ASNC 2025

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A Tale of Two Tracers – A Qualitative Comparison of the PET and SPECT Amyloid-Imaging Agents, ^{124}I-evuzamitide (AT-01) and ^{99m}Tc-p5+14 (AT-05), that are Derived from the Same Synthetic Amyloid-Binding Peptide, p5+14

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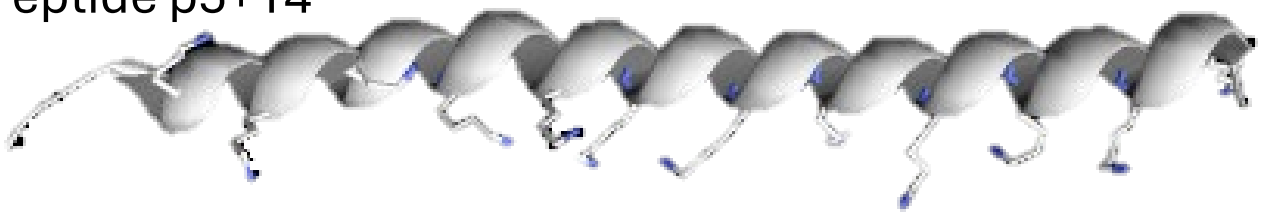
The Goal

- The goal was to develop tools that enable the detection of amyloid throughout the body and facilitate the widespread, accurate, early detection and diagnosis of amyloidosis.
- The approach was to generate both PET/CT and SPECT/CT imaging agents for maximal flexibility of use.
- Pan-amyloid imaging capabilities – For AL, ATTR, and the other 18 rare types of systemic amyloidosis. Make use of our pan-amyloid reactive peptide designated p5+14.
- Resource-tailored use: In regions without PET/CT facilities or access to iodine-124 (globally), ^{99m}Tc-p5+14 could enable amyloid imaging broadly. Where PET/CT is available, ^{124}I-evuzamitide offers superior image resolution.
- Disease monitoring and prognostication

Structure of Radiolabeled p5+14 and Amyloid Binding Hypotheses

Peptide p5+14

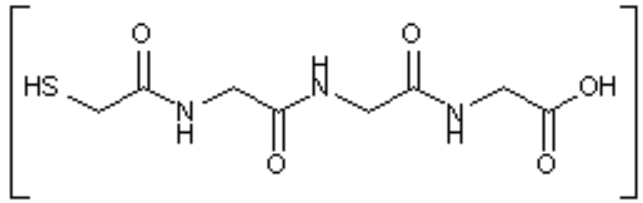


iodination site

GGGYS **K**AQ**K**A QA**K**QA **K**QAQ**K** AQ**K**AQ A**K**QA**K** QAQ**K**A Q**K**AQA **K**QA**K**Q

putative Tc-99m binding site

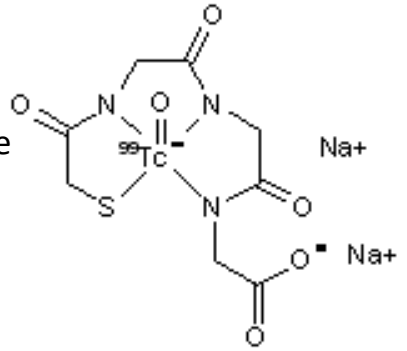
amyloid fibril and glycosaminoglycan binding site



