ASSESSMENT OF CARDIAC AMYLOIDOSIS BY USING 18F-SODIUM FLUORIDE PET/MR IMAGING.

R. Abgral, M.Trivieri, M. Dweck, P. Robson, N. Karakatsanis, A. Lala,
J. Contreras, R. Gopalan, P. Gorevic, V. Fuster, J. Contreras, J. Kovacic, Z. Fayad.

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Icahn School of Medicine at Mount Sinai
Translational and Molecular Imaging Institute

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Rationale

- Cardiac amyloidosis (CA)
  - Deposition of insoluble fibrils in the myocardium

    Falk et al. N J Eng Med 1999
    - Restrictive cardiomyopathy
    - Conduction abnormalities, arrhythmias
    - Heart failure
  - 2 most frequent types

    Falk et al. Prog Cardiovasc Dis 2011
    - Transthyrétine (ATTR)
      - Hereditary or “Mutated” : Ile68Leu, Val30Met…
      - Senile or “Wild type”
    - Acquired monoclonal immunoglobulin light-chain (AL)

Rationale

- Non invasive diagnostic modalities
  - Echocardiography

    Falk et al. Cardiovasc Imaging 2016
    - Myocardial wall and valvular thickening
    - “Granular sparkling” appearance
    - Pericardial effusion
  - MRI

    Banypersad et al. Eur Heart J 2015

    Fontana et al. JACC Cardiovasc Imaging 2014
    - Diffuse subendocardial or transmural LGE
    - Abnormalities in T1 mapping

None of them can distinguish ATTR and AL forms

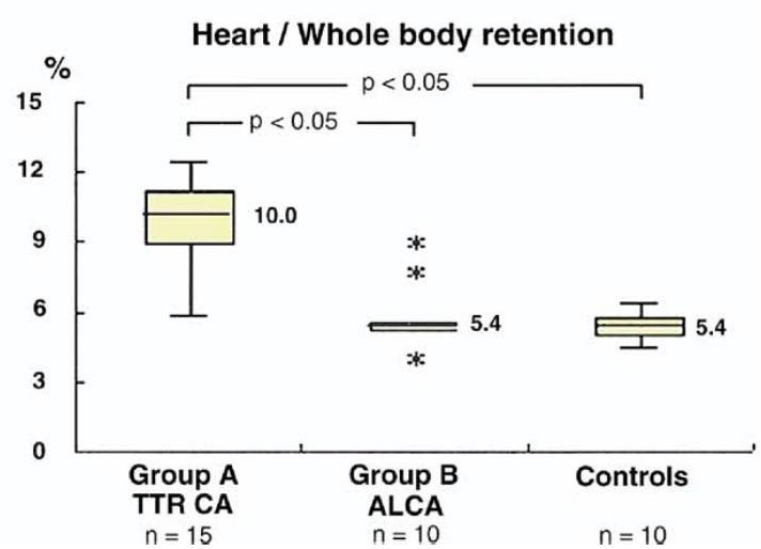
Real challenge for treatment management and prognosis

Rationale

- 99m-Tc-diphosphonate SPECT
  - Differentiation ATTR vs. AL forms
    - Diffuse uptake in ATTR

