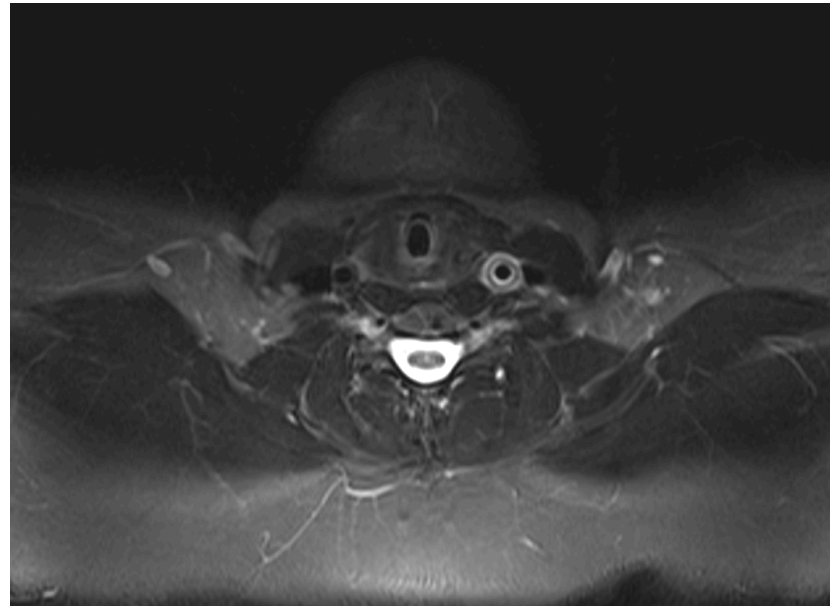
Imaging in Large Vessel Vasculitis

Peter C Grayson, MD, MSc
National Institutes of Health



Disclosures

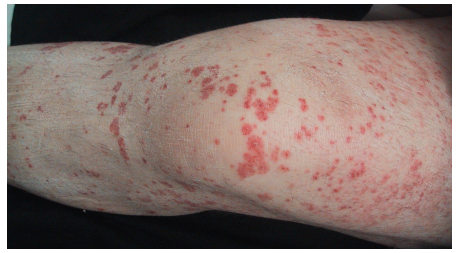
- No personal conflicts of interest to disclose.

Learning Objectives

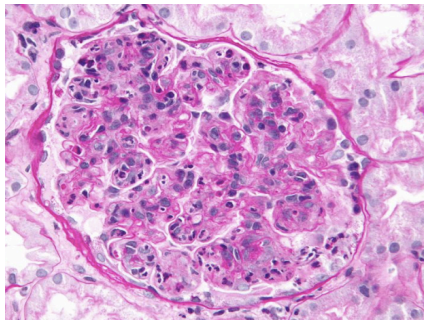
- Recognize strengths and weaknesses of different forms of vascular imaging to diagnose and monitor patients with large-vessel vasculitis