mercaptoacetyltriglycine

[^{99m}Tc]pertechnetate

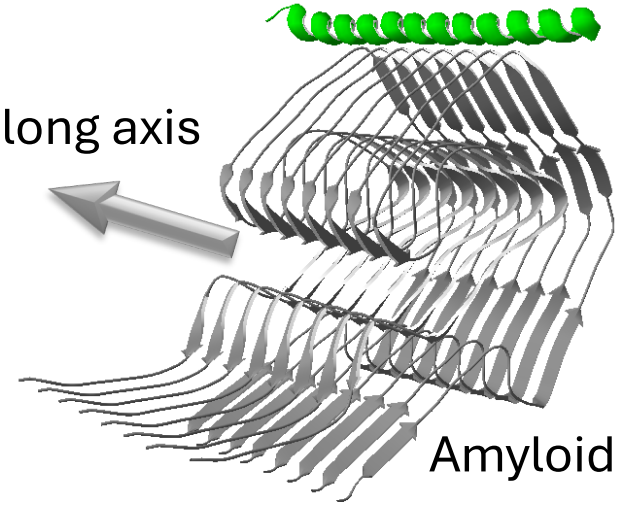
$SnCl_2$



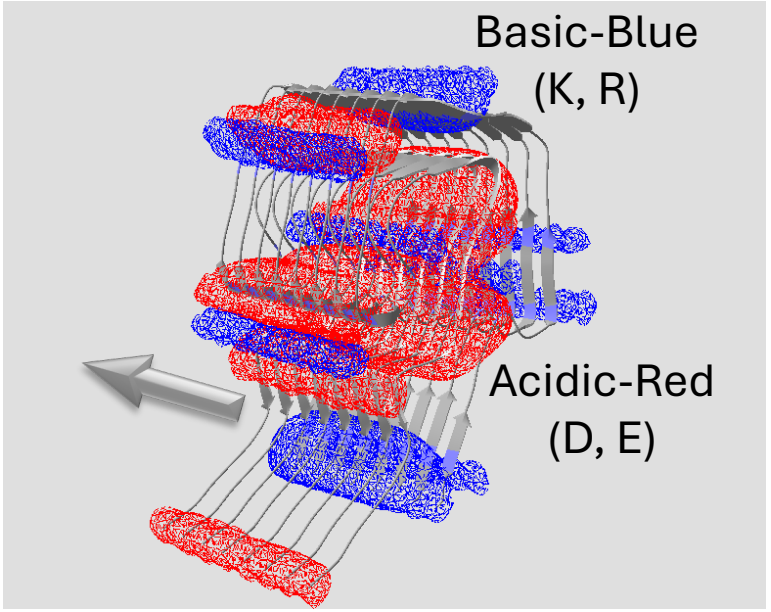
Technetium-99m-labeled mercaptoacetyltriglycine ([^{99m}Tc]MAG3)

Peptide p5+14