Perugini et al. JACC 2005

Rapezzi et al. Eur J Nucl Med Mol Imaging 2011



AL

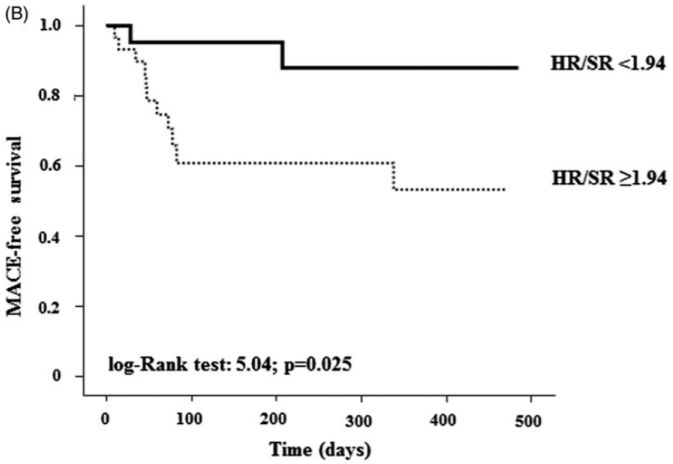
ATTR

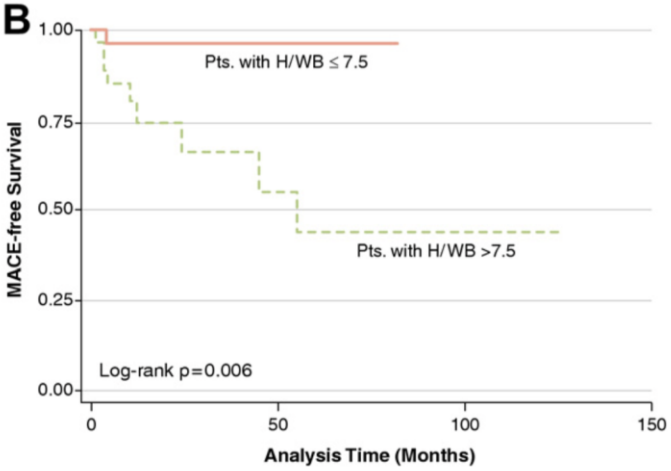
Rationale

- 99m-Tc-diphosphonate SPECT
  - Differentiation ATTR vs. AL forms
  - Prognostic information in ATTR
    - Heart retention ratios

Rapezzi et al. JACC Imaging 2011

Galat et al. Amyloid 2015

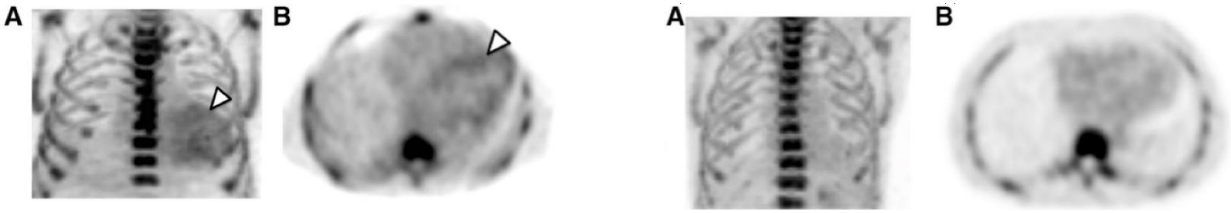




Rationale

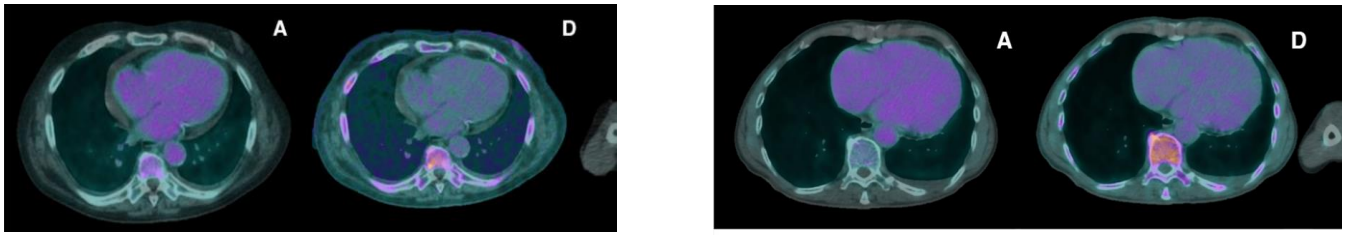
- 18F-NaF PET/CT
  - Controversial results in two series of case report
    - Higher uptake in ATTR vs AL

Van Der Gucht et al. J Nucl Cardiol 2015



    - No uptake in ATTRm or ATTRwt forms ?