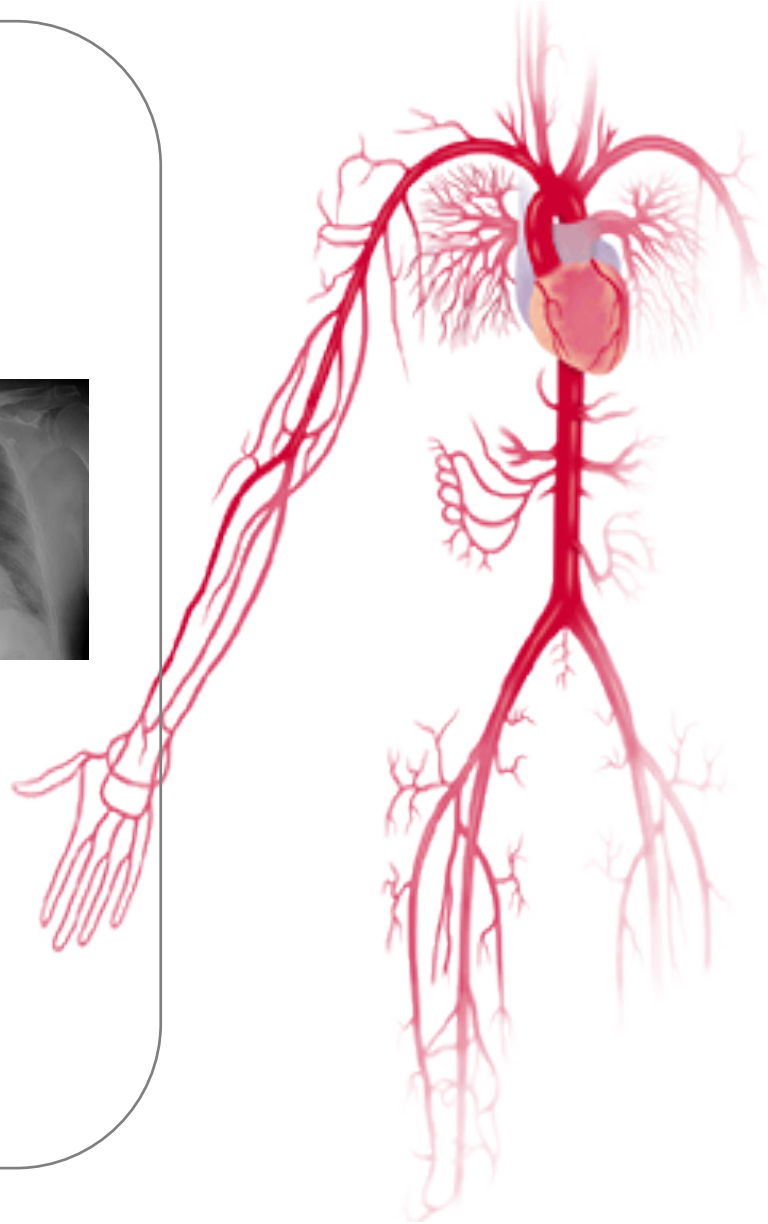
- Develop a personalized approach to incorporate vascular imaging into clinical management of your patients with large-vessel vasculitis

Forms of Vasculitis

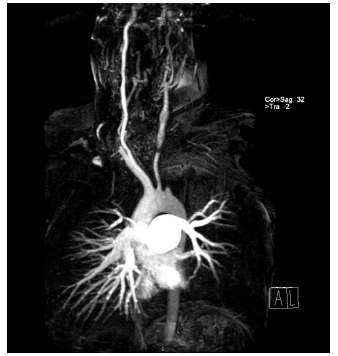


Small Vessel





Large Vessel



Takayasu’s arteritis

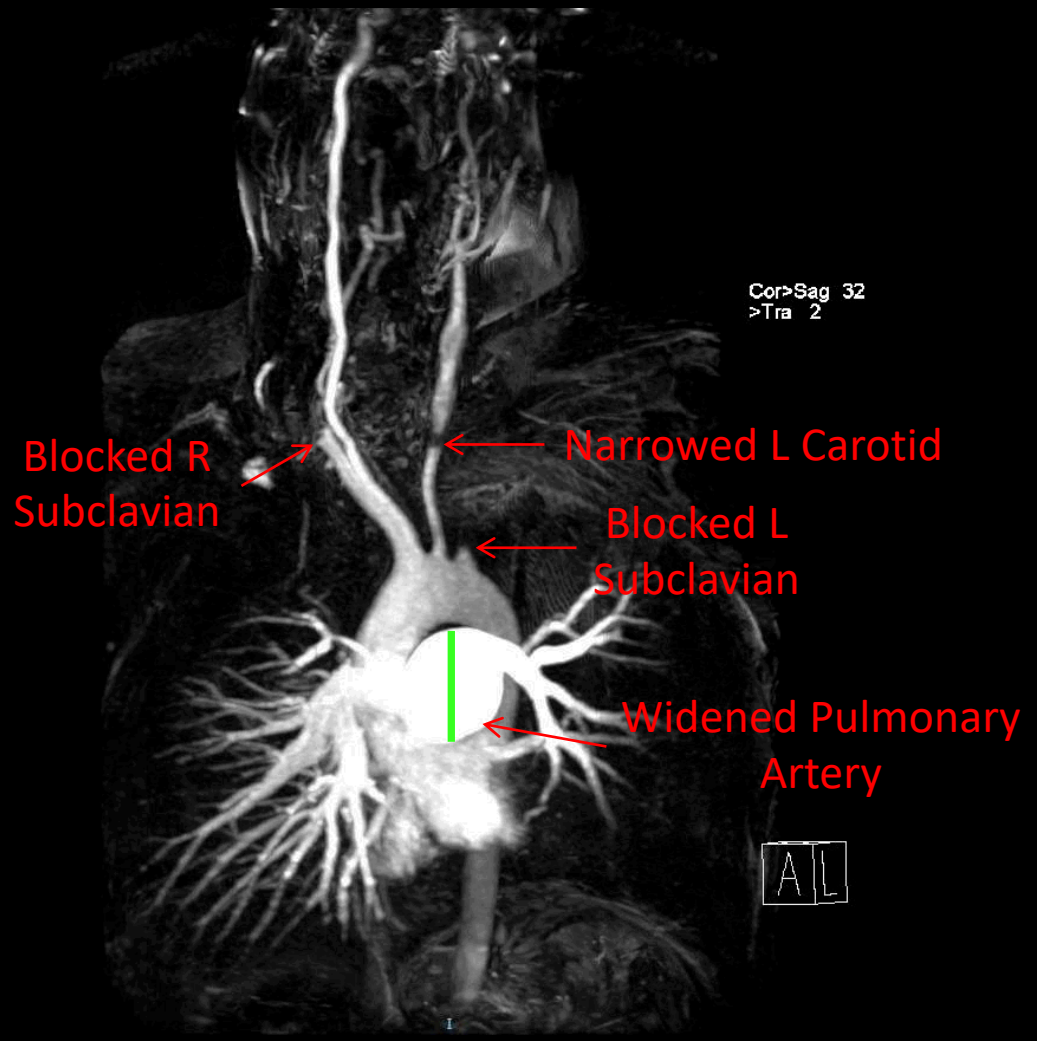
- < 40 years
- 9:1 female preponderance
- Incidence 1 per million
- Asian countries
- Aorta and branch arteries