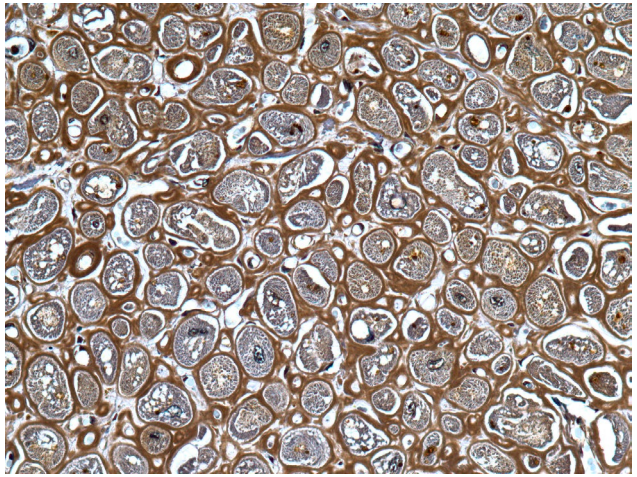
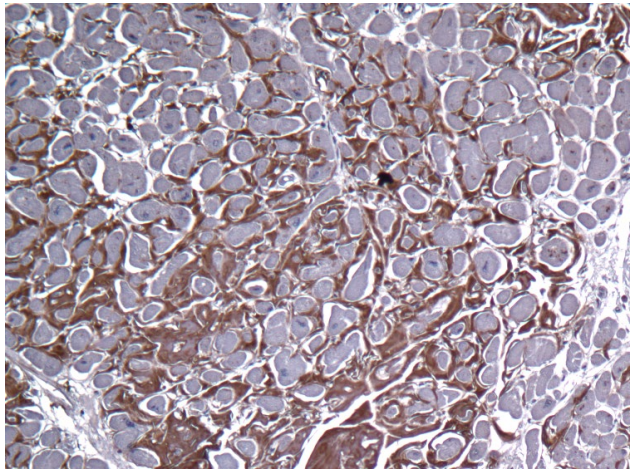
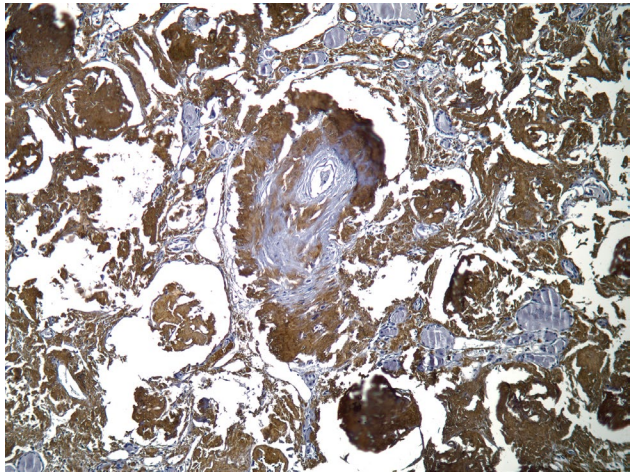
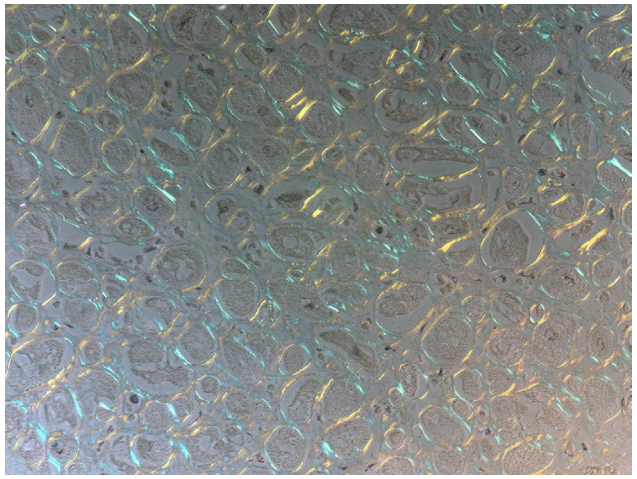
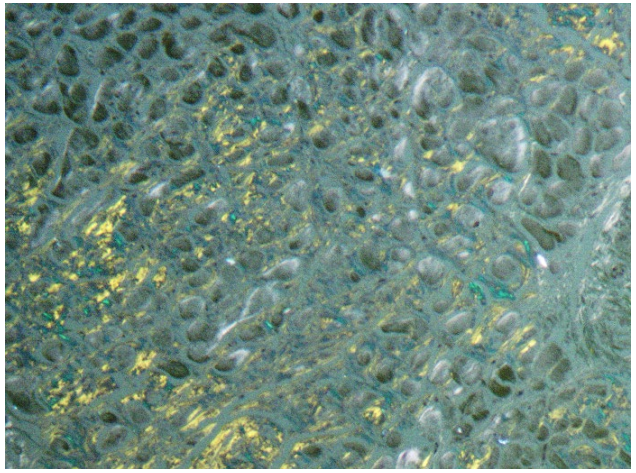
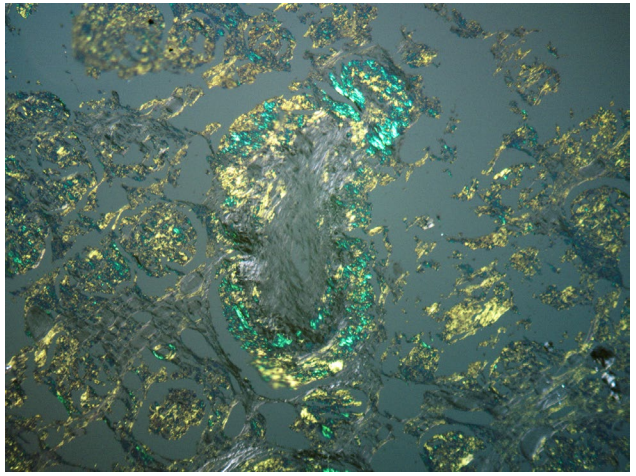
Fibril long axis



