



**Progrès réalisés
et à venir !**

Jeudi 13 juin 2024

Fondation Biermans-Lapôtre ■ PARIS

Traceurs PET des amyloses

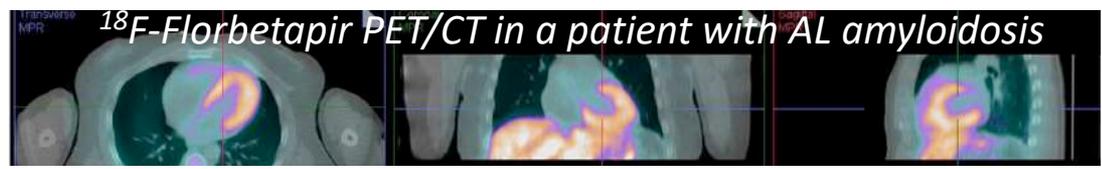
Pierre-Yves Marie

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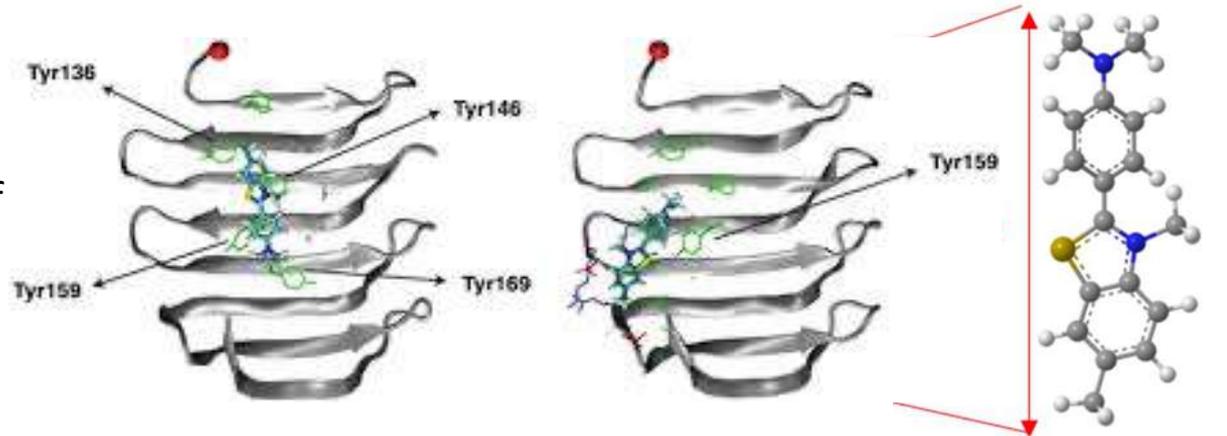
Université de Lorraine, Faculté de Médecine,

Amyloid PET/SPECT tracers



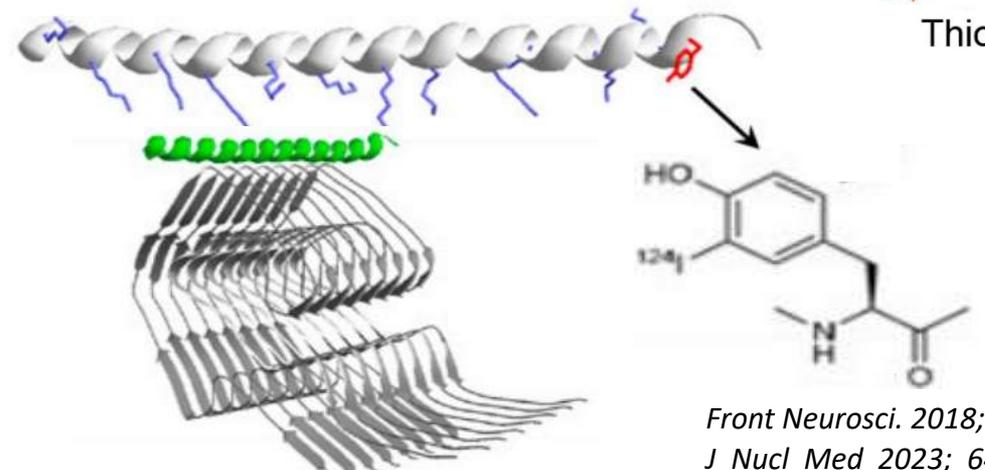
¹¹C- or ¹⁸F-labelled thioflavin-T derivatives

- binding to the beta-pleated motif of amyloid fibril
- fast kinetics (imaging < 1 hour after injection)

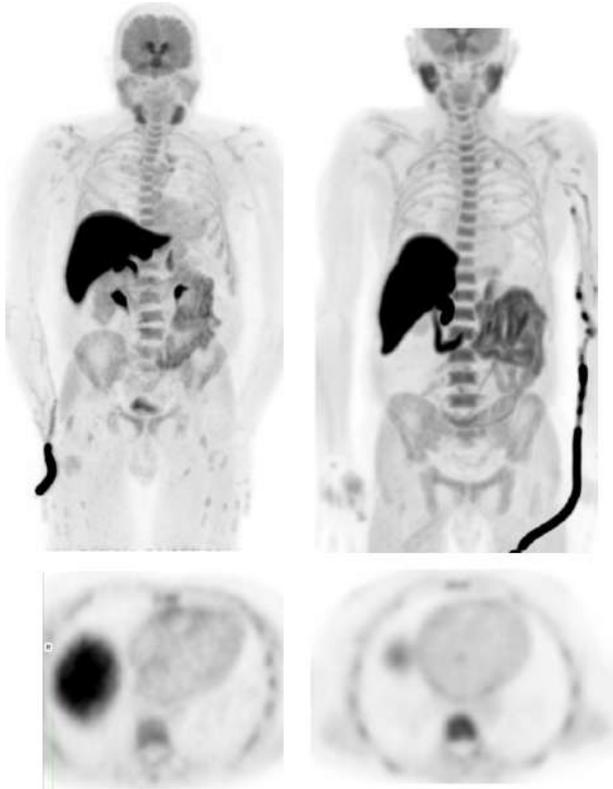


¹²⁴I- or ¹²⁵I- evuzamitide

- highly charged cationic polymer
- binding to the negative charges of amyloid fibrils
- slow kinetics