Giant cell arteritis

- > 50 years
- 3:1 female preponderance
- Incidence 17 per 100,000
- Scandinavian countries
- Cranial arteries

Healthy

Takayasu's Arteritis



Takayasu's Arteritis

Scalp Tenderness

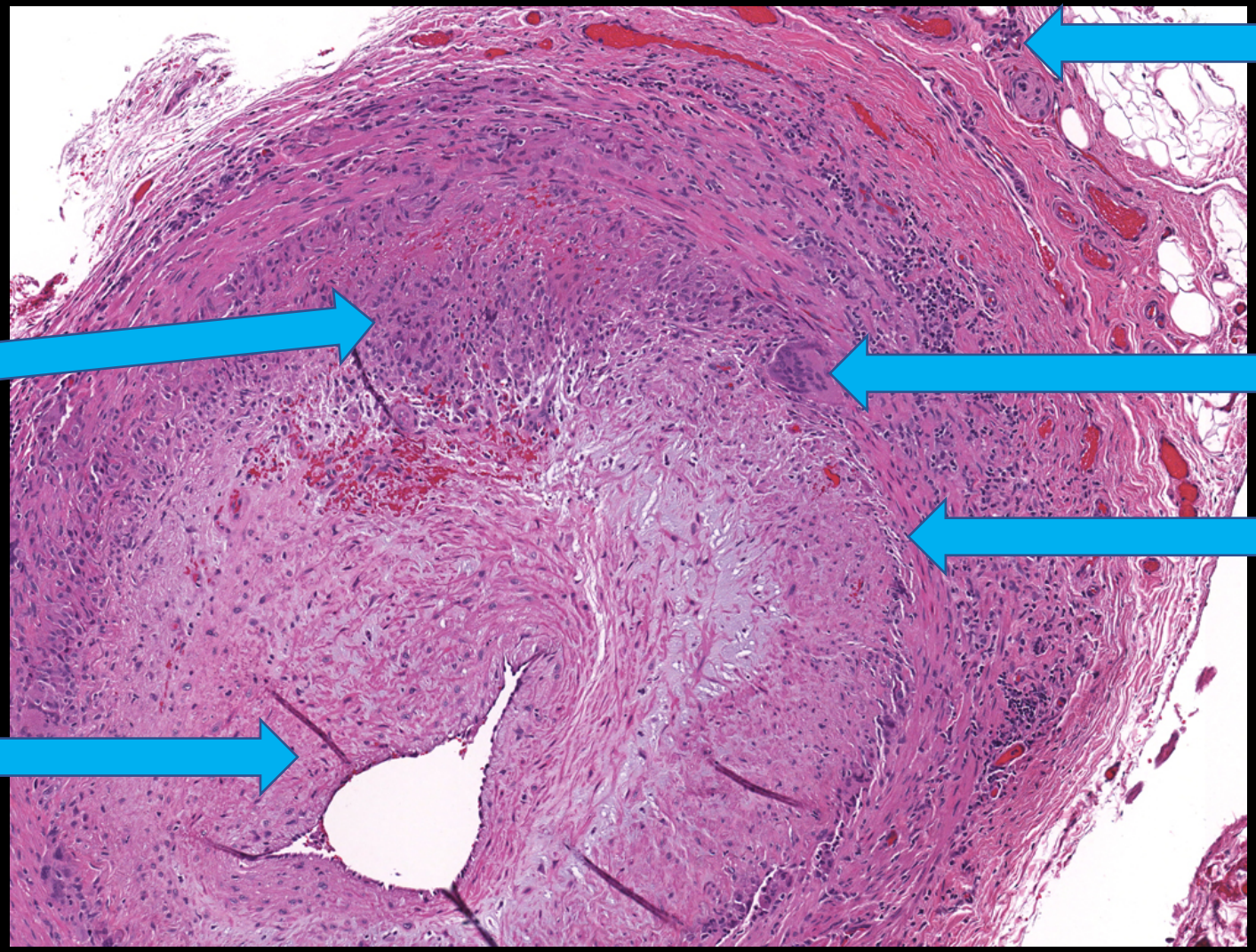
Headache