Gagliardi et al. J Nucl Cardiol 2017



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Aim

- To assess usefulness of a single low radiation scan using 18F-Sodium Fluoride PET/MR imaging for:
  - Diagnosis of cardiac amyloidosis
  - Differentiation of ATTR and AL forms

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Methods

- Population
  - Consecutive patients

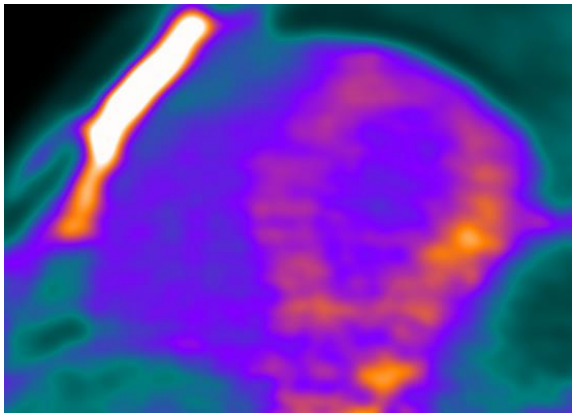
Grant NIH/NHLBI R01HL071021

    - Mount Sinai Hospital of New York
    - Histologically proven amyloidosis
    - Control group of volunteers

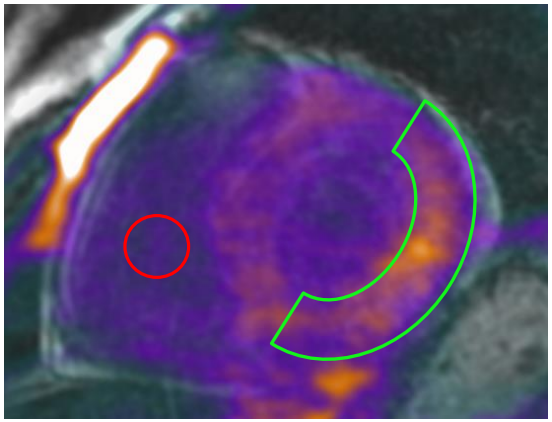
- Imaging procedure
  - PET/MR Biograph mMR system (Siemens®)
    - 90min dynamic PET after 5 MBq/Kg NaF
    - 4 classes Dixon µmap
    - T1 weighted LGE sequences after 30ml Gadolinium injection

Methods

- Image analysis
  - PET static
    - SUVmax
    - TBRmax
      - Highest uptake (green) corrected for blood pool SUVmean in RV (red)



PET



PET/MR

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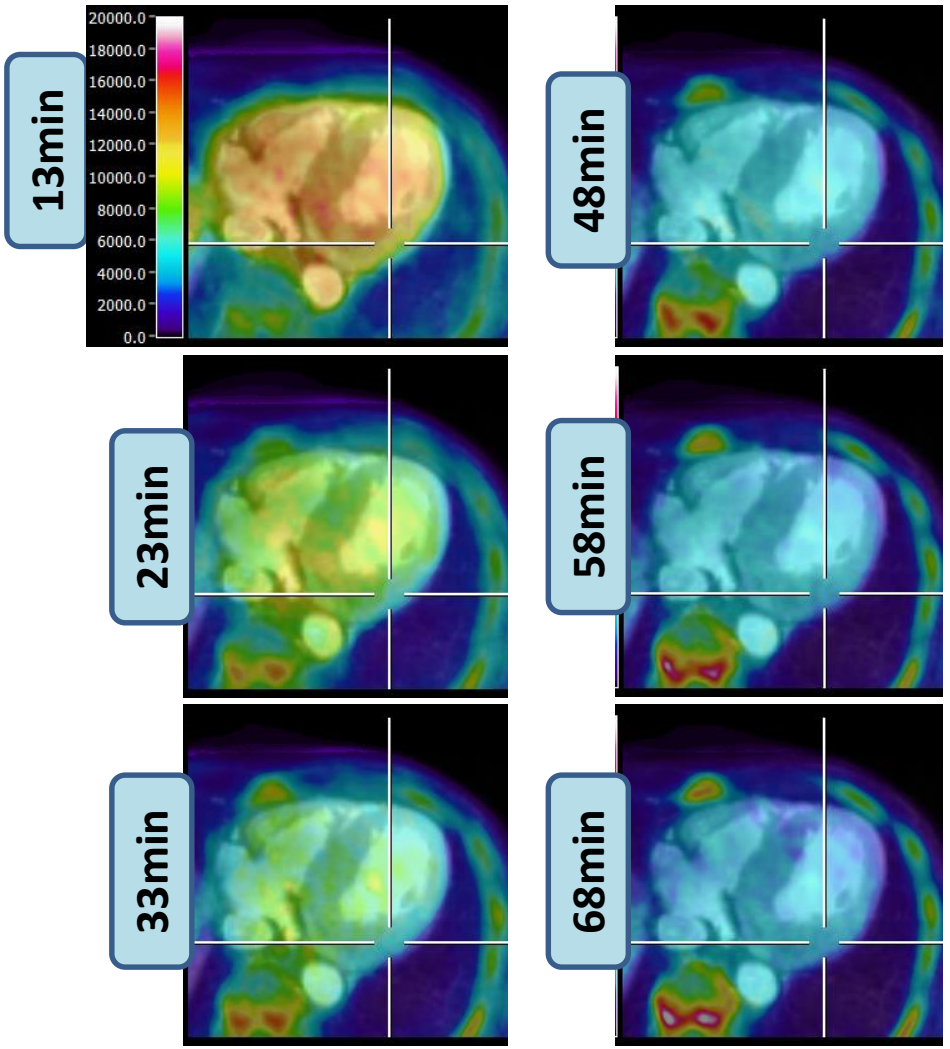
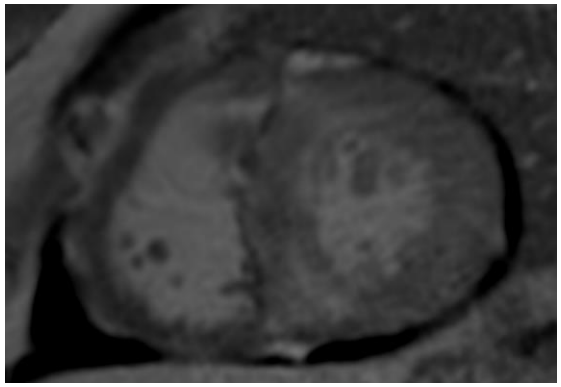
Methods