Amyloid PET tracers



¹⁸F-florbetaben: 2 patients with non-CA hypertrophic cardiomyopathies

Tracer	Half-life	Advantage
¹⁸ F-florbetapir, ¹⁸ F florbetaben, ¹⁸ F-flutemetamol	109 min	Unit dose delivery; off-label use
¹¹ C-PiB	20 min	Cyclotron needed; investigational
¹²⁴ I-evuzamitide	4.2 d	Unit dose delivery; investigational

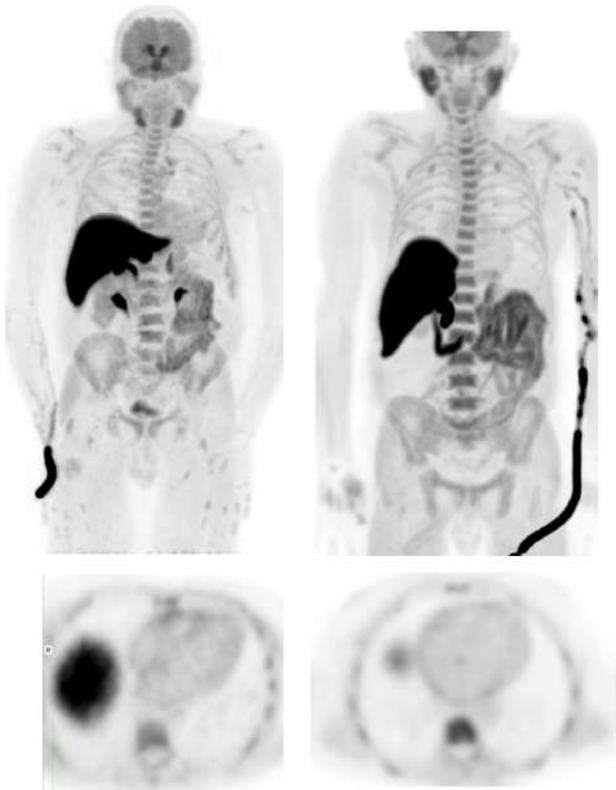
J Nucl Med 2023; 64:205

+ ¹²³I-evuzamitide SPECT 13 h Unit dose delivery
investigational

➔ **Challenges:**

- Non-specific binding due to lipophilia
- Areas of urinary and hepatobiliary clearance