Jaw Claudication

Vision Loss

Temporal Artery Biopsy

Minimal histologic diagnostic criteria?



Inflammation in vasa vasorum

Inflammatory infiltrate

Giant Cells

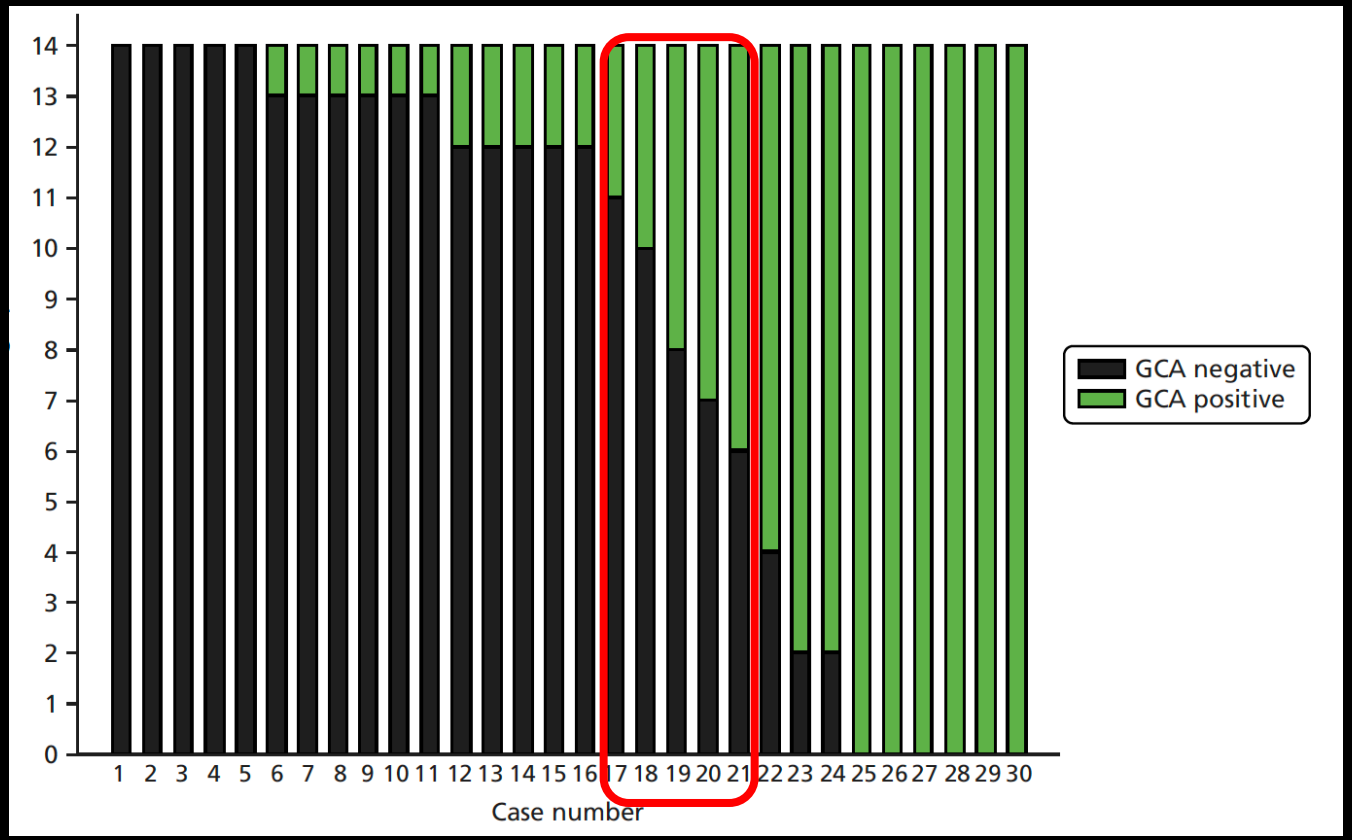
Fragmentation of internal elastic lamina