- Image analysis
  - PET static
    - SUVmax
    - TBRmax
  - PET dynamic
    - TBRmean
    - CNR



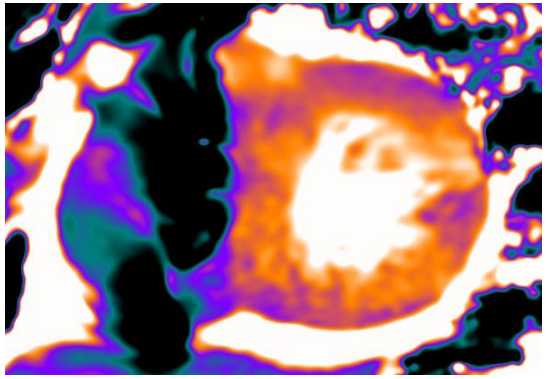
Methods

- Image analysis
  - MRI
    - LGE
    - Wall thickening
    - LVEF

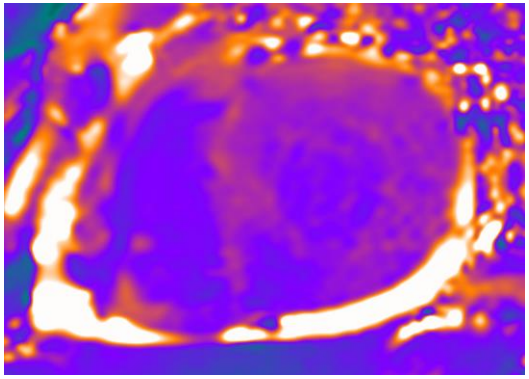


LGE MRI

- T1 values in pre-/post-contrast mapping



Pre T1



Post T1

Results

- Population (n=18)

November 2015-December 2016

  - 9 cardiac amyloidosis
    - 6 ATTR
      - 2 Ile68Leu mutated
      - 4 wild type
    - 3 AL
  - 9 control subjects
    - Healthy volunteers

	Amyloid (n=9)	Controls (n=9)
Characteristics		
Age (mean SD)	66.3 ± 8.9	56.3 ± 10.7
Gender (M/F)	8/1	4/5
Symptoms (n,%)	9 (100)	0(0)
ECG abnormalities (n,%)	6 (67)	0(0)