Amyloid PET tracers

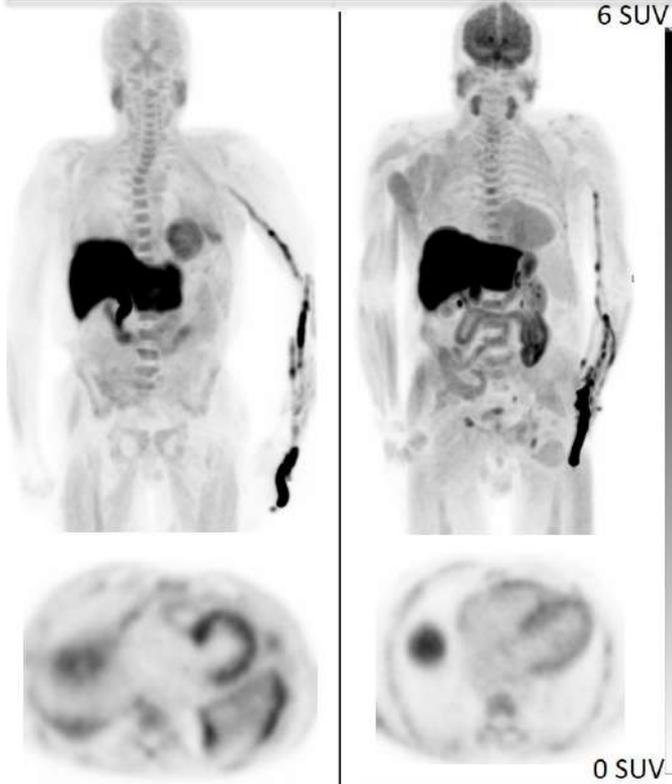


^{18}F -florbetaben: 2 patients with non-CA hypertrophic cardiomyopathies

^{18}F -florbetaben

AL patient

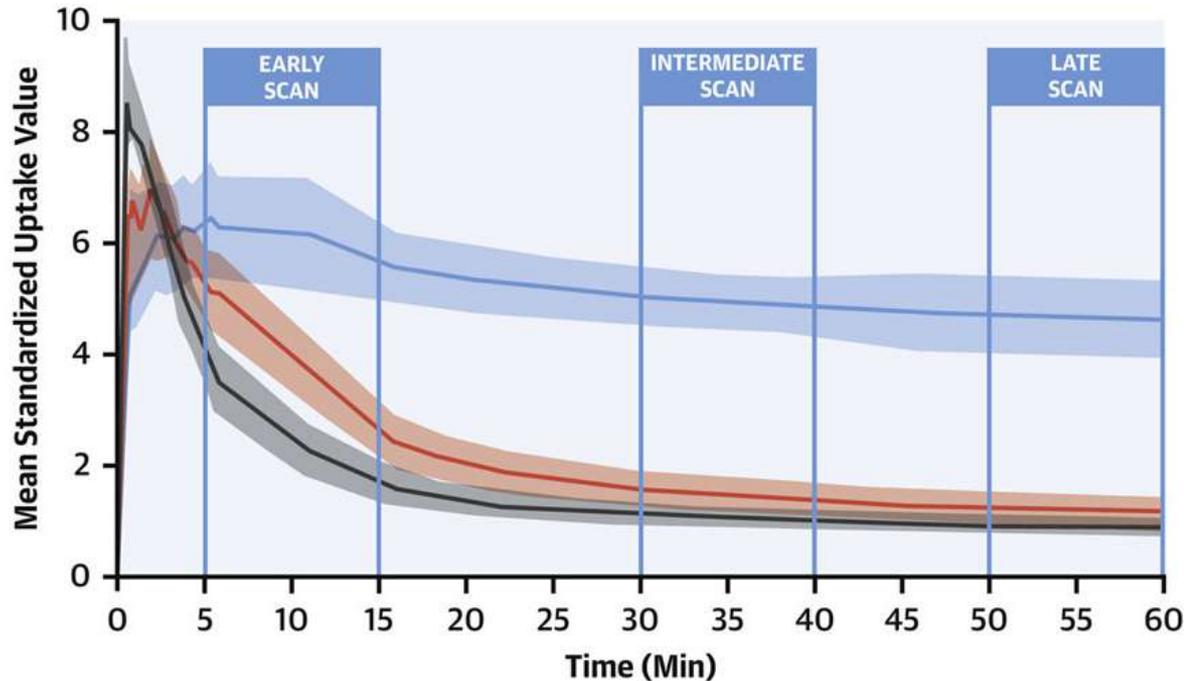
ATTR patient



Higher uptakes are observed on the heart and other organs of CA patients

Amyloid PET tracers

→ Better affinity (and diagnostic accuracy) for AL than ATTR cardiac amyloidosis



- Immunoglobulin Light-Chain Amyloidosis
- Transthyretin-Related Amyloidosis
- Non-Cardiac Amyloidosis

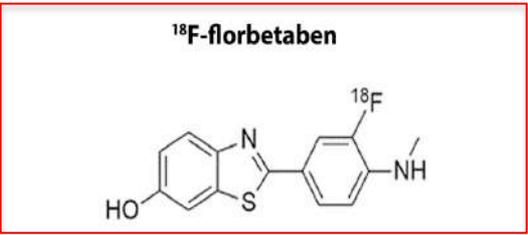
Dynamic [^{18}F]-florbetaben PET acquisitions performed in:

- ✓ 40 patients with biopsy-proven diagnoses of CA (20 ALs, 20 ATTRs)
- ✓ 20 patients diagnosed with non-CA pathology.

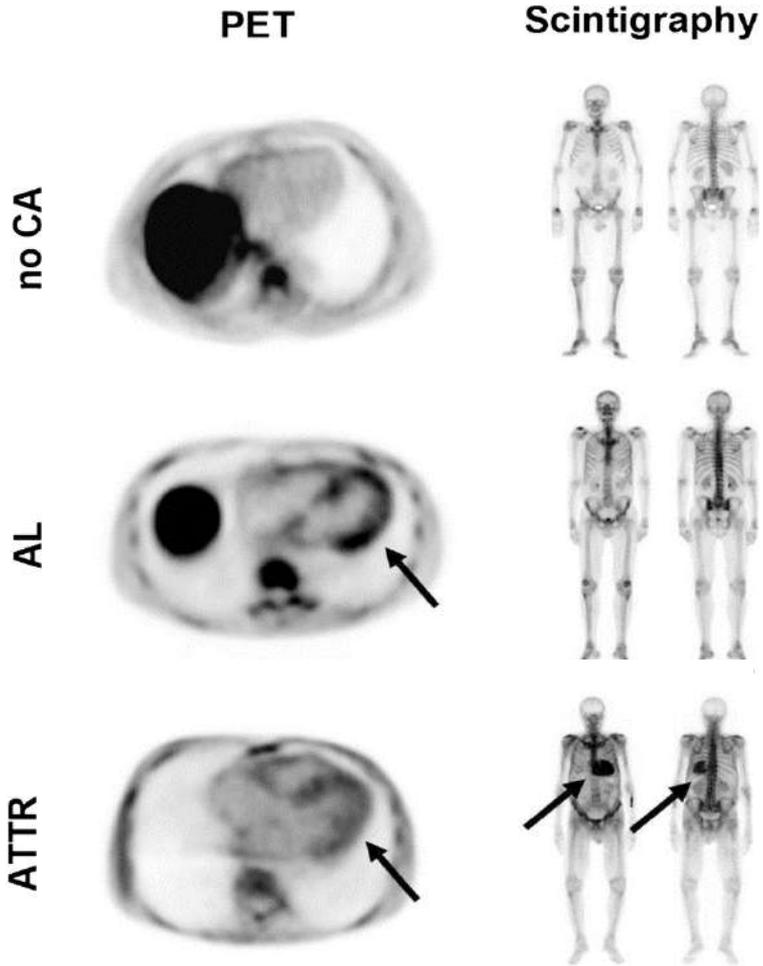
Amyloid PET tracers

What is the method of choice?

→ 1) Combining bone scintigraphy with amyloid PET tracers for the diagnosis of AL and ATTR CA



Eur J Nucl Med Mol Imaging.
2019;46(7):1407-1416.