Intimal hyperplasia

Temporal Artery Biopsy

Pathologist interpretation

Pathologists often disagree about TAB



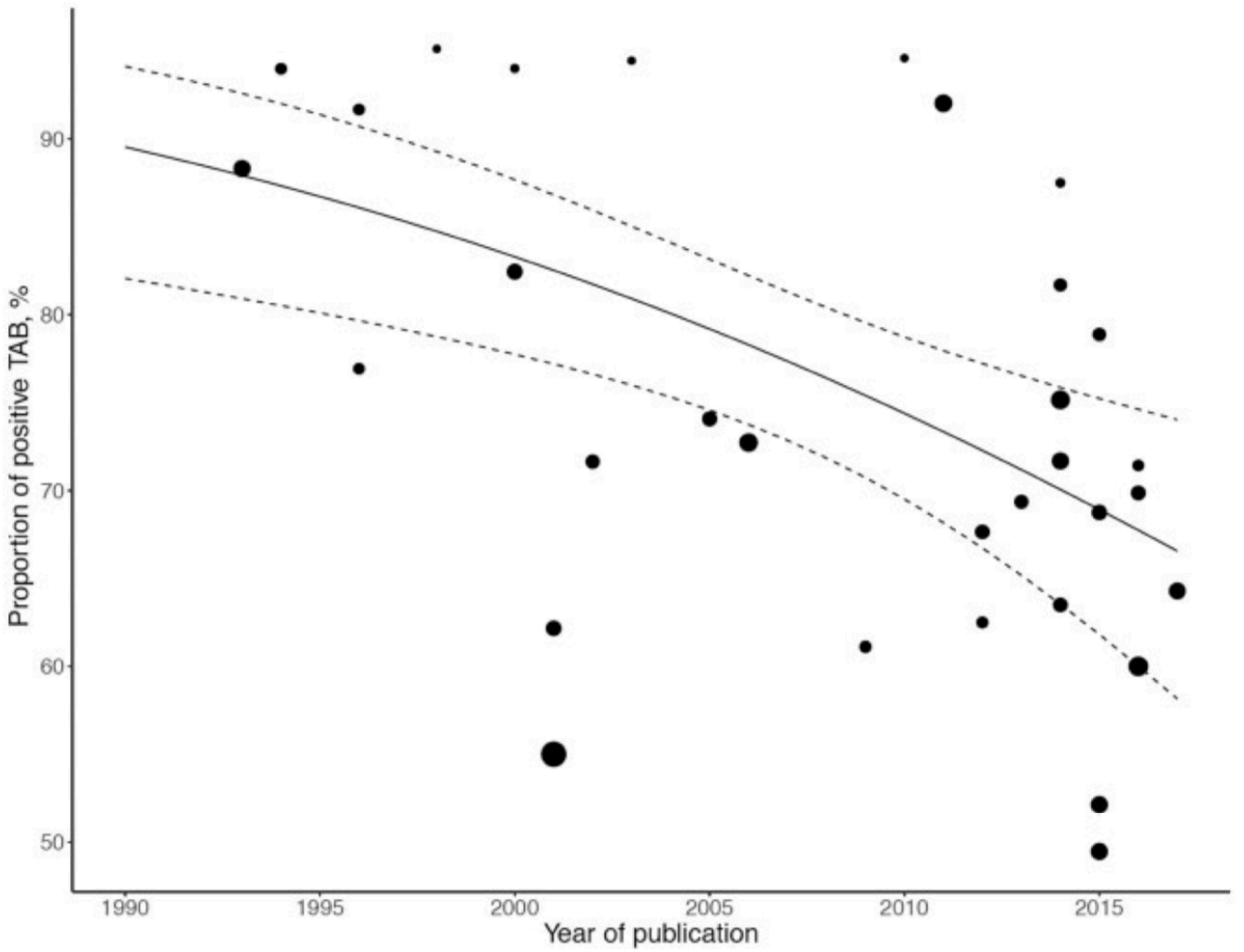
Luqmani et al, Health Technol Assess 2016