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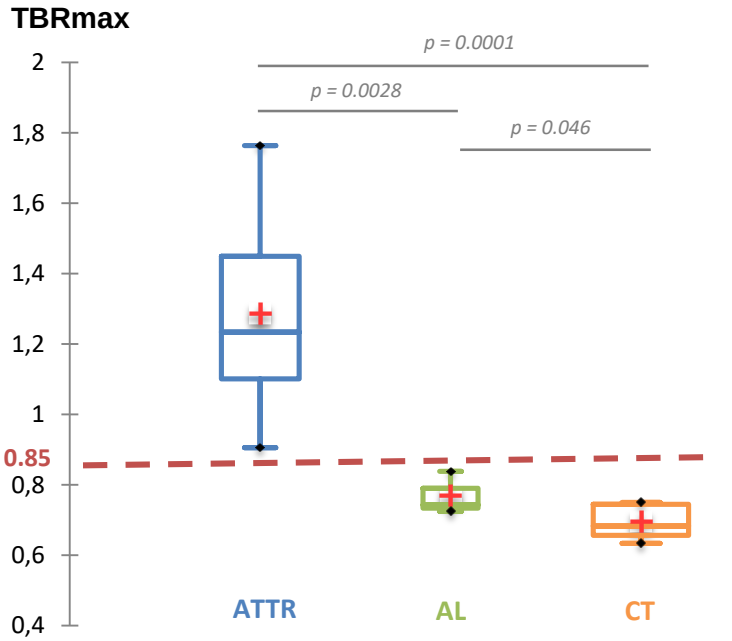
Results

- PET/MR analysis
  - Visual
    - No LGE or abnormal NaF uptake in control patients
    - Characteristic LGE in all CA with different PET patterns
      - Low NaF uptake < BP level in AL
      - Moderate NaF uptake ≥ BP level in ATTR

Results

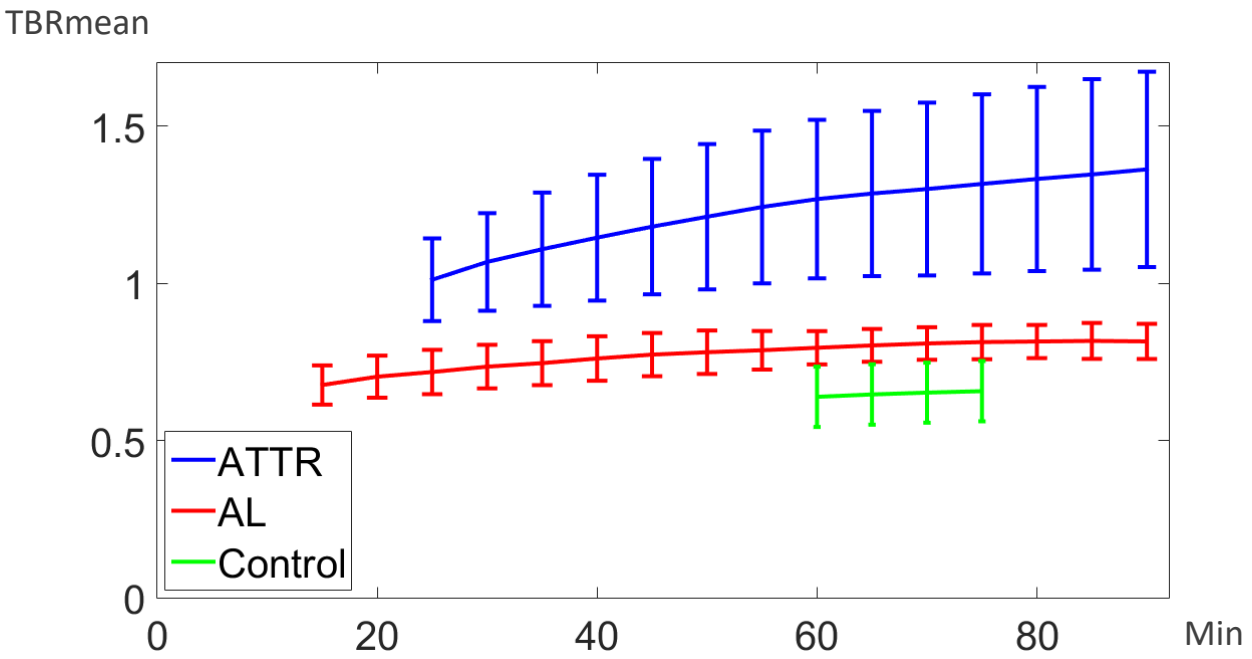
- PET/MR analysis
  - Visual
  - Quantitative

