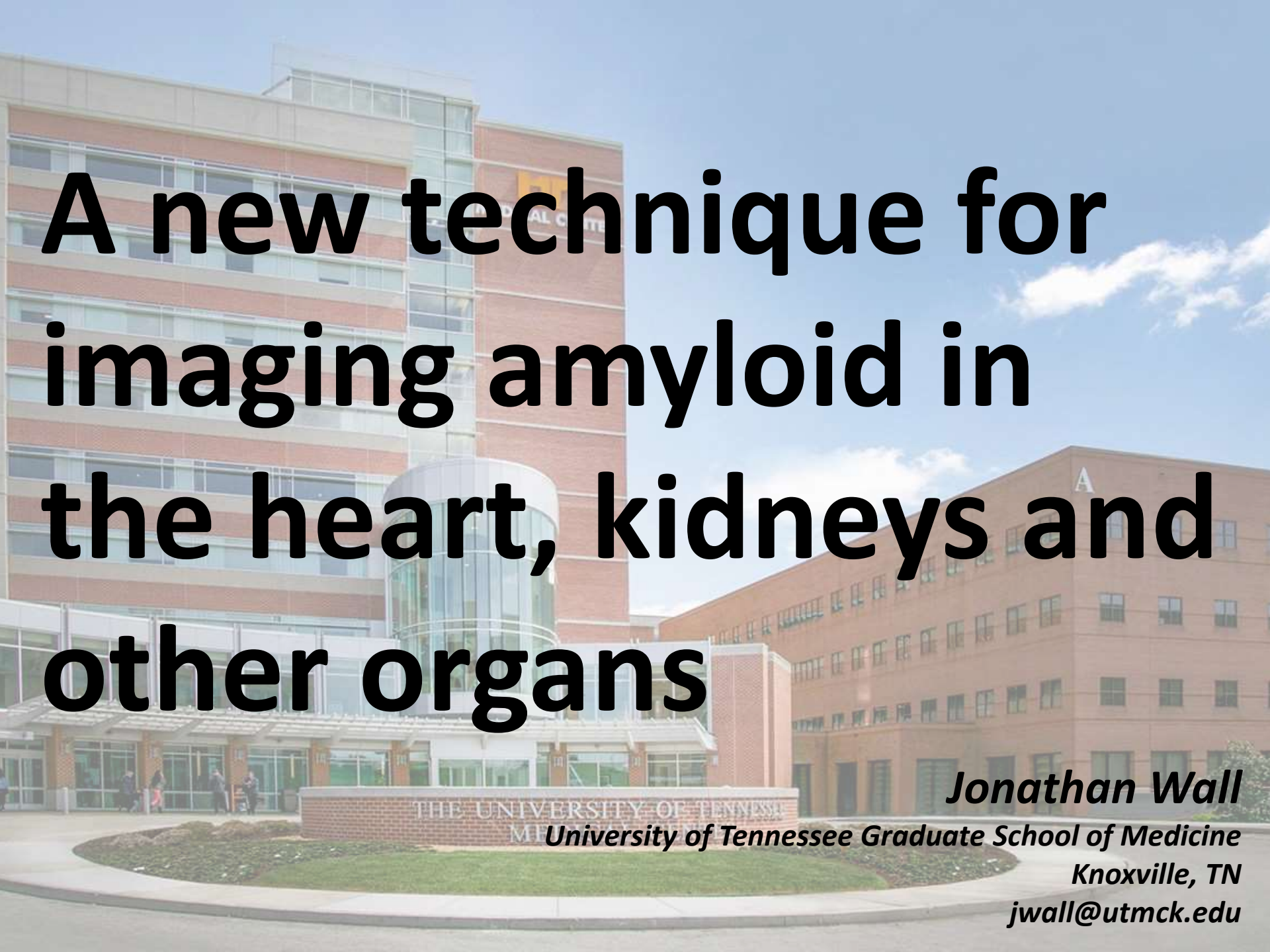

A new technique for imaging amyloid in the heart, kidneys and other organs

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NIH National Institute of Diabetes and Digestive and Kidney Diseases

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amyloidosis foundation

Pharmaceutical Industry

THE UNIVERSITY OF TENNESSEE MEDICAL CENTER
Wisdom for Your Life.

Amyloid Research Program: Addressing Patient Problems

Measuring risk of disease PREDICTION

Amyloid DETECTION

Patient and Doctor EDUCATION

Amyloid THERAPY

Rare Disease Day at UTMC

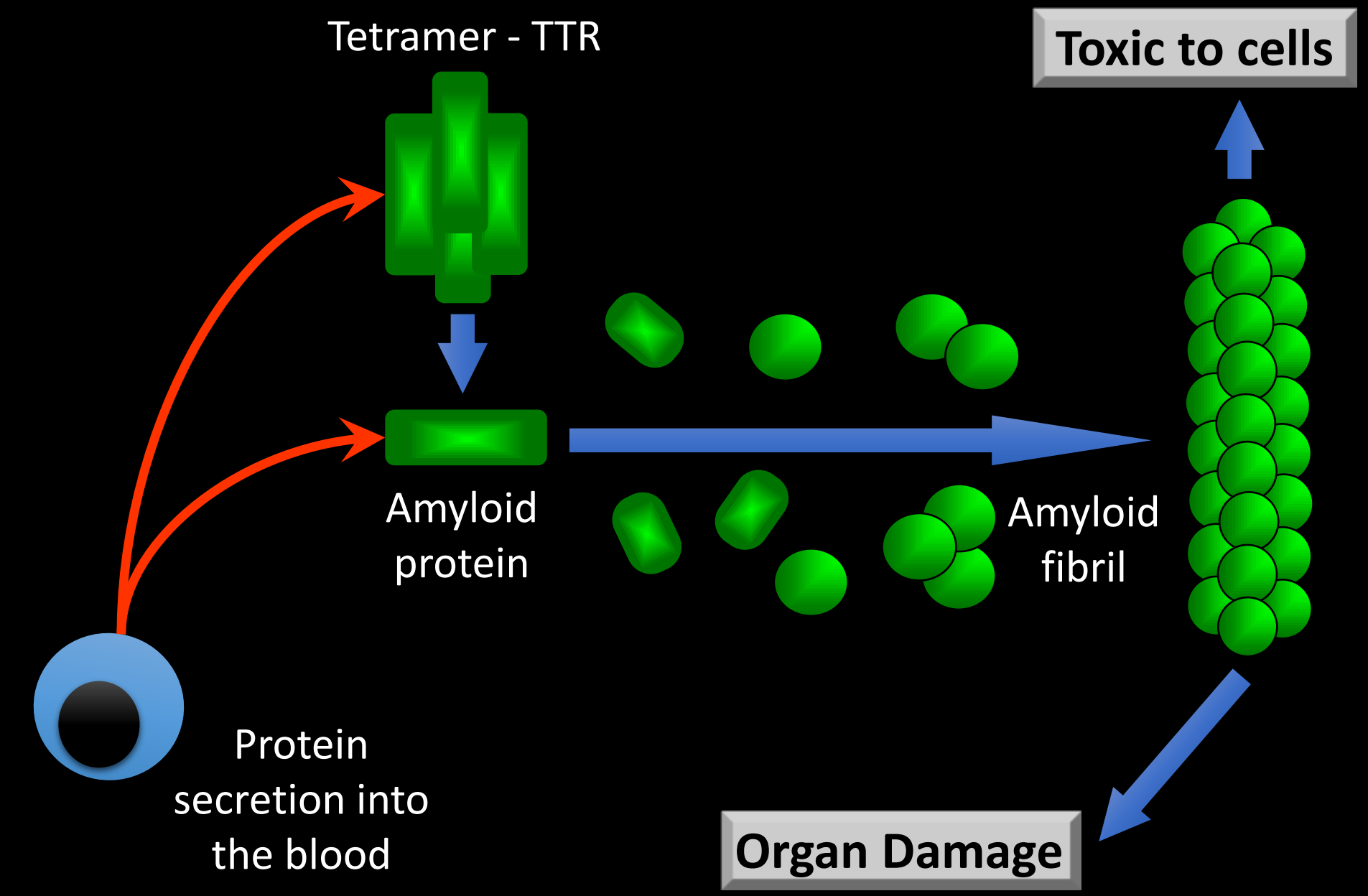
Amyloidosis Patient Support Group at UTMC

Amyloidosis Awareness Month (2018)

Gov. Haslam signs resolution making **March Amyloidosis Awareness** month for the state of **Tennessee**

How Does Amyloid Form?