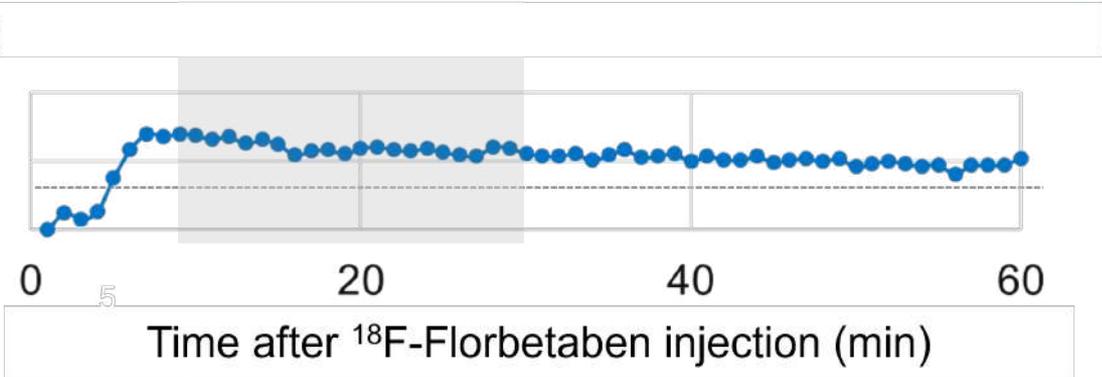


Amyloid PET tracers

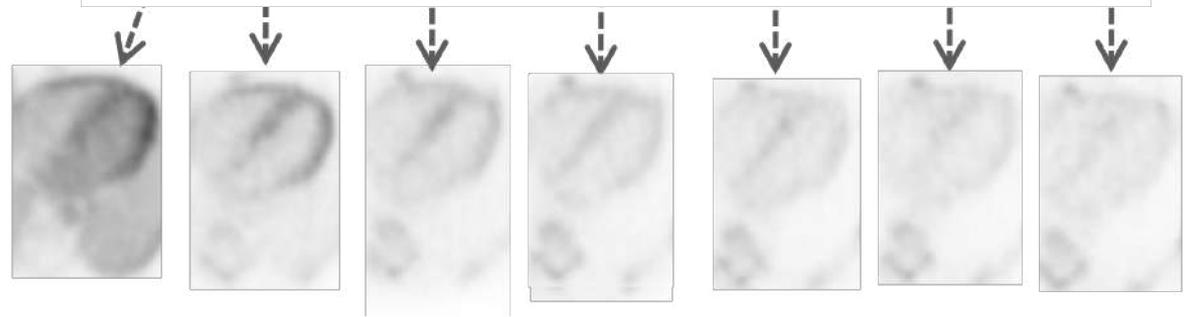
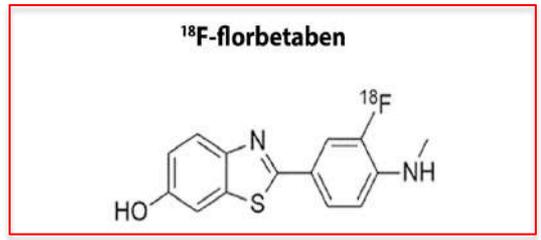
What is the method of choice?

→ 2) Determining myocardial uptake indexes

Myocardium / blood
SUV mean ratio



→ high diagnostic accuracy in preliminary results from the French multicentric CAPRI study

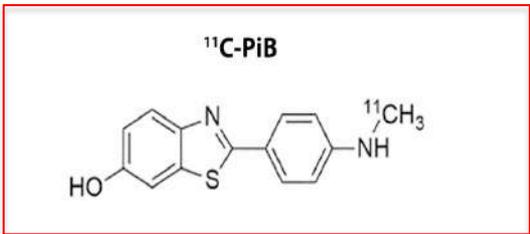


Amyloid PET tracers

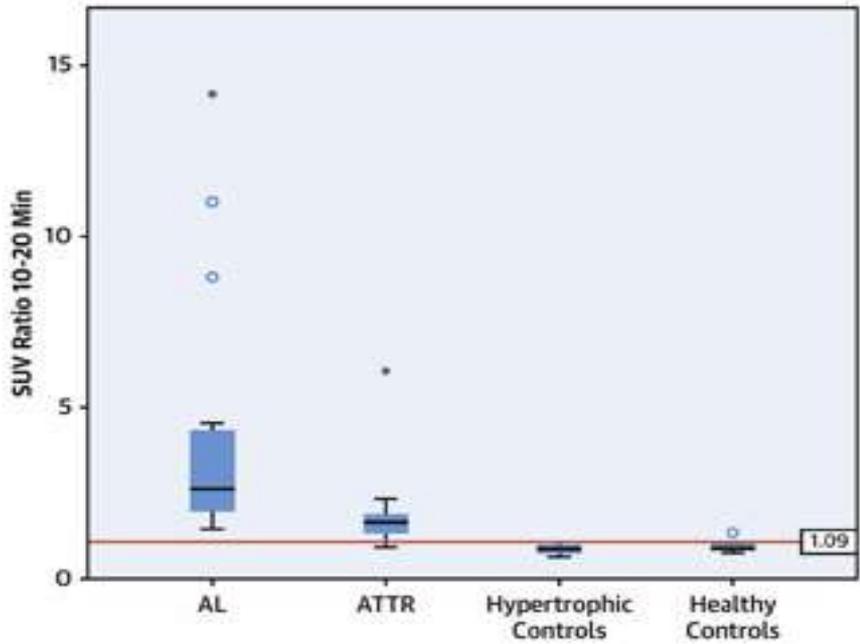
What is the method of choice?