Amyloid fibril

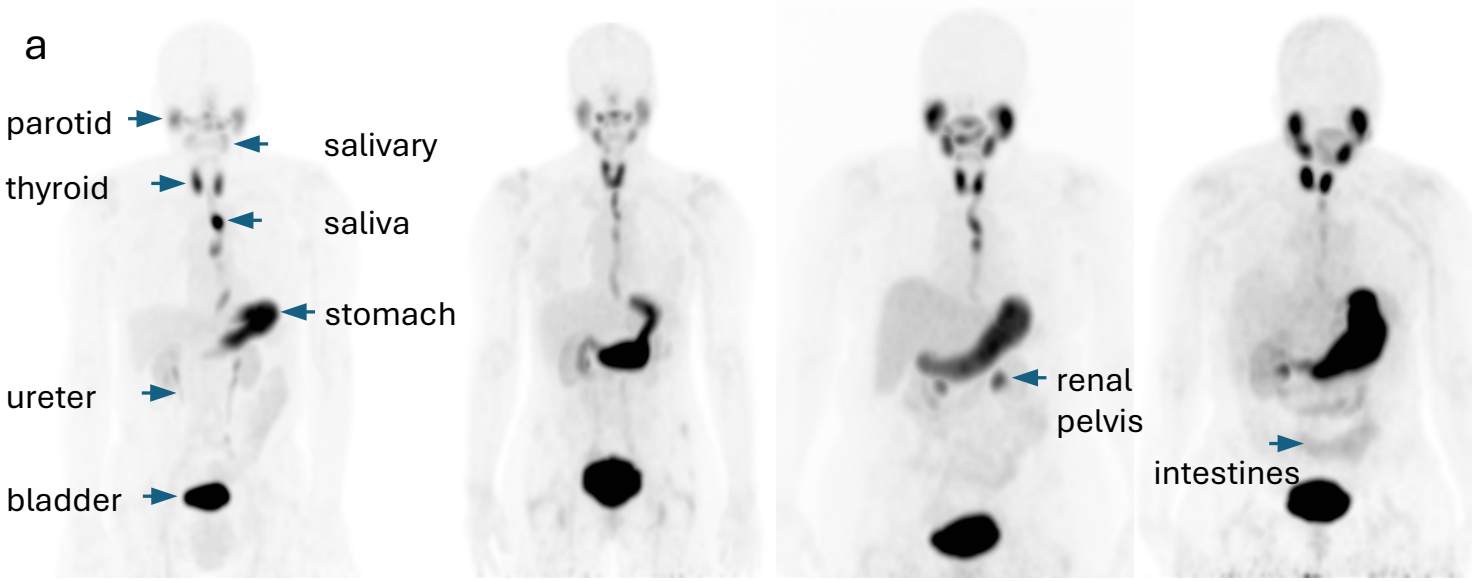


Binding of Biotinyl-p5+14 to Tissue Amyloid

	AL Heart	ATTR Heart	AL Kidney
Biotin-p5+14			
Congo red			

Physiologic Distribution of Radiolabeled p5+14 in Healthy Volunteers

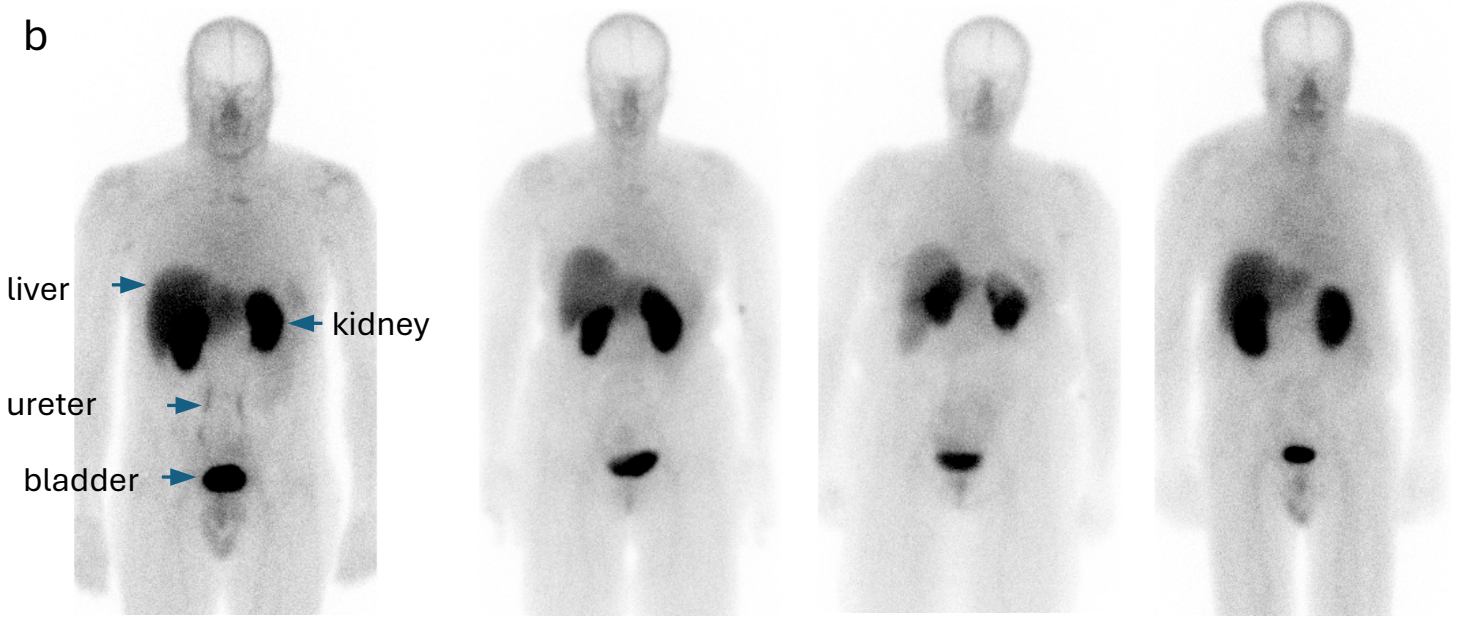
^{124}I-evuzamitide
(5 h pi)



^{124}I-evuzamitide

- Parotid gland
- Salivary gland
- Saliva
- Thyroid
- Stomach lumen
- Ureter
- Urinary bladder
- *Intestines*

^{99m}Tc-p5+14
(1 h pi)