Amyloidosis – A Protein Misfolding Disorder



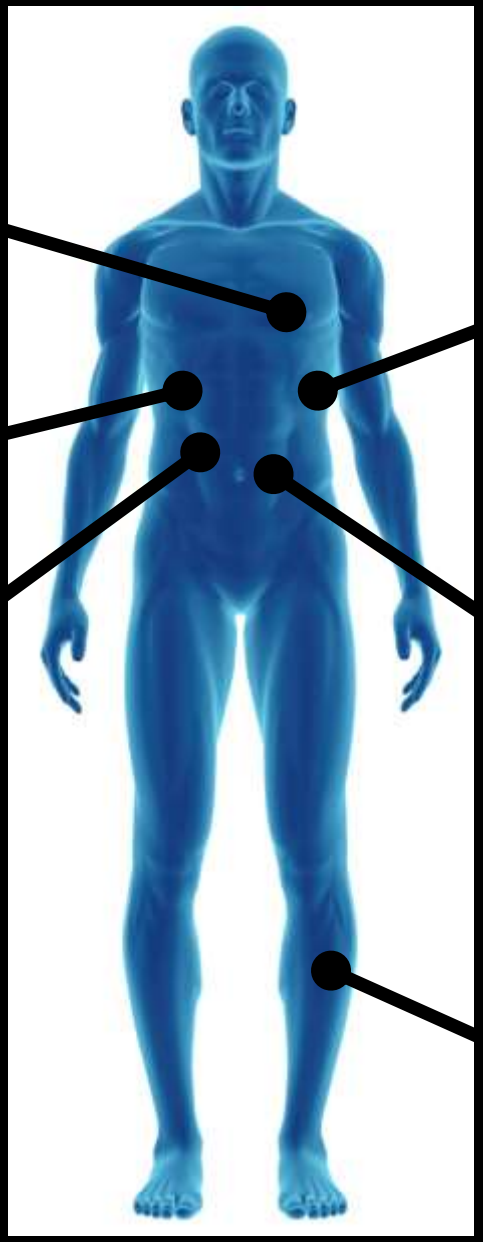
Systemic Amyloidosis

Heart

Liver

Kidney

- Eyes
- Adrenal glands
- Lymph nodes
- Stomach



Spleen

Intestines

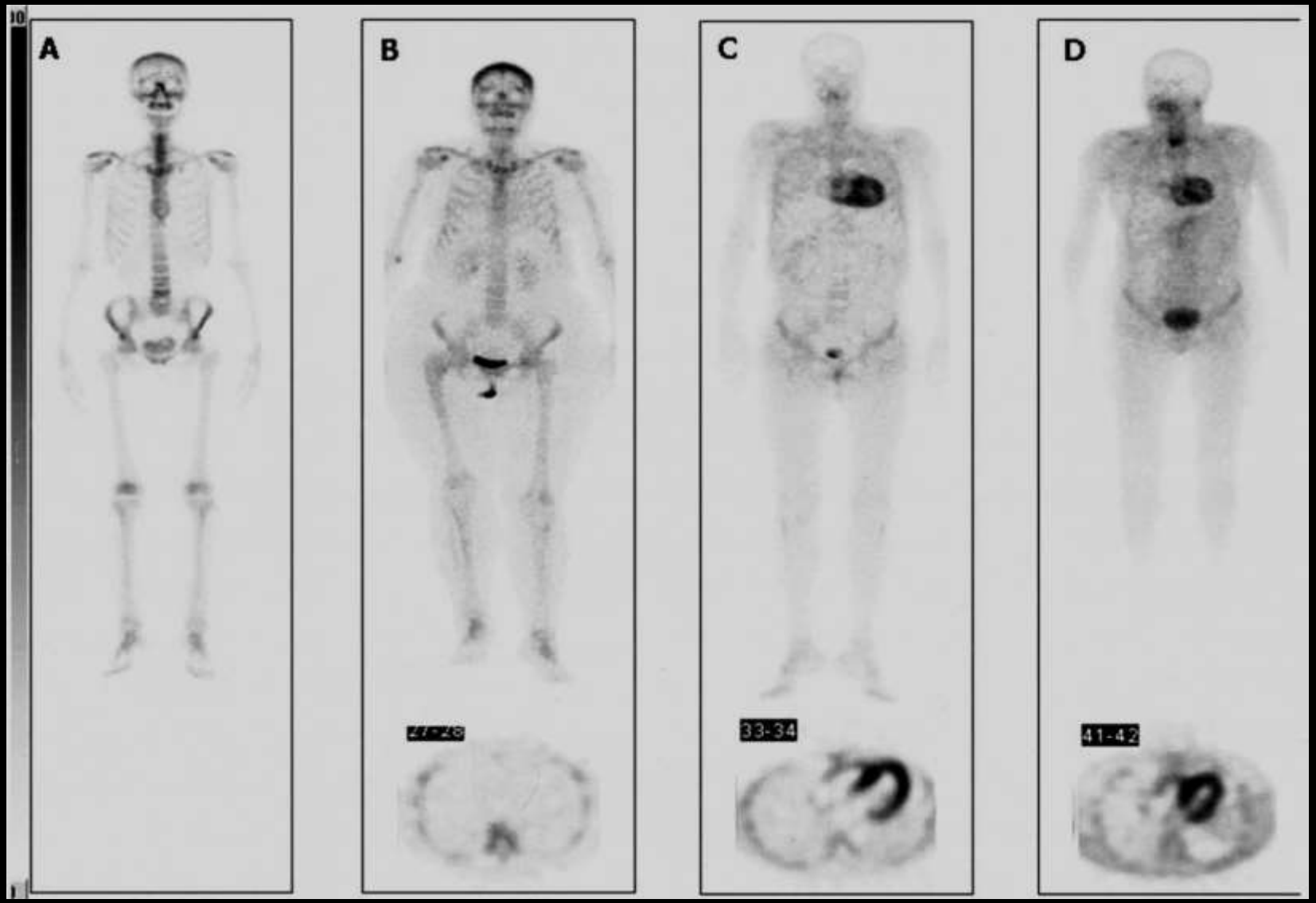
Nerve

Imaging Amyloidosis

Why Image Systemic Amyloidosis?

- Detection of amyloid in the heart, lung, kidney, liver, and spleen (and nerve) using one agent is not currently possible.
- Imaging amyloid can provide more effective and rapid diagnosis.
- The extent of deposition may be of prognostic value and might influence treatment options – and allow physicians to monitor the effect of treatments.
- Currently only one approved method for imaging ATTR in the heart with no agents approved for other forms of amyloidosis.