→ 2) Determining myocardial uptake indexes:

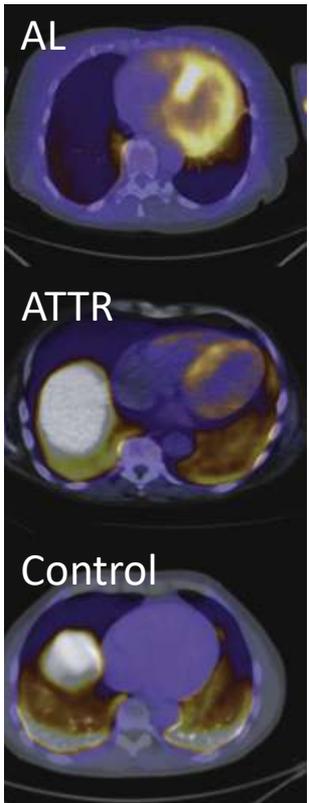
→ Discrimination of AL CA from controls and ATTR CA.



JACC Cardiovasc Imaging. 2020;13:1337.



Myocardial/blood SUV ratio determined in 36 patients with CA (15 ALs, 21 ATTRs) and 15 non-CA subjects.

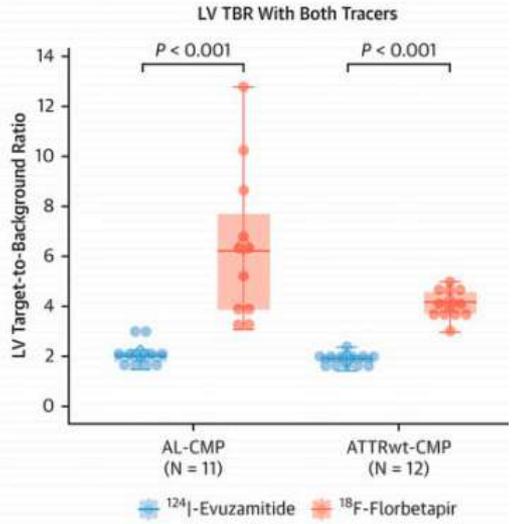
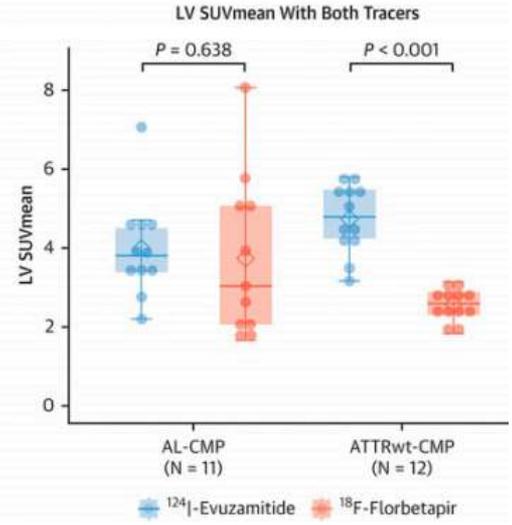
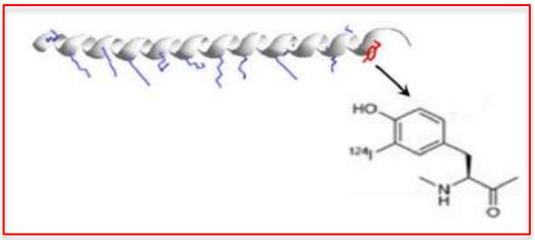


Amyloid PET tracers

What is the method of choice?

→ 3) Use of ¹²⁴I-evuzamitide

- The first pan-amyloid radiotracer
- Accurate identification of AL CA and ATTR CA
- But high blood level 5 hours after injection.



JACC Cardiovasc Imaging. 2023; 16: 1419.

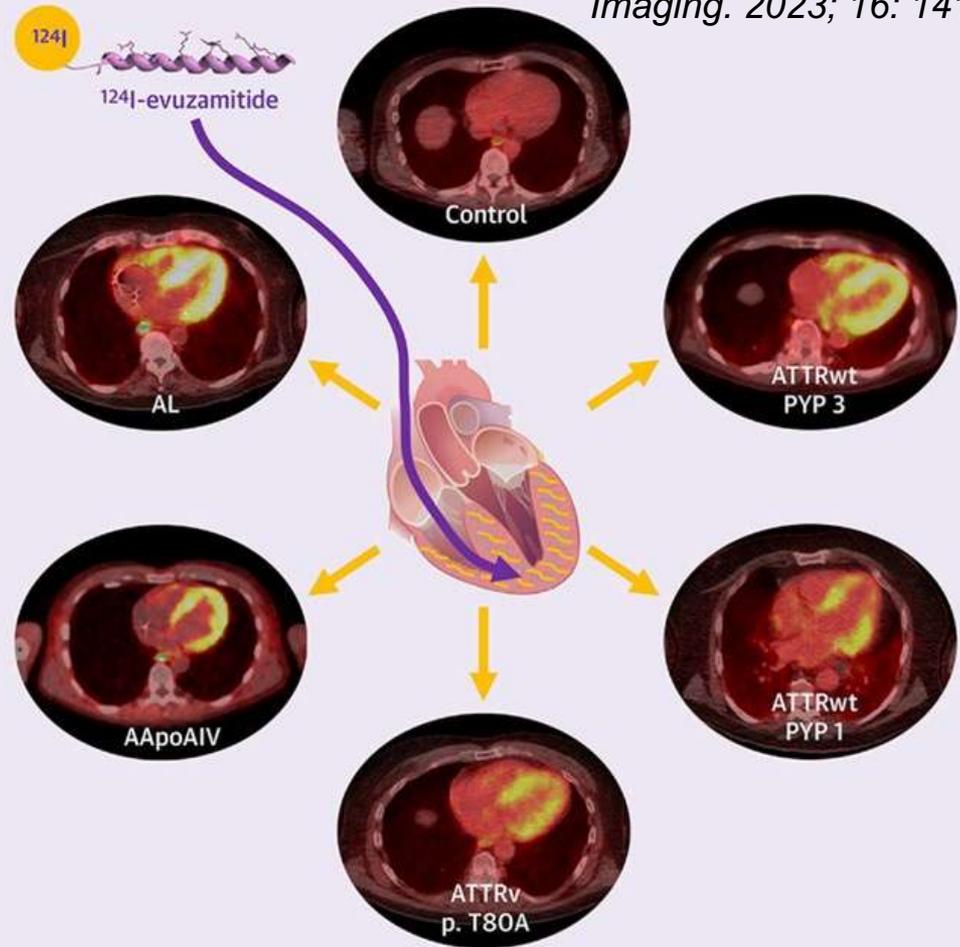
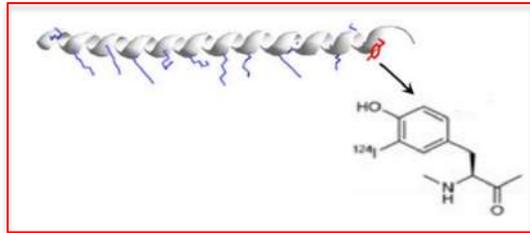
- 46 participants:
- 12 AL, 12 ATTRwt),
 - 2 hereditary amyloidosis,
 - 20 control subjects