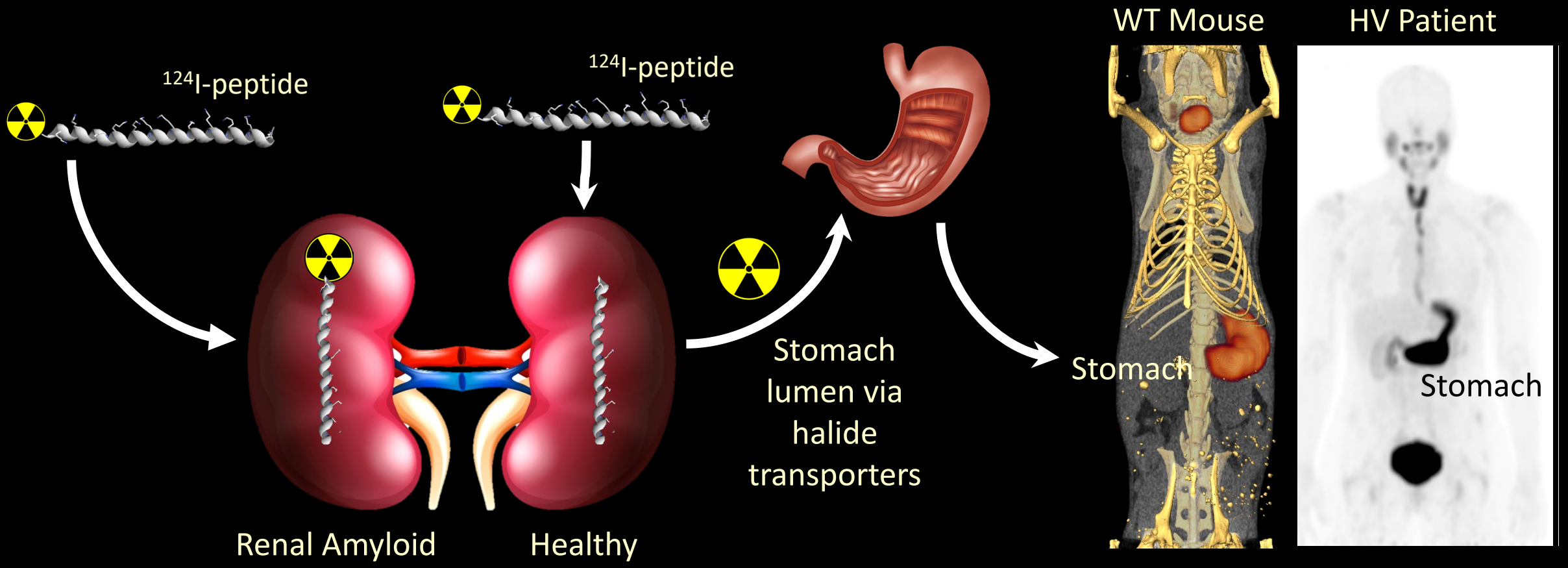
^{99m}Tc-p5+14

- Liver
- Kidney
- Ureter
- Urinary bladder
- *Intestines*

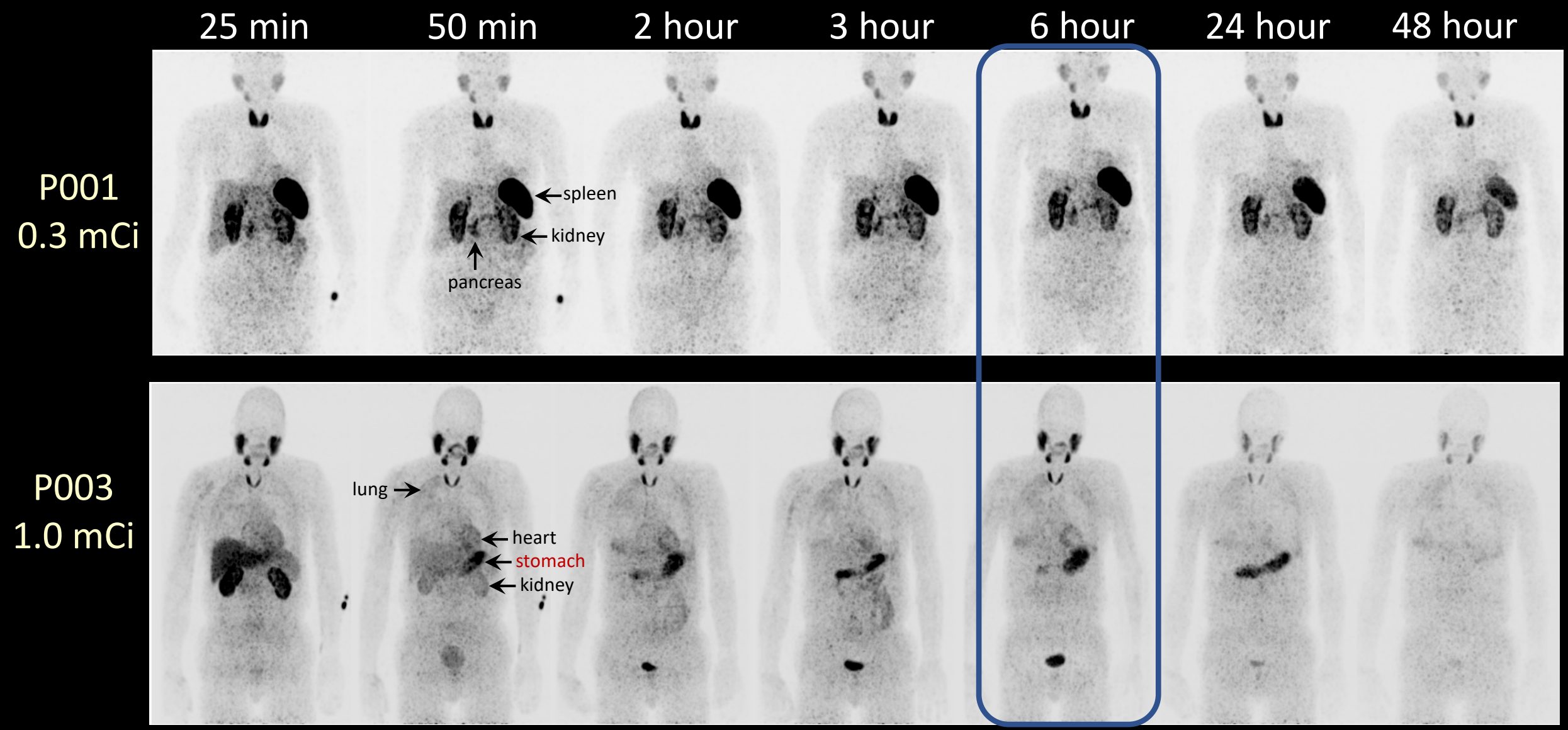
Why use iodine-124 for PET imaging of the p5+14?

We take advantage of enzymes in the kidneys and liver (dehalogenases) that strip the iodide from the peptide that is not bound to amyloid (in intracellular compartments).