Imaging ATTR with ^{99m}Tc-PyP

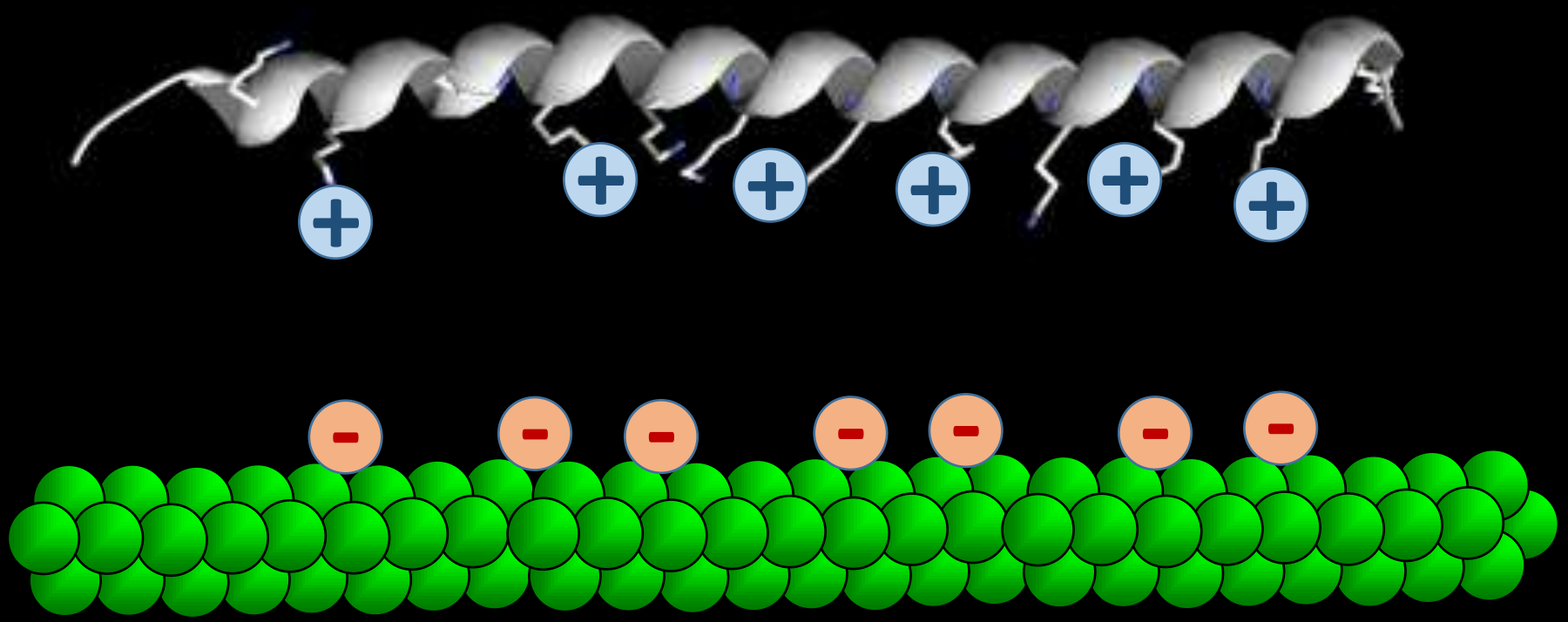


normal AL - negative ATTR – positive patients

A First-in-Human Amyloid Imaging Study at UTMC

Not an industry-sponsored trial.
Supported by donations to our program from our researchers and patients.

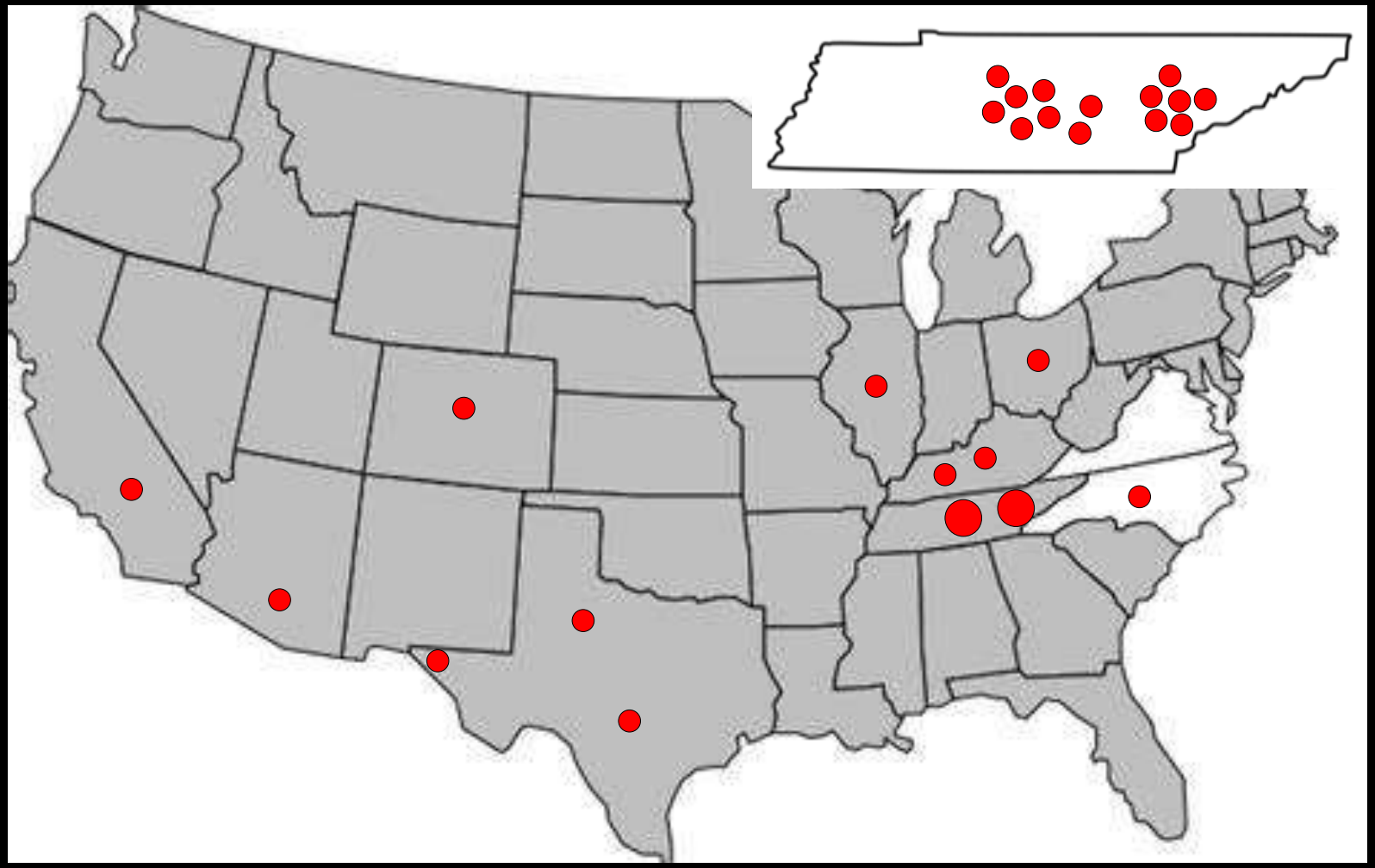
Peptide p5+14 – A Novel Agent for Amyloid Imaging



Amyloid fibril

Patient Recruitment

Patients Come From Central and Eastern Tennessee and Around the US

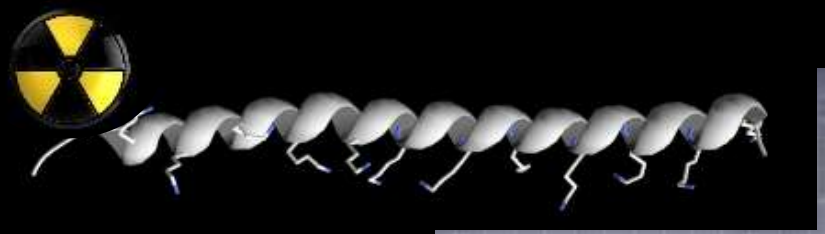


More than half the patients are Tennesseans

First-in-Human Clinical Trial of Peptide p5+14

Phase 1

A Very, Very Brief Introduction to Imaging



Phase 1 Clinical Trial of ^{124}I-p5+14 PET/CT Imaging of Patients with Systemic Amyloidosis