	ATTR (n=6)	AL (n=3)	p value
PARAMETERS (mean+/-SD)			
SUVmax	1.3 ± 0.3	1.2 ± 0.1	*0.526*
TBRmax	1.3 ± 0.3	0.8 ± 0.1	***0.028***
SW thickness (mm)	1.5 ± 0.4	1.5 ± 0.5	0.962
LVEF (%)	55 ± 6	63 ± 3	0.066
Pré T1 (ms)	1465 ± 134	1405 ± 26	*0.479*
Post T1 (ms)	342 ± 63	311 ± 99	*0.571*



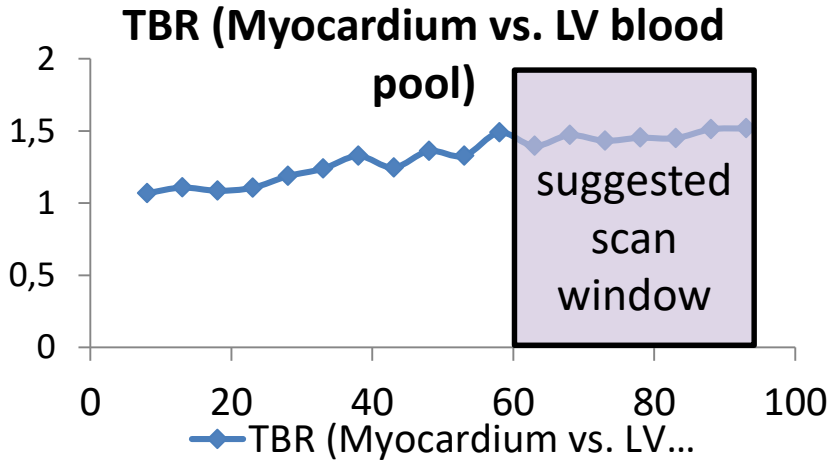
Results

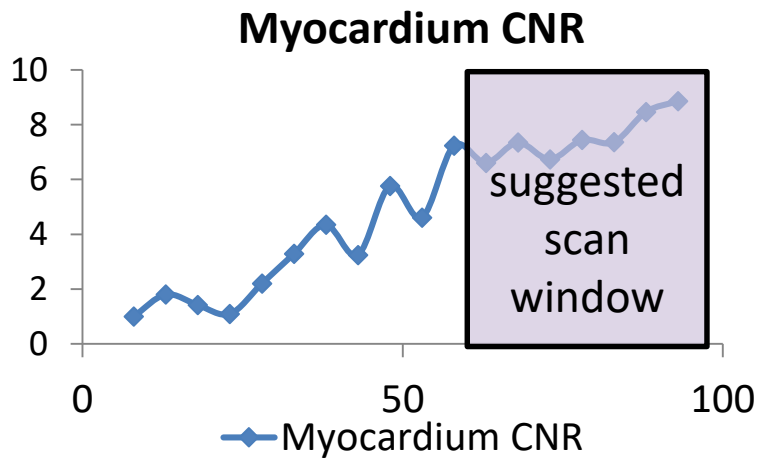
- Dynamic PET analysis
  - 3 significant different patterns of TBRmean
    - Supports previous results