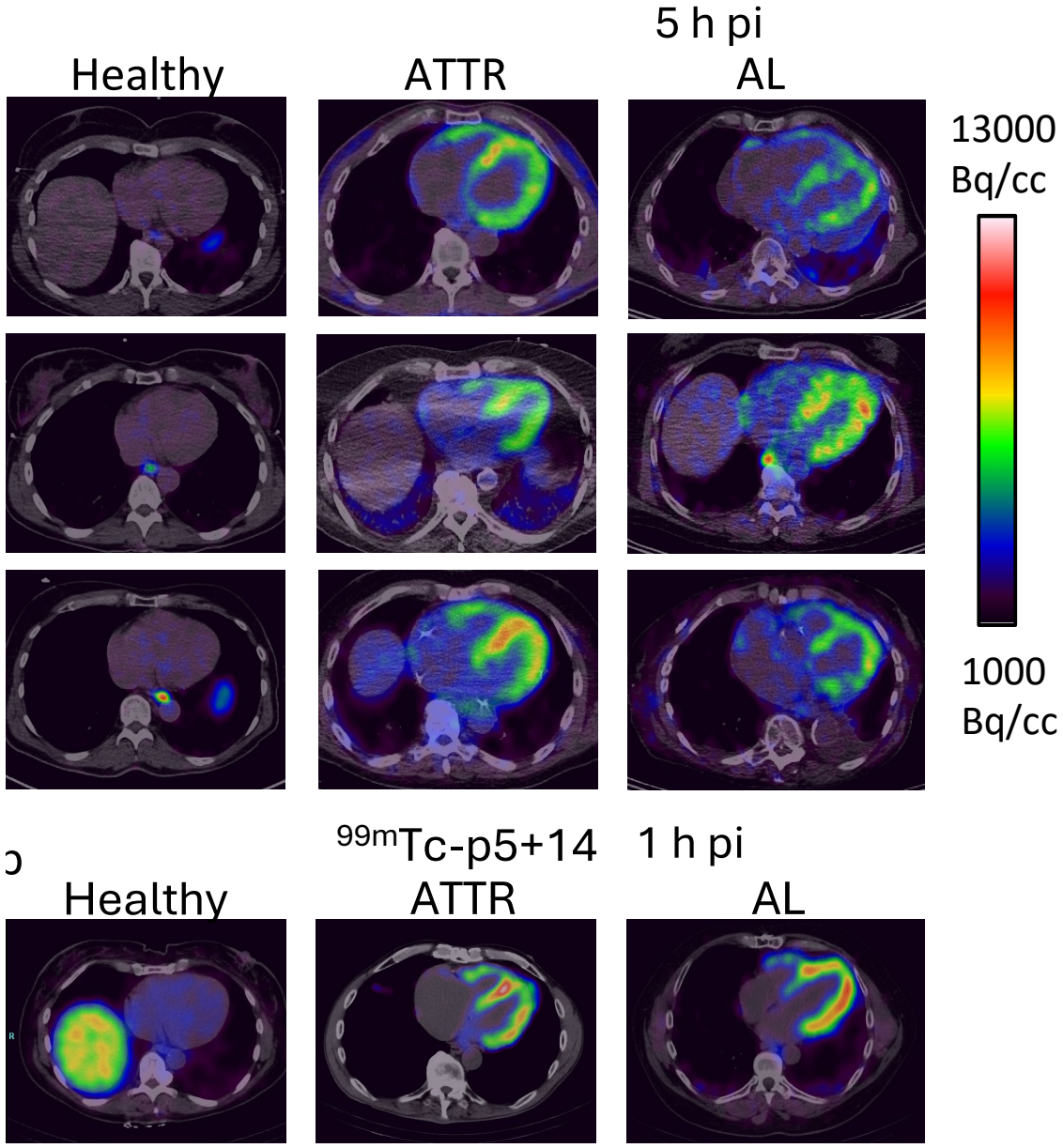
This allows us to choose a time post injection when we can image the kidney amyloid, which is a problem in most type of systemic amyloidosis.



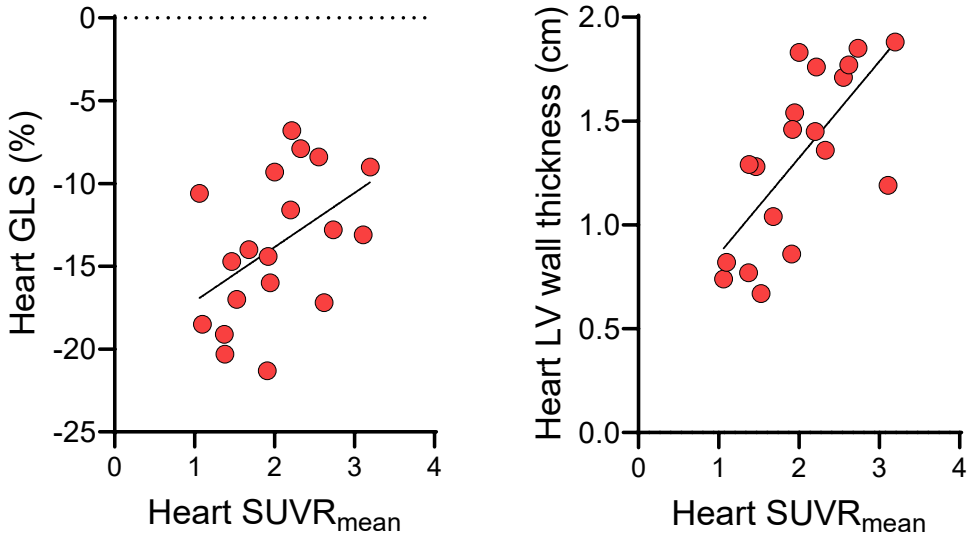
^{124}I-Evuzamitide Clearance in AL Patients