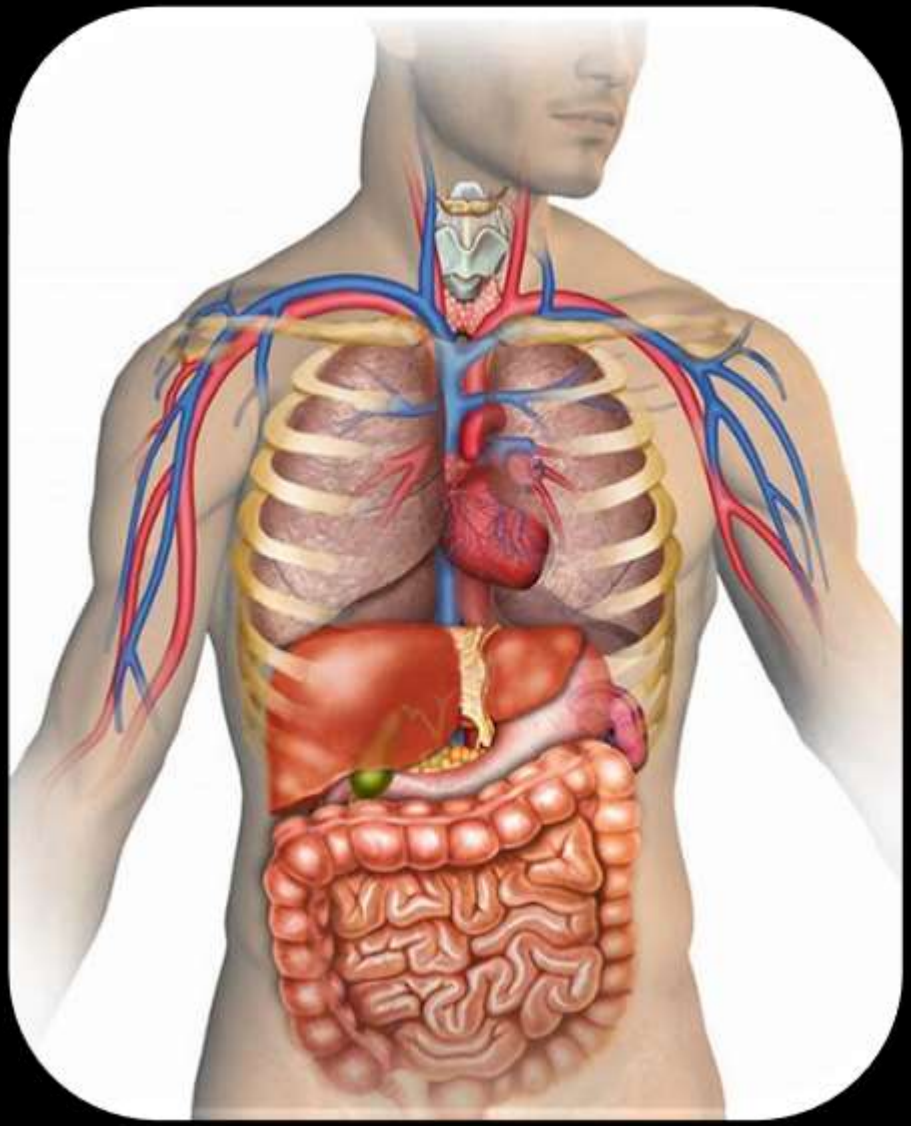
- Part 1 – Three patients with AL given radioactive p5+14 peptide for initial evaluation of safety. Patients were imaged 7 times over 48 h – COMPLETED.
- Part 2 – Forty patients:
  - 20 AL (*6 imaged to date*)
  - 10 ATTR (*4 imaged, all hereditary*)
  - 5 ALect2 (*1 imaged*)
  - 5 Other (*1 recruited*)
- Each patient receives a low dose of the peptide and low dose of radioactivity and is imaged at 5 h and 24 h post injection.
- Study is assessing safety and determining whether we can image individual organs that are known or suspected of containing amyloid based on the clinical work-up.
- Patients receive copies of their images as part of the study.

Imaging Protocol

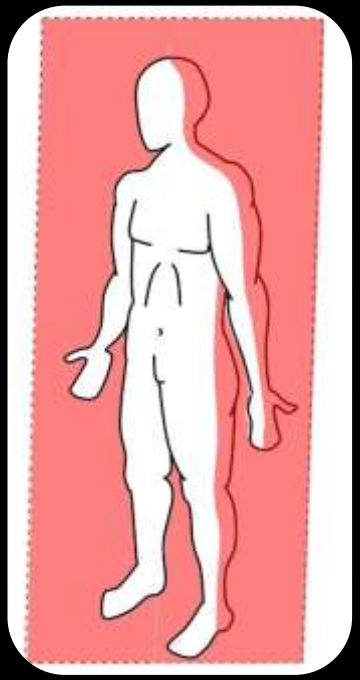
- Patients visit our Study Physician for a check up
  - The radioactive drug is prepared at UTMC
- The patients come to the Nuclear Medicine Dept

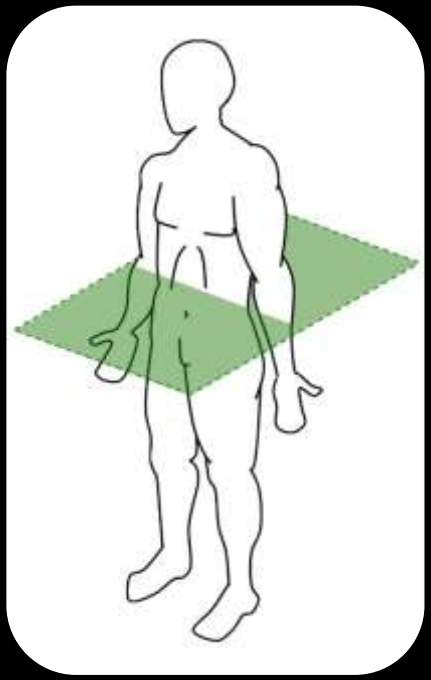
Imaging Protocol

A Very, Very Brief Introduction to Imaging

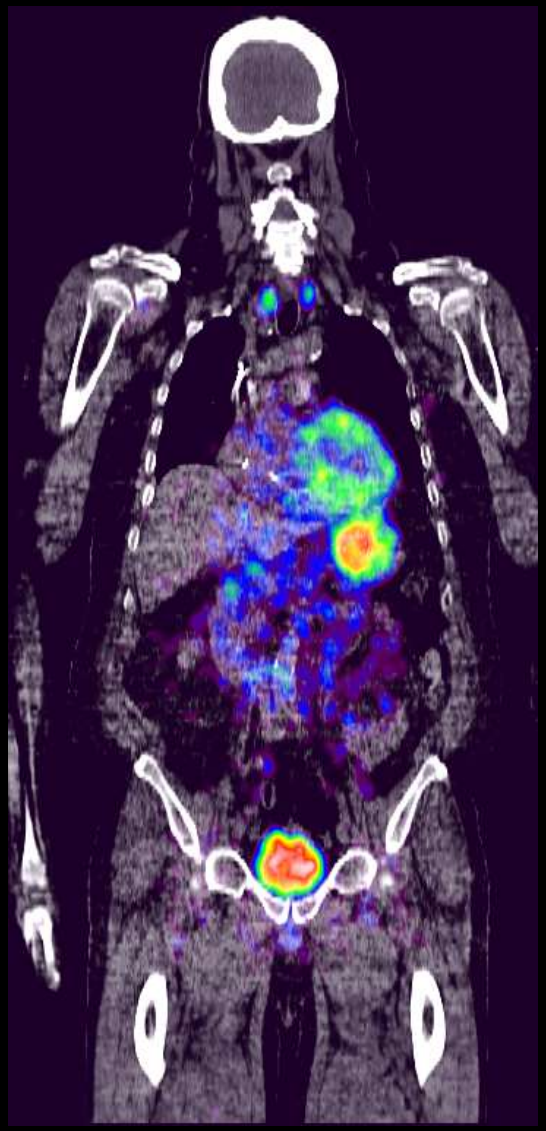


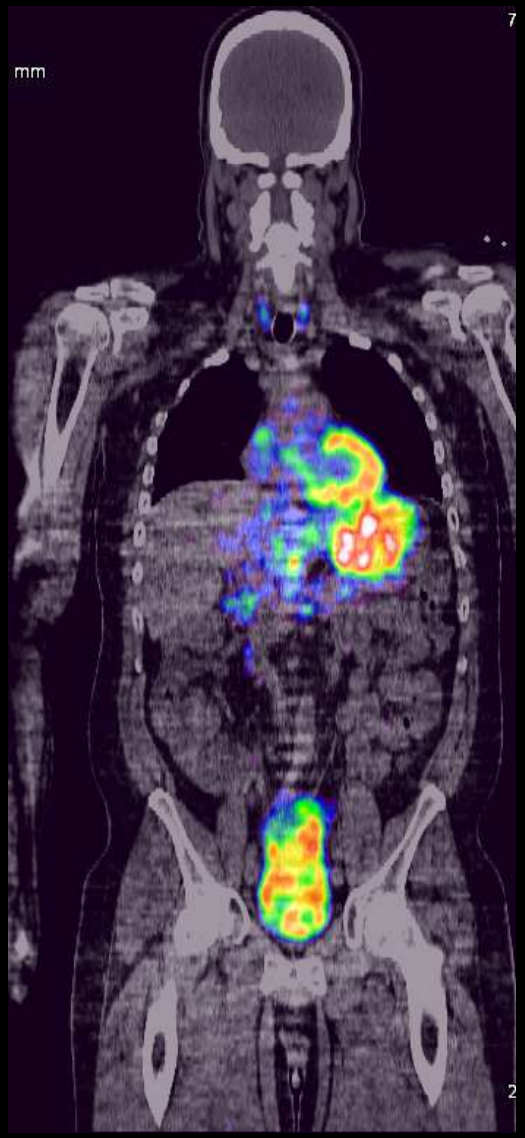
3D PET/CT Imaging allows us to look at many views of the patient