Amyloid PET tracers

What is the method of choice?

→ 3) Use of ^{124}I -evuzamitide

- The first pan-amyloid radiotracer
- Accurate identification of AL CA and ATTR CA
- But high blood level 5 hours after injection.

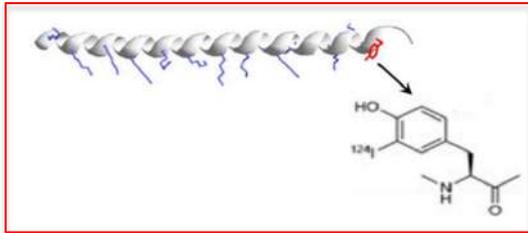


Amyloid PET tracers

What is the method of choice?

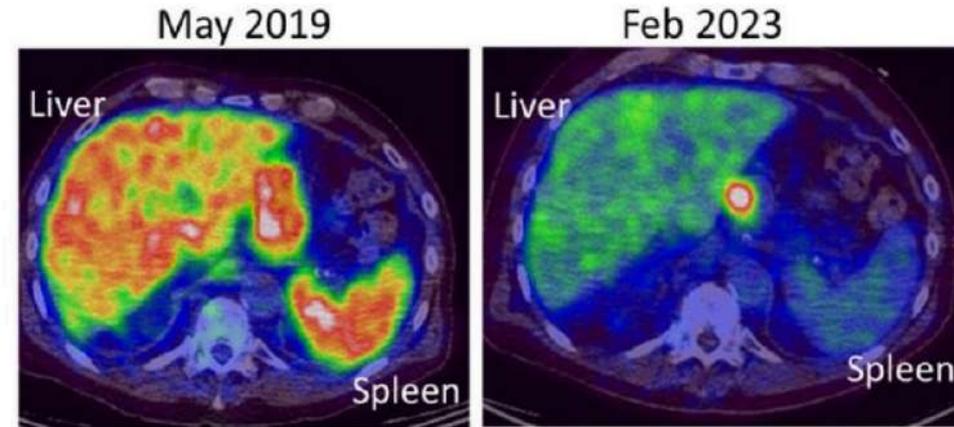
→ 3) Use of ^{124}I -evuzamitide

- The first pan-amyloid radiotracer
- Accurate identification of AL CA and ATTR CA
- But high blood level 5 hours after injection.
- Possible quantification of hepatic and renal amyloid



Lands R, et al. Longitudinal PET/CT imaging with iodine (^{124}I) evuzamitide reveals organ response to plasma cell immunotherapy in a patient with AL amyloidosis.

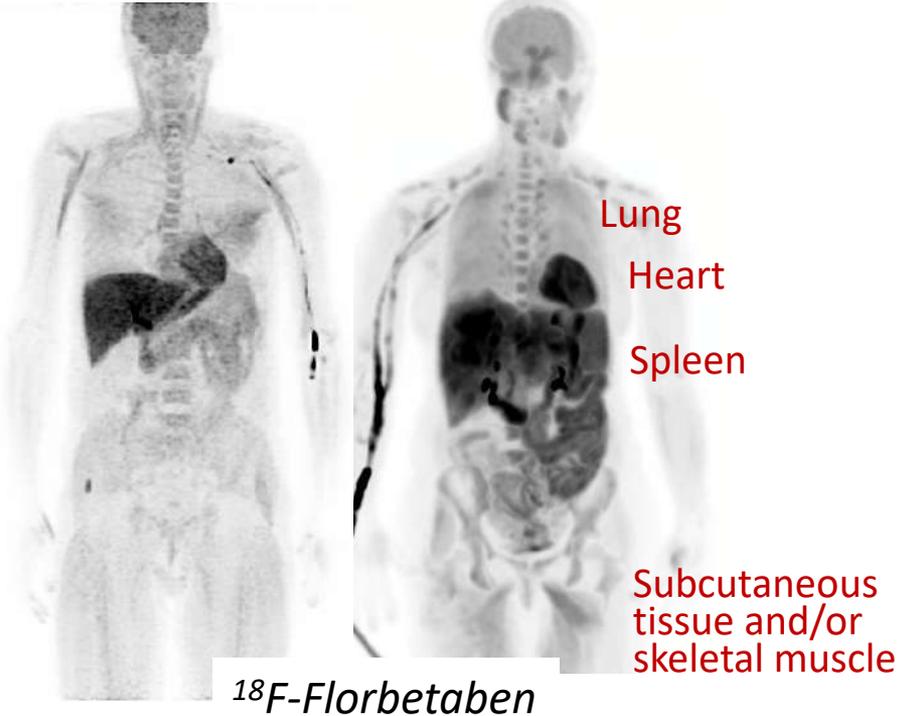
Amyloid. 2024;31(2):148-149.