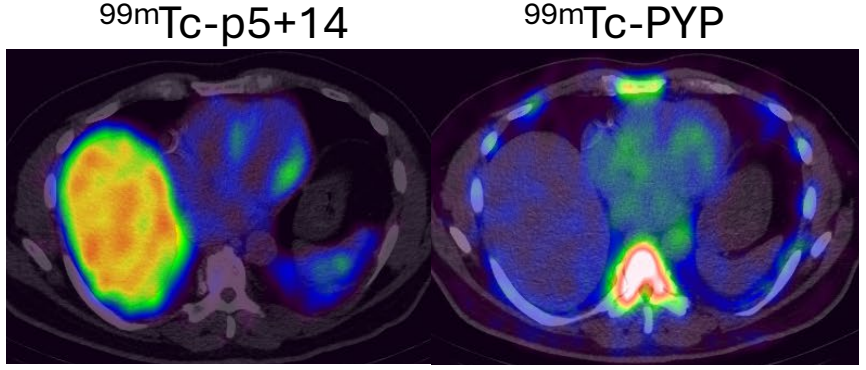
Cardiac Uptake of Radiolabeled p5+14



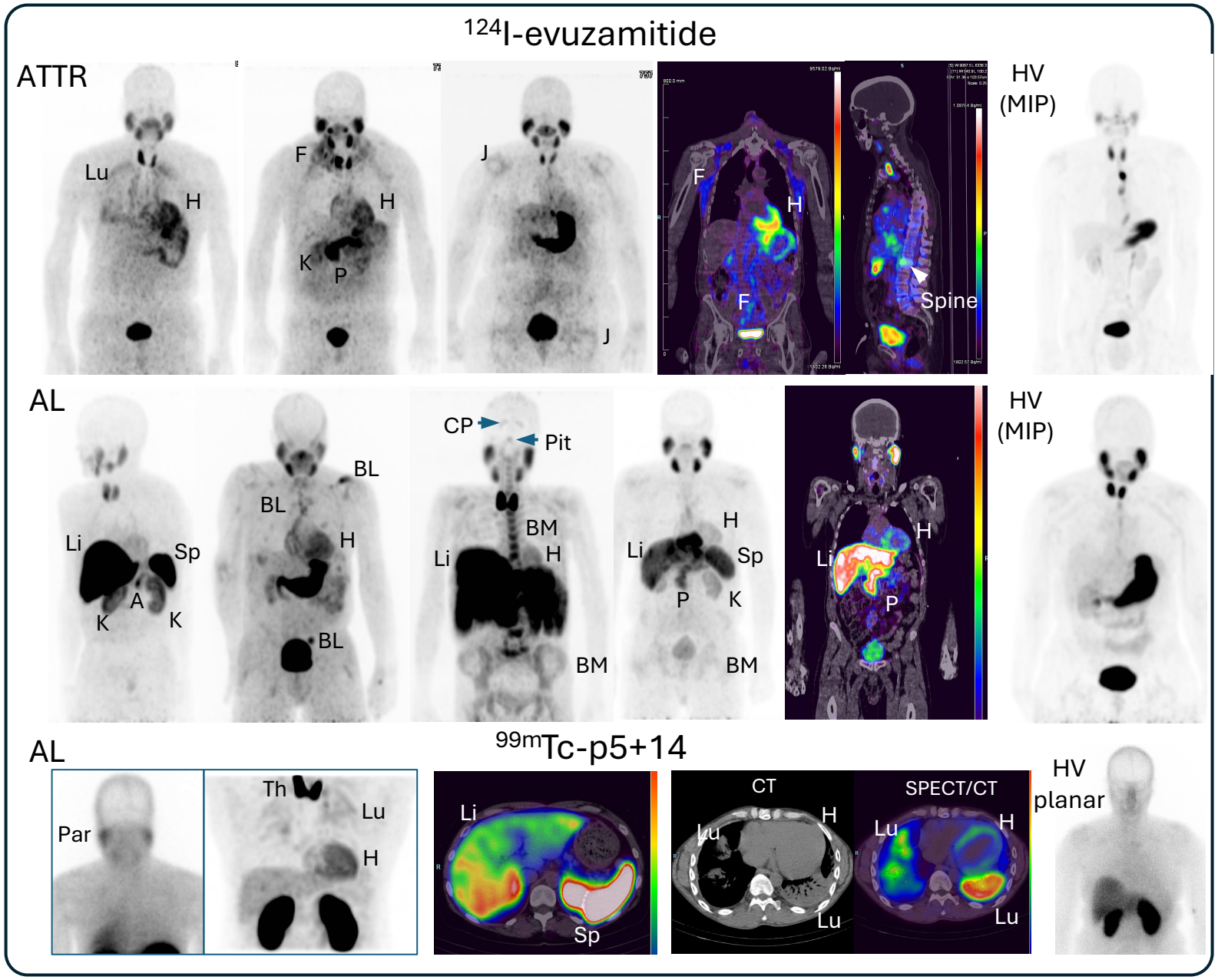
Uptake of ^{124}I-evuzamitide Correlates with Measures of Cardiac Function and Structure and QoL