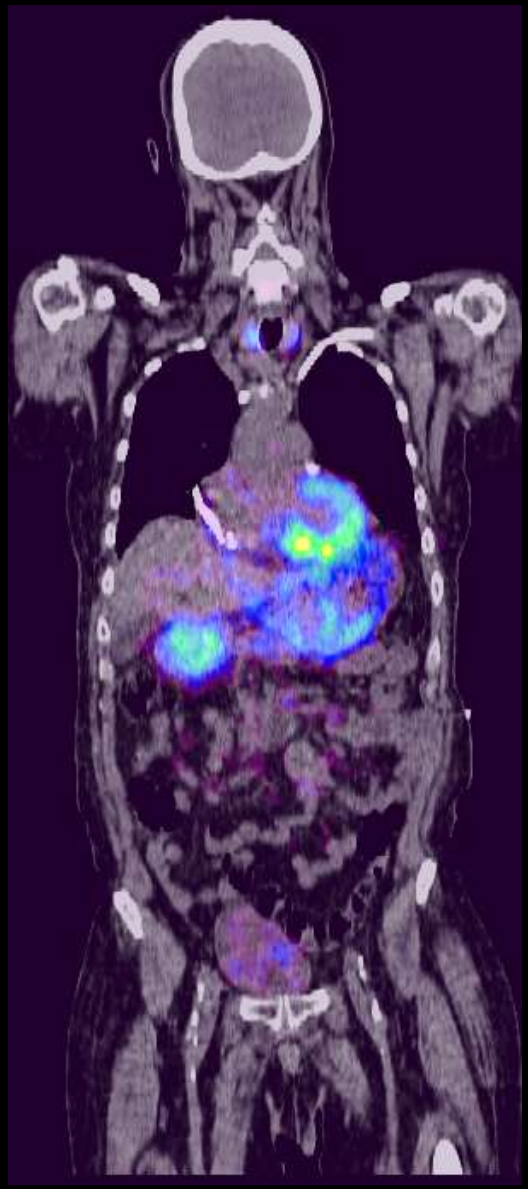


ATTR Patients – Diagnosed with Cardiac Amyloid

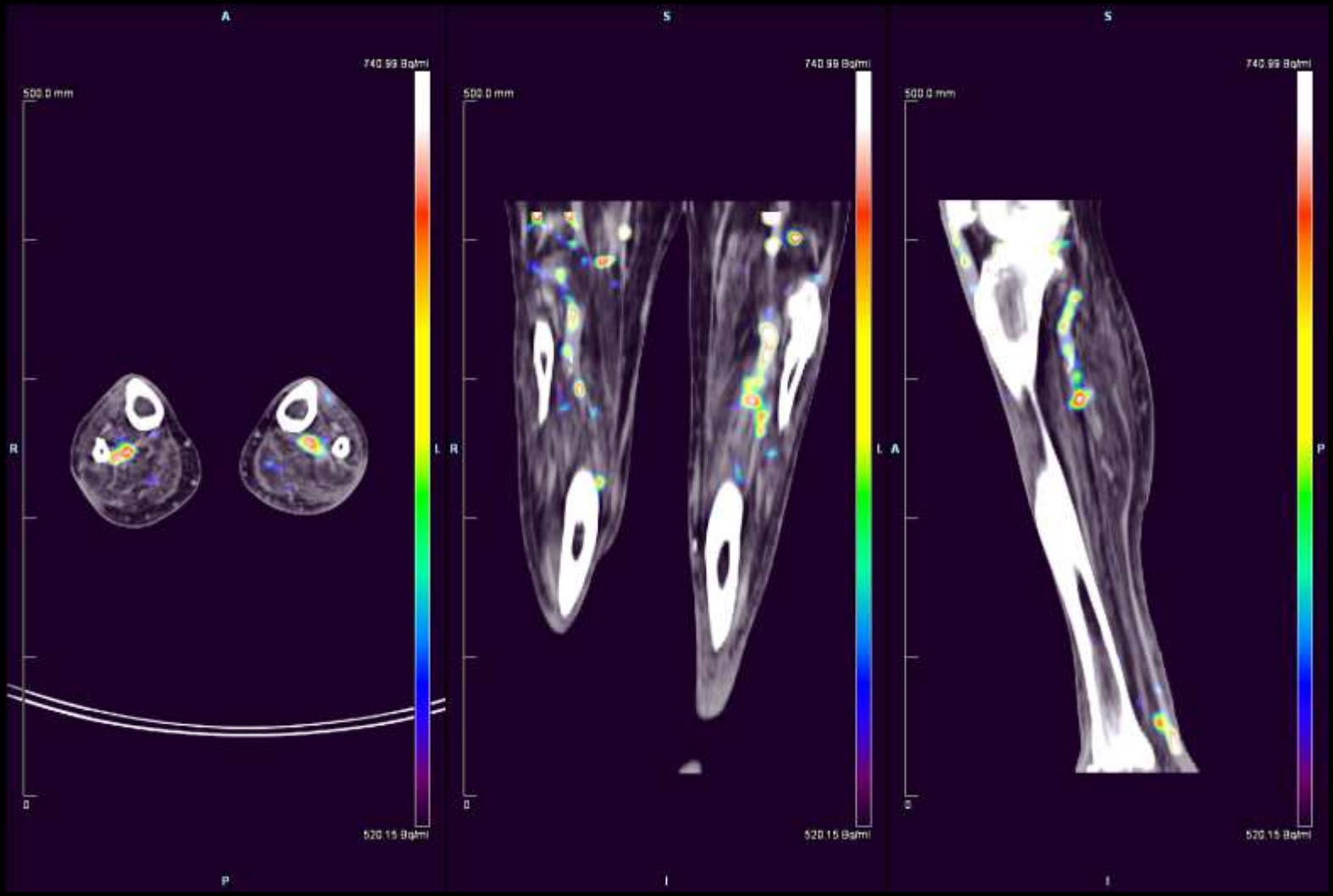




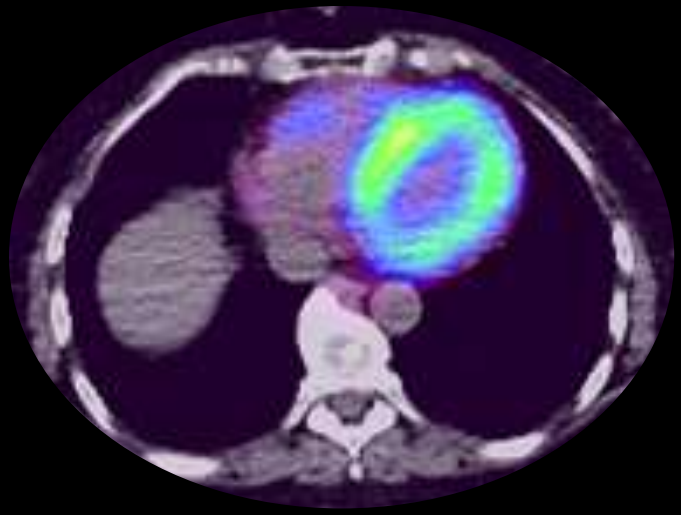
ATTR – Diagnosed with neuropathy

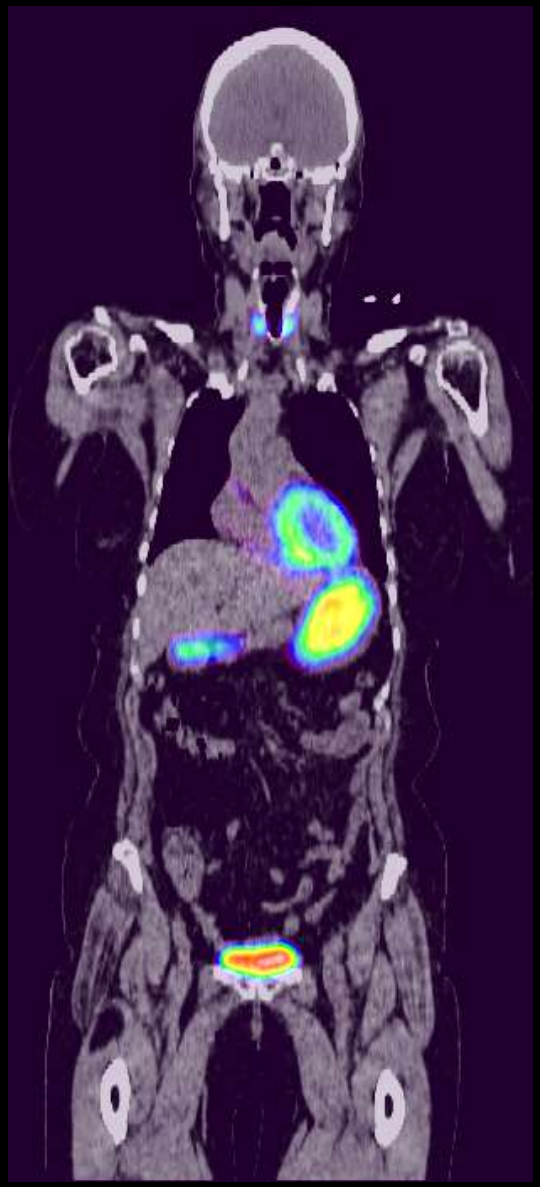


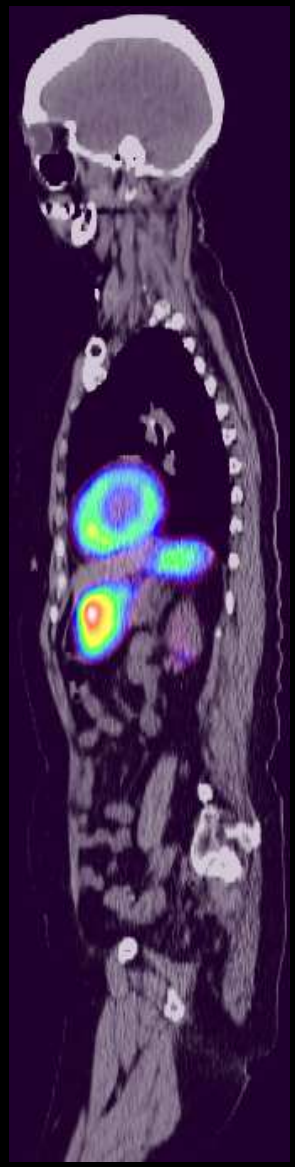
Peripheral nerve amyloid



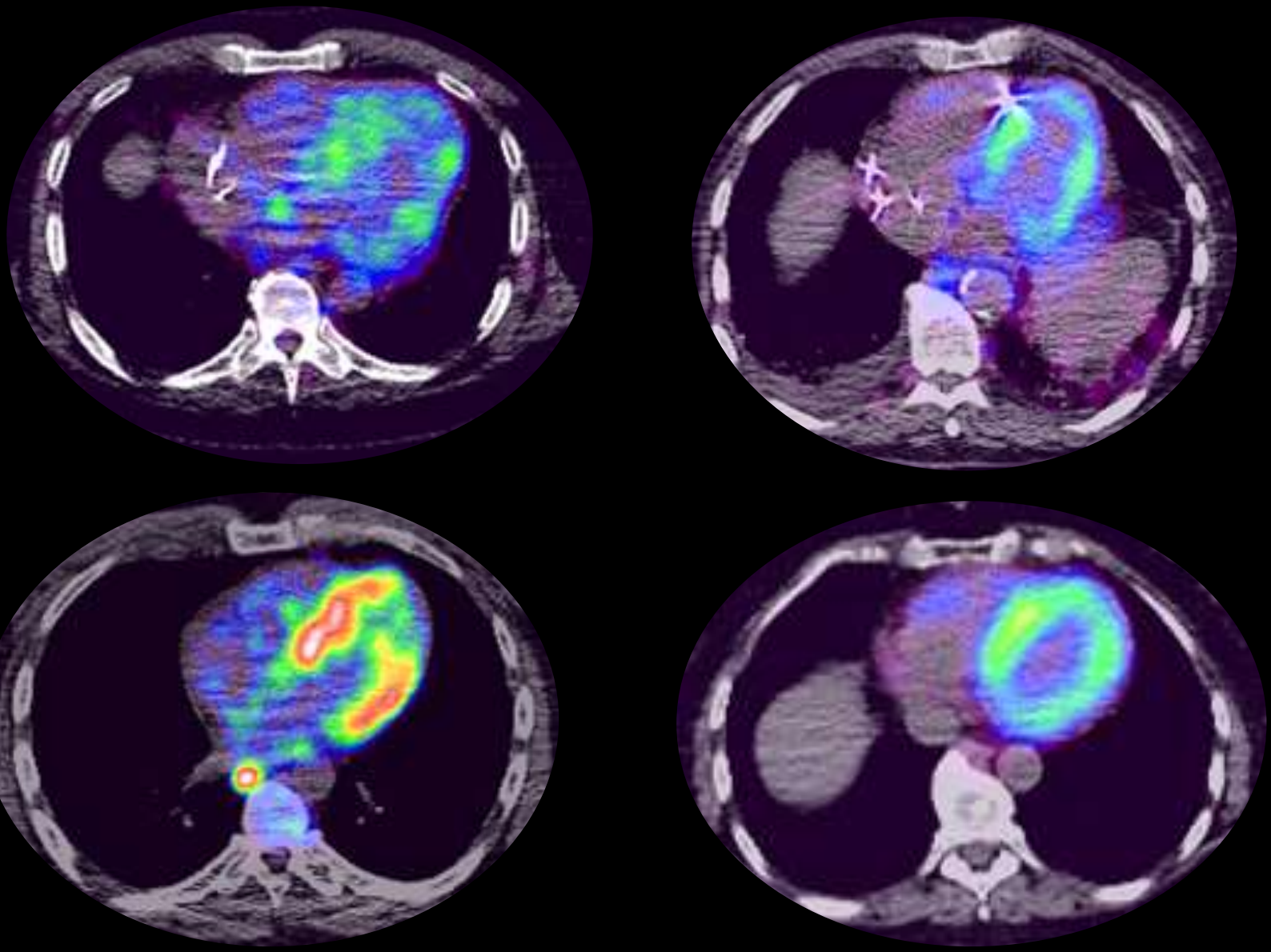
ATTR Patient