Amyloid PET tracers

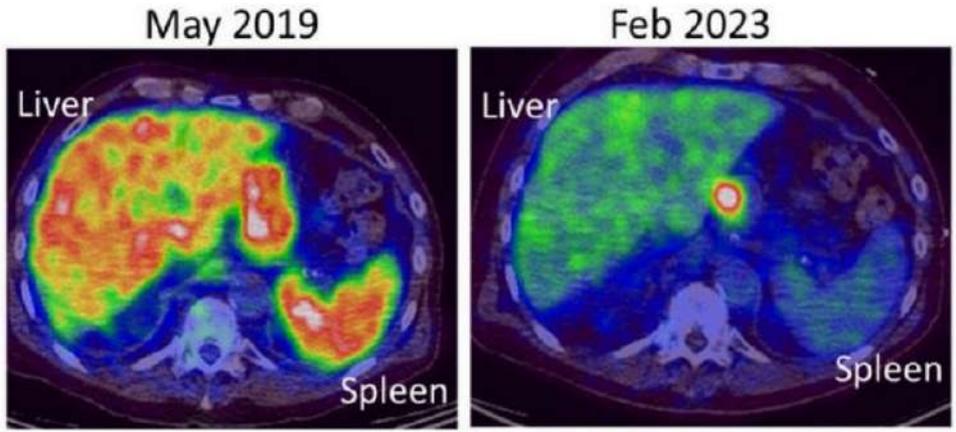
For assessing a whole-body amyloid charge?

Two AL patients from the CAPRI study



Lands R, et al. Longitudinal PET/CT imaging with iodine (¹²⁴I) evuzamitide reveals organ response to plasma cell immunotherapy in a patient with AL amyloidosis.

Amyloid. 2024;31(2):148-149.

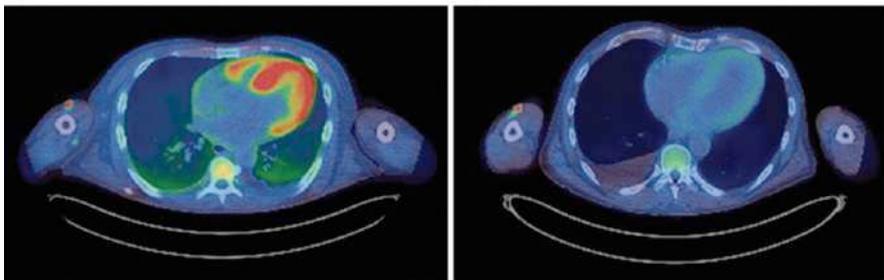


Amyloid PET tracers

For monitoring the treatment of AL patients?

Manwani R. et al. A pilot study demonstrating cardiac uptake with ^{18}F -florbetapir PET in AL amyloidosis patients with cardiac involvement.

Amyloid. 2018;25(4):247-252.

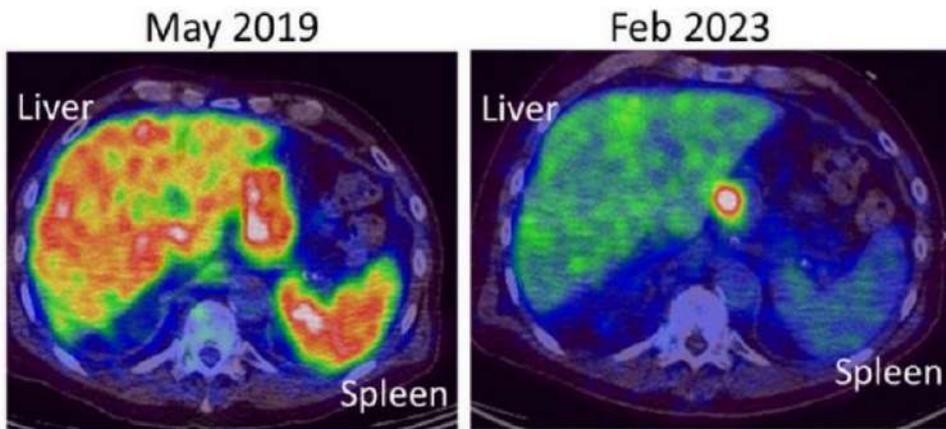


Prior chemotherapy initiation

After chemotherapy (complete response)

Lands R, et al. Longitudinal PET/CT imaging with iodine (^{124}I) evuzamitide reveals organ response to plasma cell immunotherapy in a patient with AL amyloidosis.

Amyloid. 2024;31(2):148-149.



May 2019

Feb 2023

Liver

Liver

Spleen

Spleen

Amyloid PET tracers

For determining the prognosis of AL patients?