Results

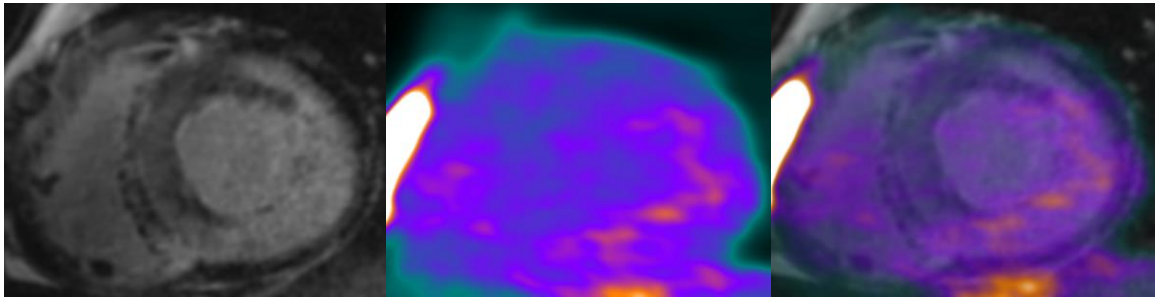
- Dynamic analysis
  - 3 significant different patterns of TBRmean
    - Supports previous results
  - Highest CNR ≥ 60min with TBR plateau
    - Suggests a 60-90min scan window





Examples

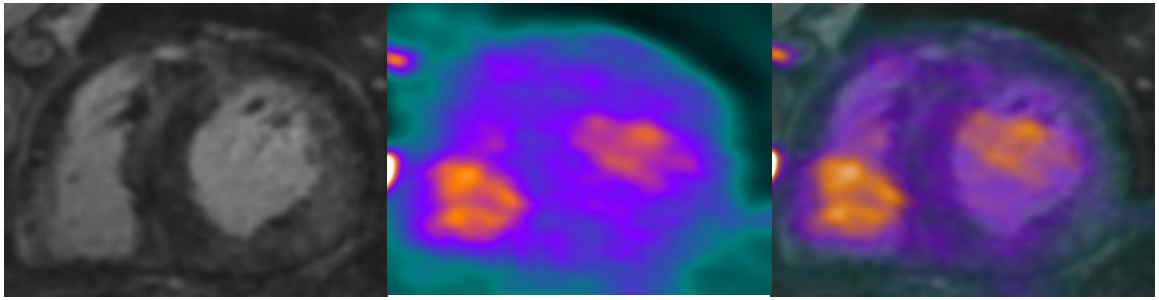
ATTR



SUVmax = 1.7

TBRmax= 1.4

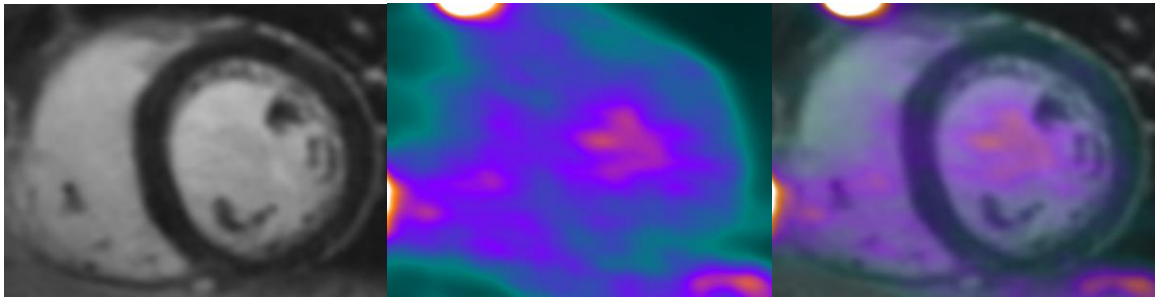
AL



SUVmax = 1.1

TBRmax= 0.7

Control



SUVmax = 0.8

TBRmax= 0.7

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Conclusions

- Usefulness of NaF PET/MR for both diagnosis of cardiac amyloidosis (LGE, T1 mapping) and differentiation of AL and ATTR (quantification) within a single scan.
  - Myocardial NaF uptake lower than the blood-pool in healthy volunteers and patients with AL.
  - By contrast increased in ATTR with a TBRmax=0.85 cut-off appearing to provide discrimination.

^{18}F-Sodium Fluoride PET/MR for the Assessment of Cardiac Amyloidosis

Maria Giovanna Trivieri, Marc R. Dweck, Ronan Abgral, Philip M. Robson, Nicolas A. Karakatsanis, Anuradha Lala, Johanna Contreras, Gagan Sahni, Radha Gopalan, Peter Gorevic, Valentin Fuster, Jagat Narula, Zahi A. Fayad

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Thanks for attention