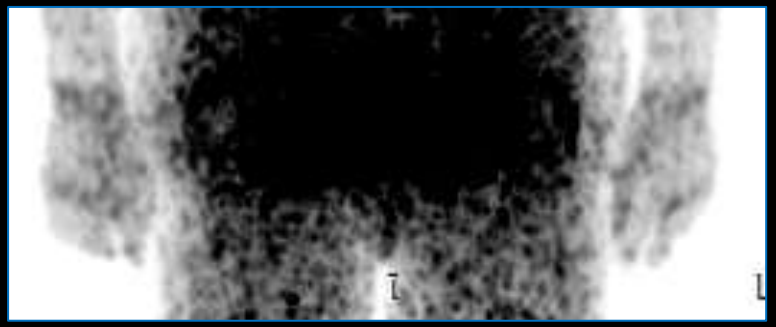


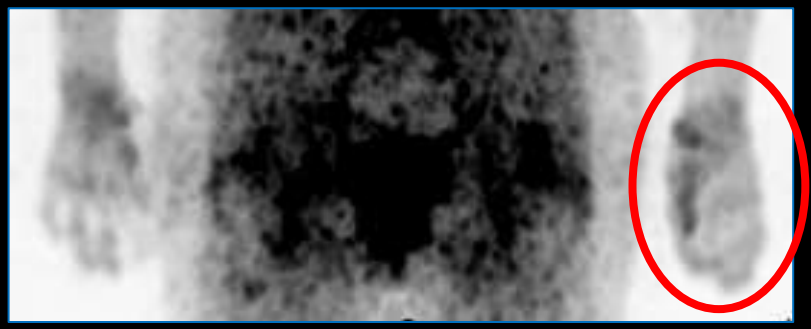


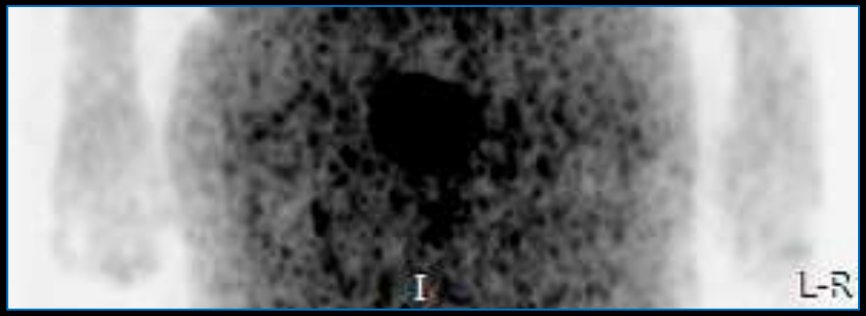
ATTR Cardiac Amyloid Images

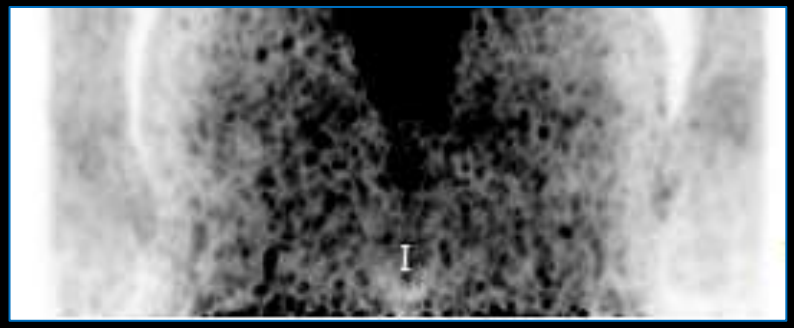


ATTR Patients





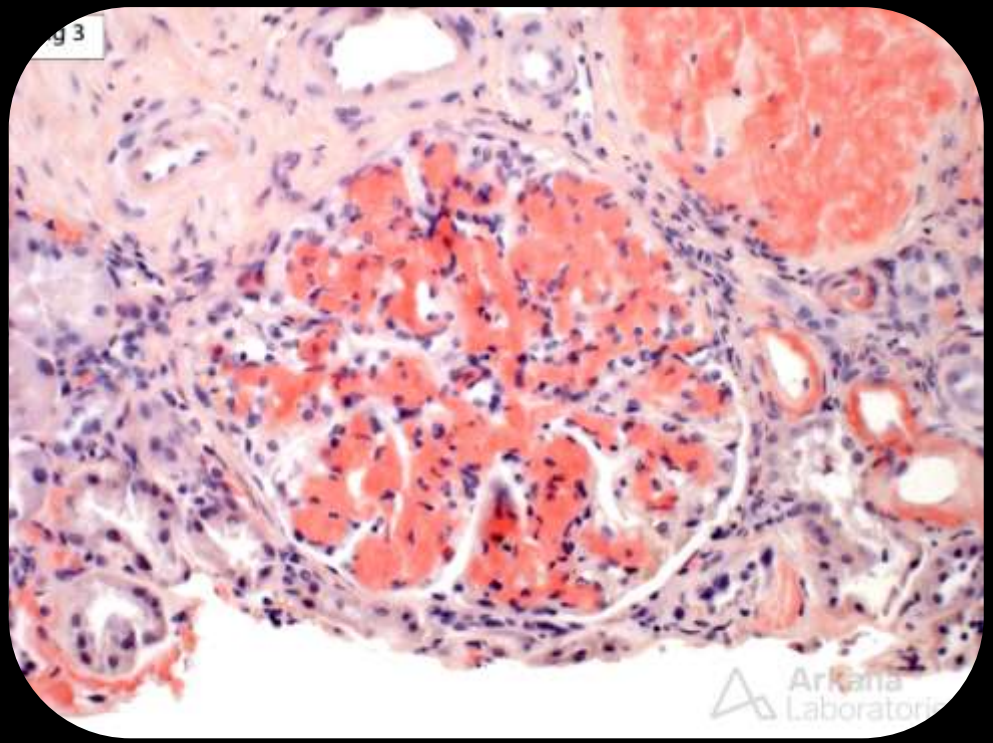




We continue to study the images from all the patients to understand how the peptide works and what it can “see” but the images suggest that it may be possible to see nerve-associated ATTR