Sensitivity of TAB is declining

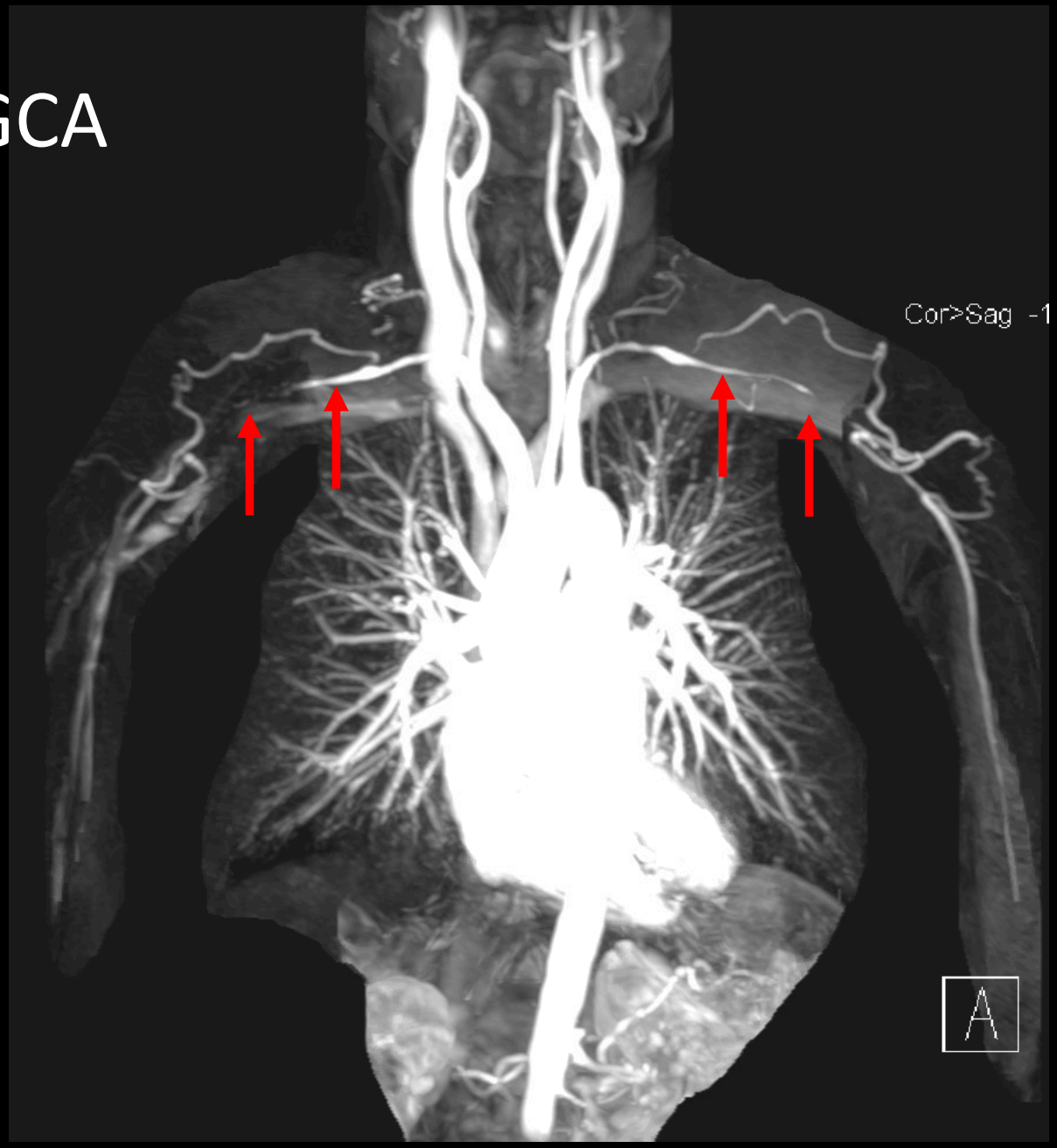
Rubenstein et al
Rheumatology 2020

Clinical diagnosis without biopsy