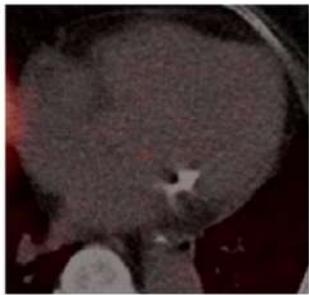
Choi YJ, et al. Independent prognostic utility of ¹¹C-Pittsburgh compound B PET in patients with light-chain cardiac amyloidosis. *J Nucl Med.* 2022;63:1064

Conventional Serum Biomarkers

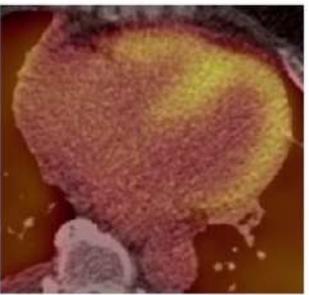


Troponin I
NT-proBNP
Free light chain difference

¹¹C-PIB PET/CT

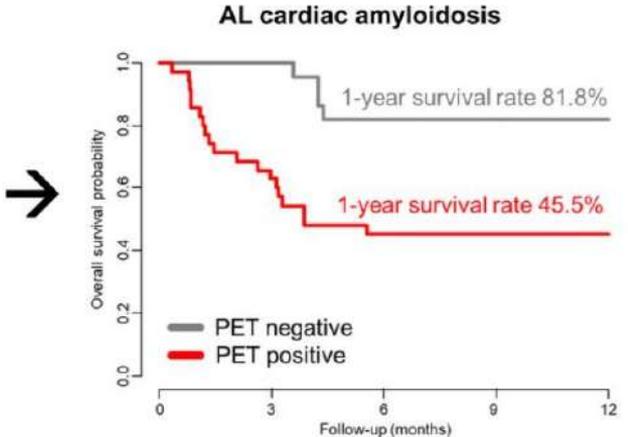


Negative



Positive

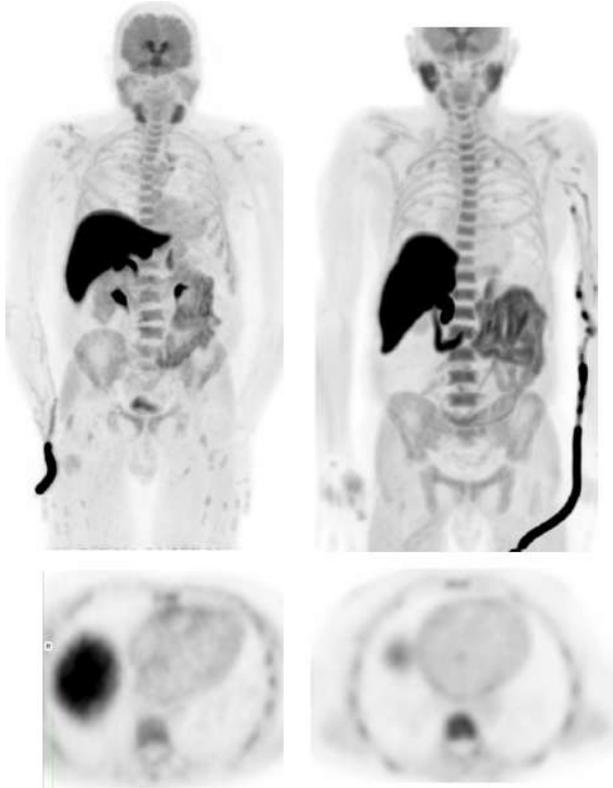
Improvement of Outcome Prediction



Traceurs PET des amyloses : Conclusion

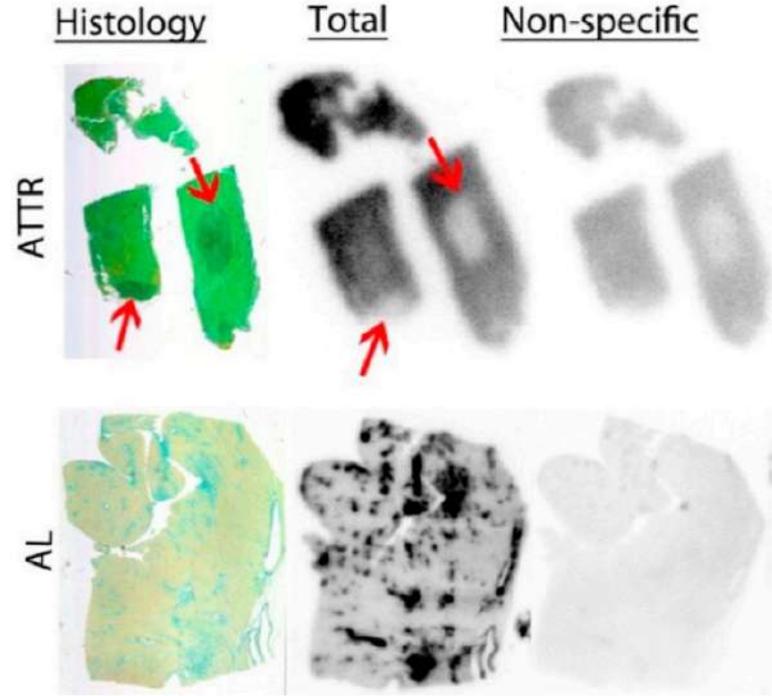
- La capacité des traceurs « Thioflavine-like » à **identifier l'amylose AL** est établie.
 - ✓ extensions d'indication envisagées pour ^{18}F -Flutemetamol et ^{18}F -Florbetaben
 - ✓ mais le coût est élevé (1 200 euros)
- **Etudes supplémentaires** nécessaires pour les évaluations :
 - ✓ des formes ATTR
 - ✓ du pronostic, de l'effet des traitements et la charge amyloïde globale dans les AL
- Les **polymères cationiques** constituent une nouvelle famille de traceurs de l'amylose
 - ✓ imageries PET mais aussi SPECT potentiellement possibles
 - ✓ sans les captations aspécifiques des traceurs lipophiles
 - ✓ mais clearance sanguine lente

Amyloid PET tracers



^{18}F -florbetaben: 2 patients with non-CA hypertrophic cardiomyopathies

^{18}F -florbetapir binding



Circ Cardiovasc Imaging. 2015;8:10.



Challenges:

- Non-specific binding due to lipophilia
- Areas of urinary and hepatobiliary clearance