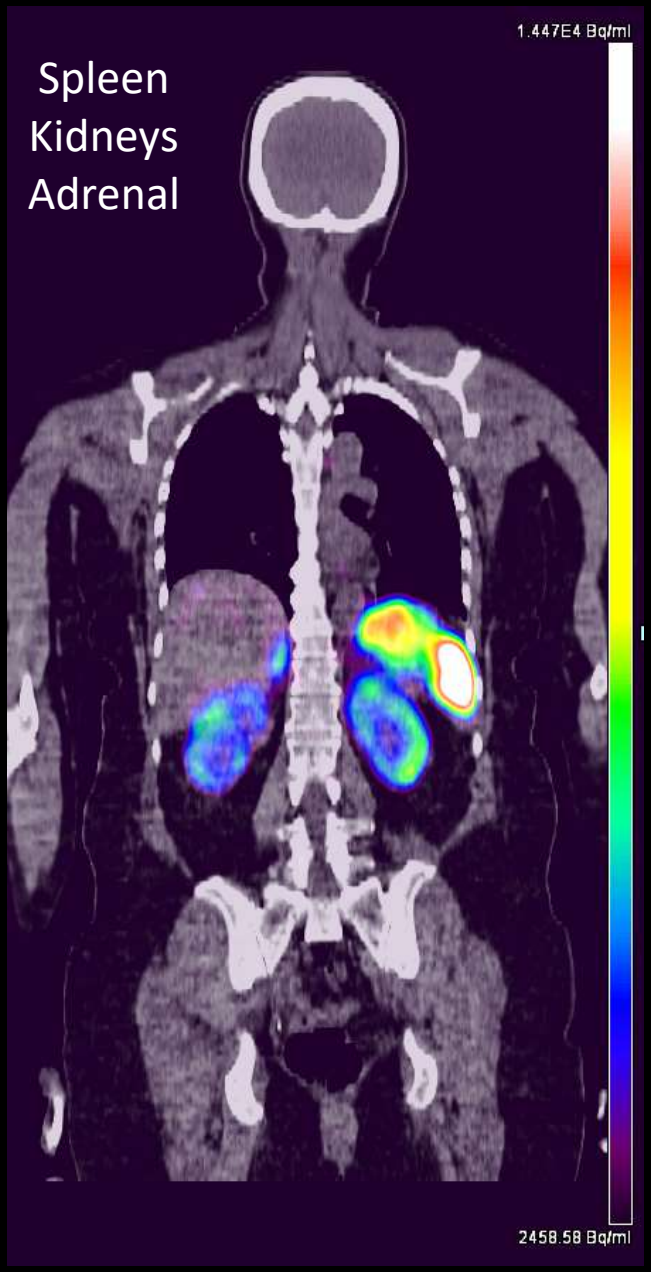
ALECT2 Amyloidosis

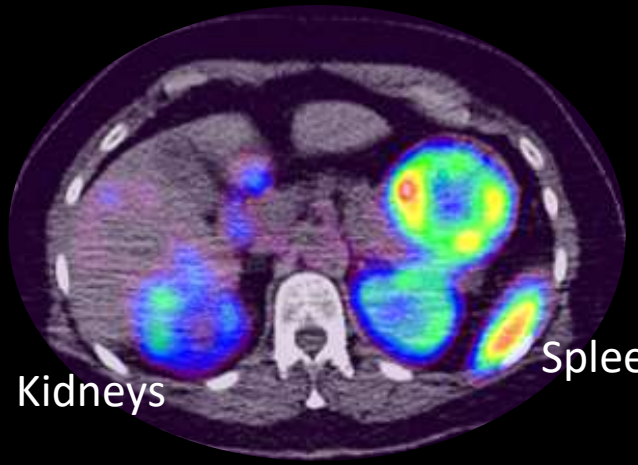
- ALECT2 amyloidosis is the third most common form of systemic amyloidosis in the US.
- Common in people of Mexican descent with most patients in the Southwest US.
- Amyloid deposits most commonly found in the kidneys, liver, and spleen.