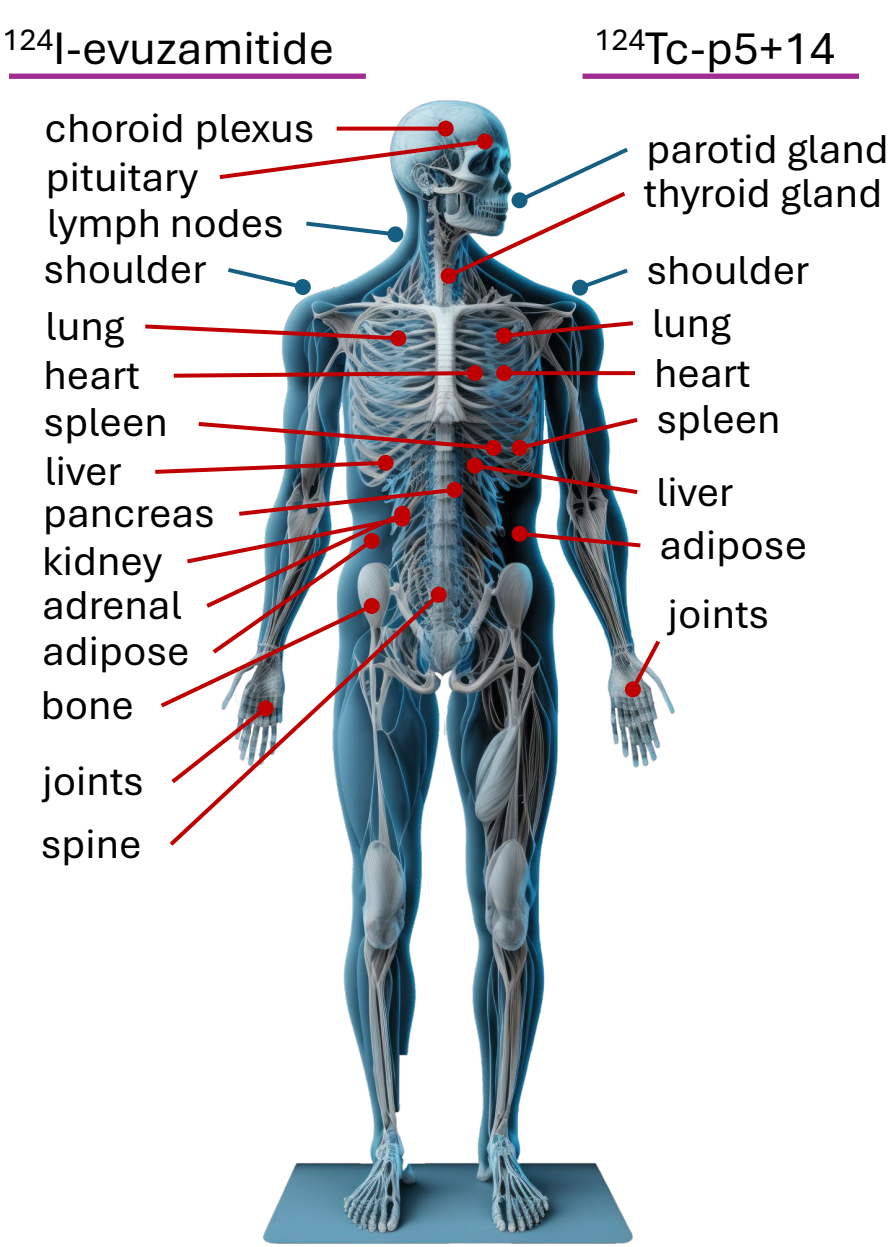


Uptake of ^{99m}Tc-p5+14 (1 h pi) may Detect Early Cardiac Amyloid



Extracardiac Uptake of Radiolabeled p5+14





Summary

- **^{124}I-evuzamitide (PET)**:
  - *High resolution and quantitative imaging*. Enabling accurate assessment of early focal as well as diffuse amyloid deposits.
  - *High sensitivity*. Demonstrated ~96% cardiac detection in AL and ATTR patients with amyloidosis, with uptake observed in multiple organs.
  - *Therapy monitoring*. Quantitative PET/CT imaging may allow tracking changes in organ-specific amyloid load in response to therapy.
  - *Whole-body imaging*. PET/CT can survey all organs in one study that can be rapidly performed.
  - *Regulatory support*. BTD has been granted by the US FDA. Orphan drug designation has been granted for AL and ATTR, both in the US and European Union. The Phase 3 REVEAL study is underway with results expected in early 2026 (NCT06788535). – Dr. Dorbala and Spencer Guthrie.
- **^{99m}Tc-p5+14 (SPECT)**:
  - *Accessibility*. Technetium-99m is generator-produced and radiotracer synthesis is rapid. Kits can be developed allowing widespread adoption; SPECT cameras are ubiquitous.
  - *Rapid imaging workflow*. Scans at 1 h post-injection fit routine practice.
  - *Pan-amyloid binding*. Like ^{124}I-evuzamitide, it binds and images both AL and ATTR amyloid.

Acknowledgements

The patients and their families for participating

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