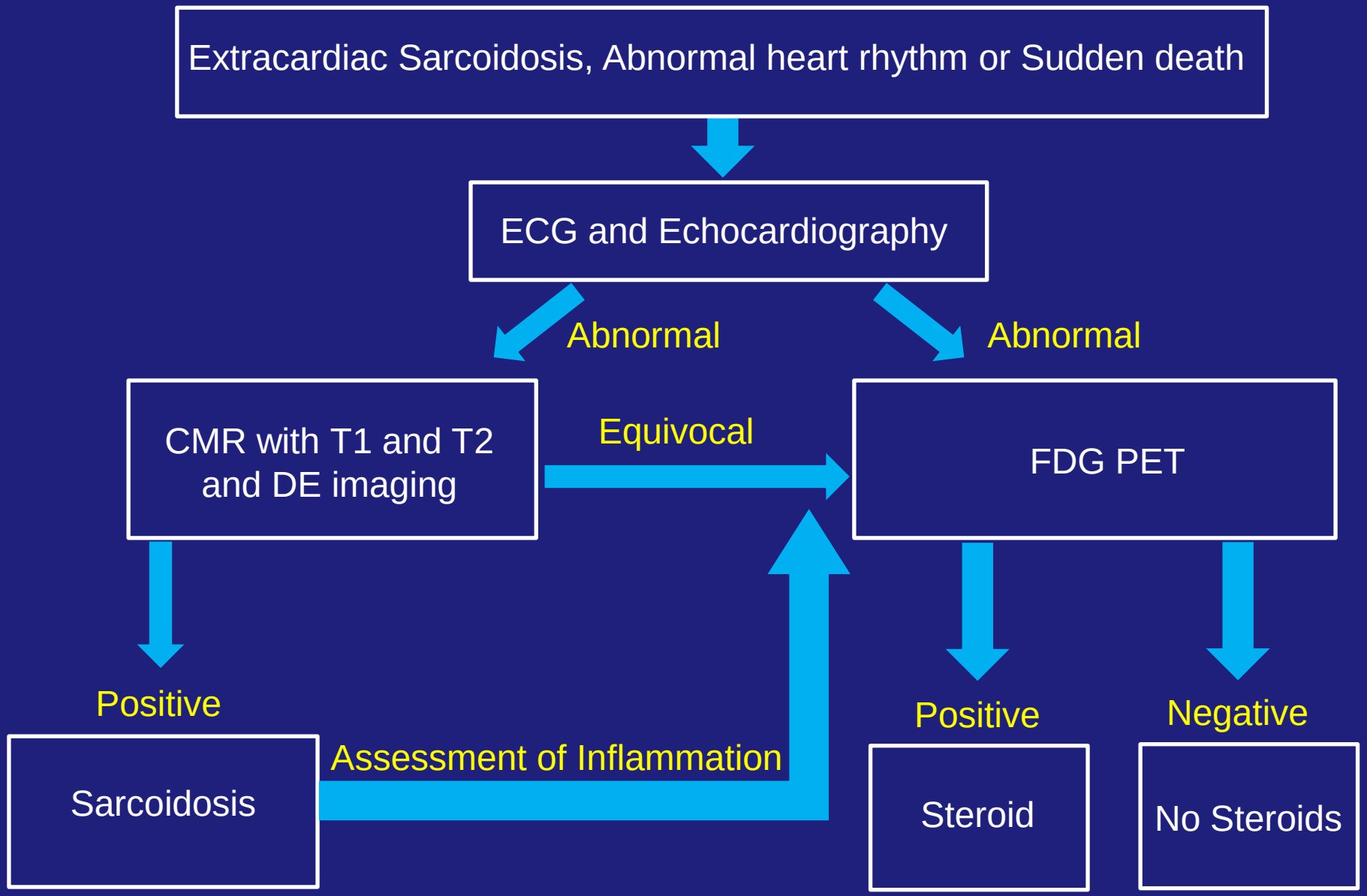
Quantitative Measurement of FDG Uptake for Prognostication



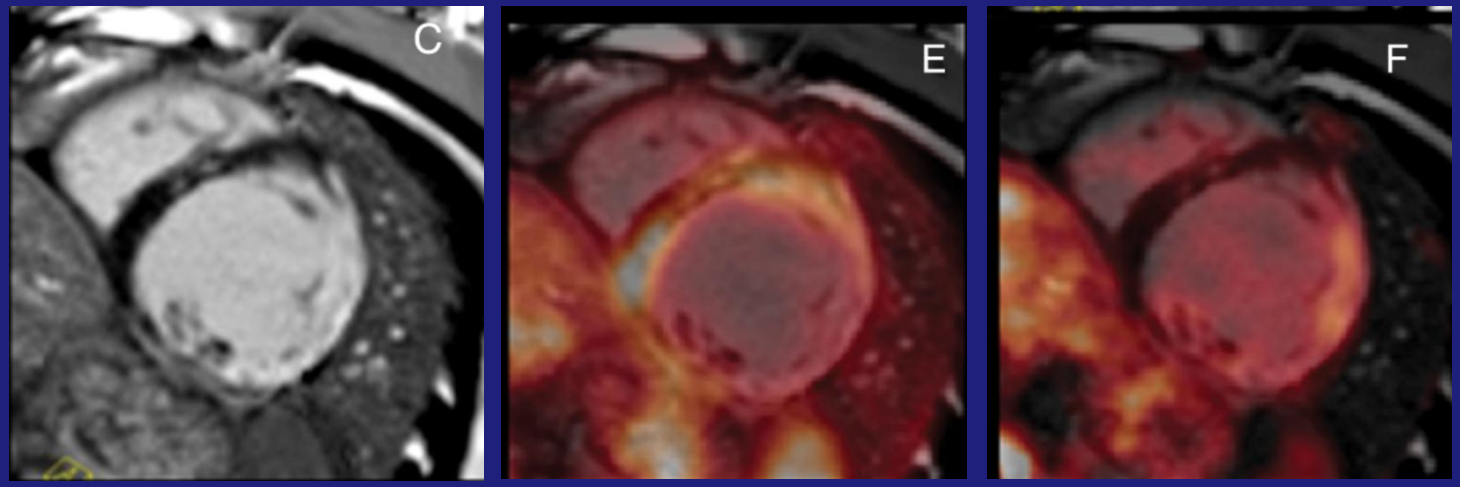
63 patients out of 203 suffered adverse events over a mean followup of 1.8y

Sperry et al., Prognostic Impact of Extent, Severity, and Heterogeneity of Abnormalities on ^{18}F-FDG PET Scans for Suspected Cardiac Sarcoidosis JACC Imag 2017

Diagnostic Imaging in Sarcoidosis



PET-MRI for Sarcoid Imaging



MRI PET Perfusion PET FDG

Eur Heart J. 2013;35(5):312

Cardiac Imaging in Sarcoidosis

- Diagnosis: MRI/PET
- Prognosis: MRI/PET
- Quantification of FDG uptake can be useful for guiding therapy and monitoring response
- PET-MRI combines the best of both modalities