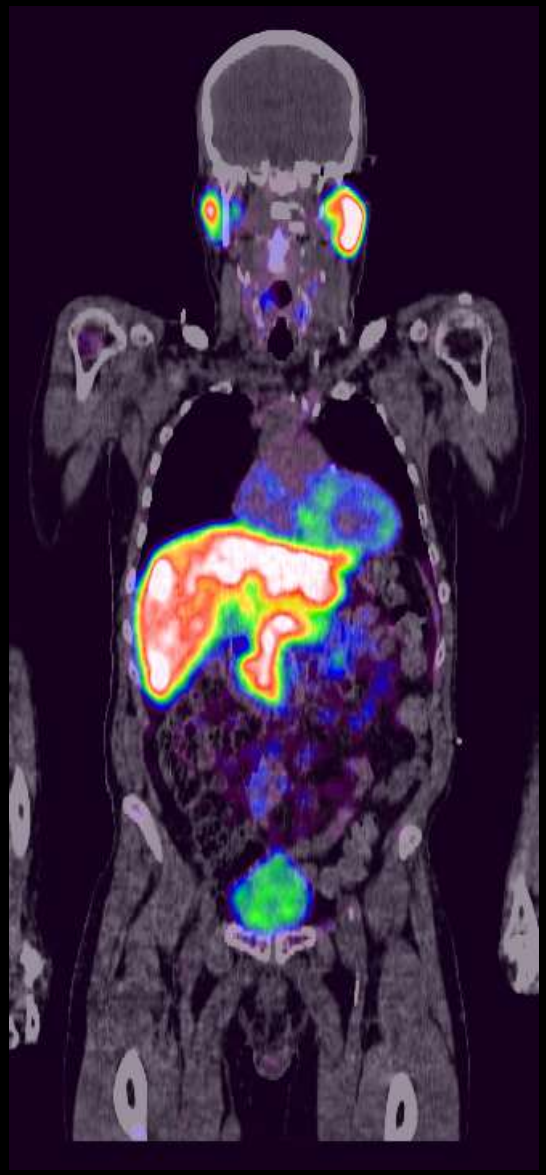
Dr. Chris Larsen, Arkana Laboratories

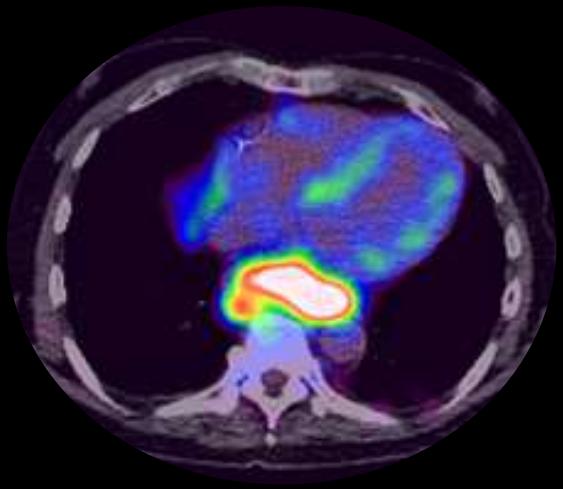
ALECT2


Spleen
Kidneys
Adrenal
1.447E4 Bq/ml
2458.58 Bq/ml

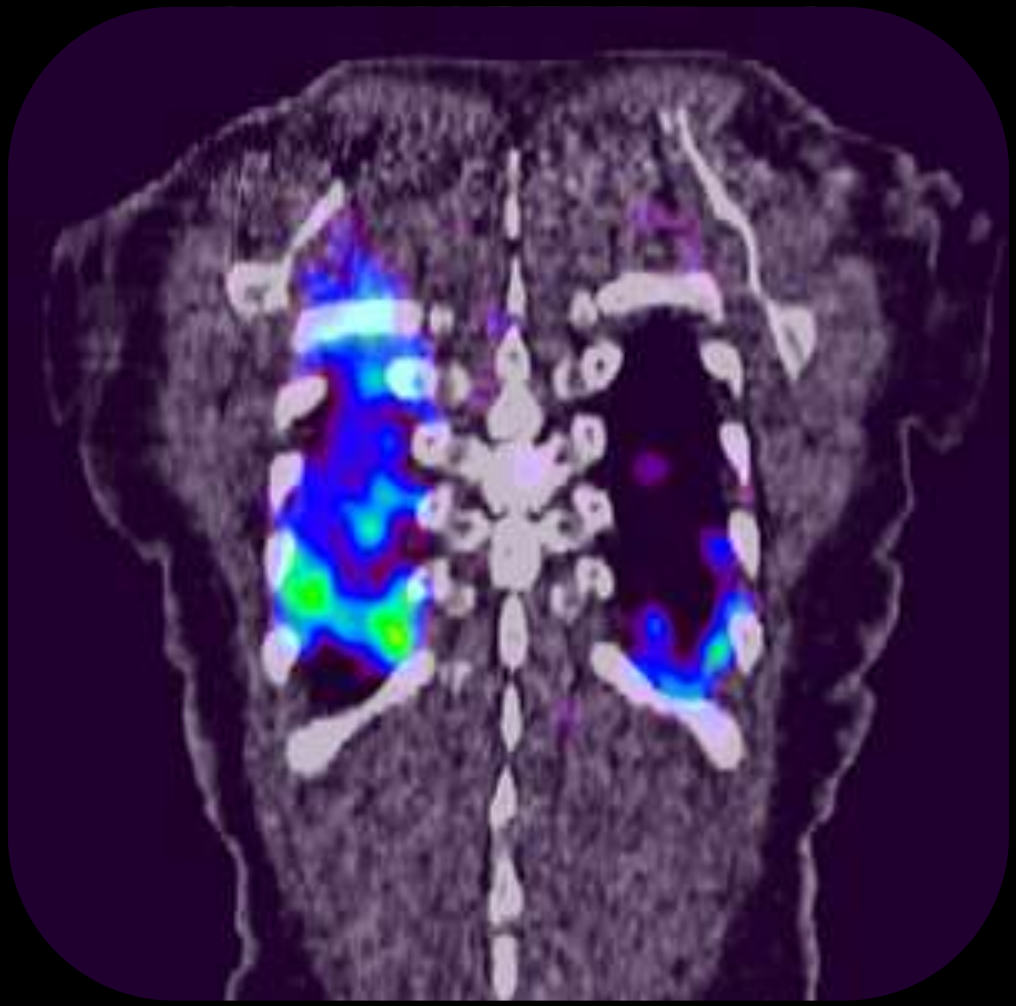

Kidneys
Spleen

Imaging AL Amyloidosis





Lung uptake



Future Plans

- The Phase 1 study will continue to recruit for another year (or so) – after which we will extend the study and image as many patients as we can.

- Based on feedback from many of the patients that we have imaged we hope to begin the following studies:
    1. Perform repeat imaging on patients at 12 month intervals so that we can monitor response to therapy.
    2. Recruit TTR mutant carriers who are asymptomatic to see if very early amyloid detection is possible.
    3. Recruit amyloid-free “heathy” subjects.
    4. Increase the availability for imaging of rare forms of amyloidosis.

Future Directions

- The Phase 1 study will continue to recruit for another year (or so) – after which we will extend the study and image as many patients as we can.
- We continue to work on understanding the peptide and how the images can be used to benefit patients.
- The specific reactivity of the peptide for amyloid is being further exploited to develop therapeutics designed to enhance the clearance of tissue amyloid.
- The peptide is being developed by a company (Aurora Bio) to make this imaging agent available for widespread use.

Amyloidosis and Cancer Theranostics Program

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