Expansion of the phenotype to include large artery disease

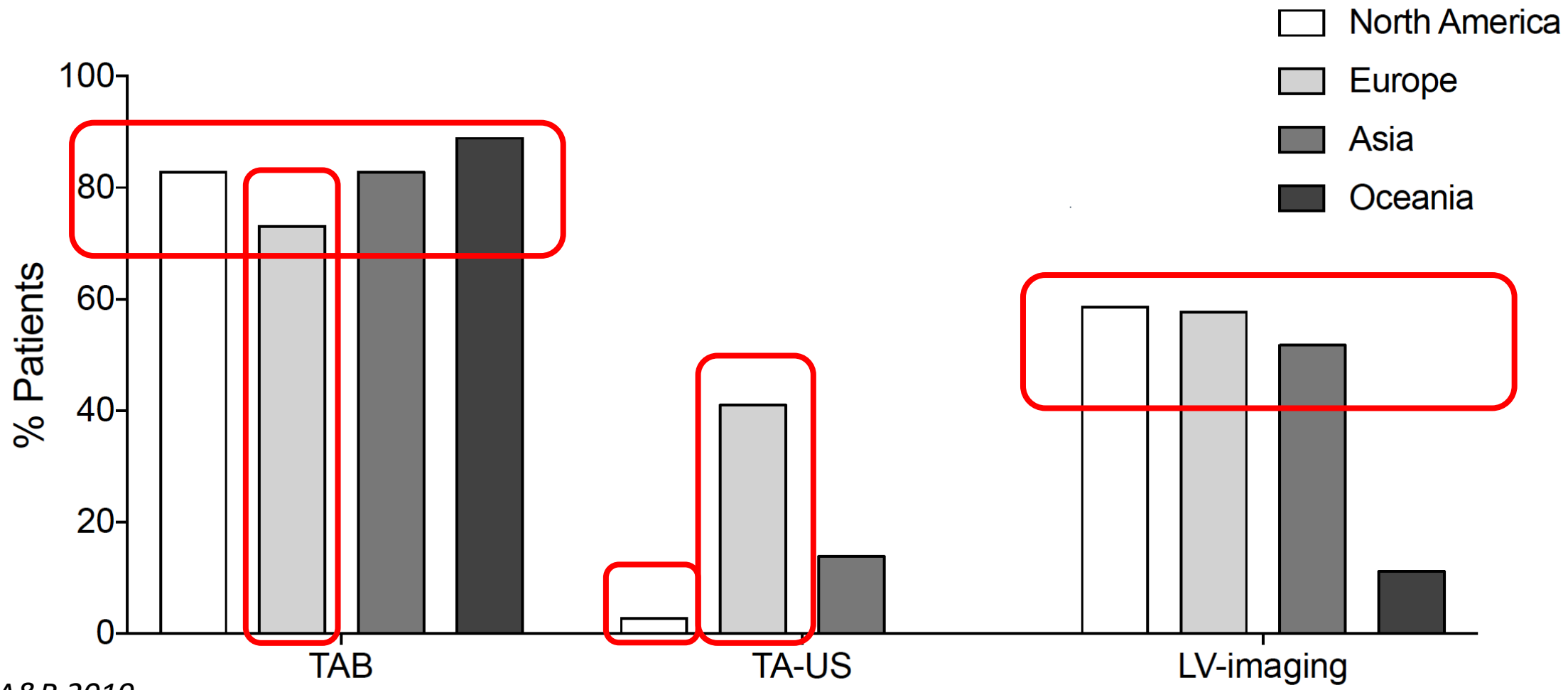


Large Vessel GCA



DCVAS Study

Multi-modal assessment is happening in GCA

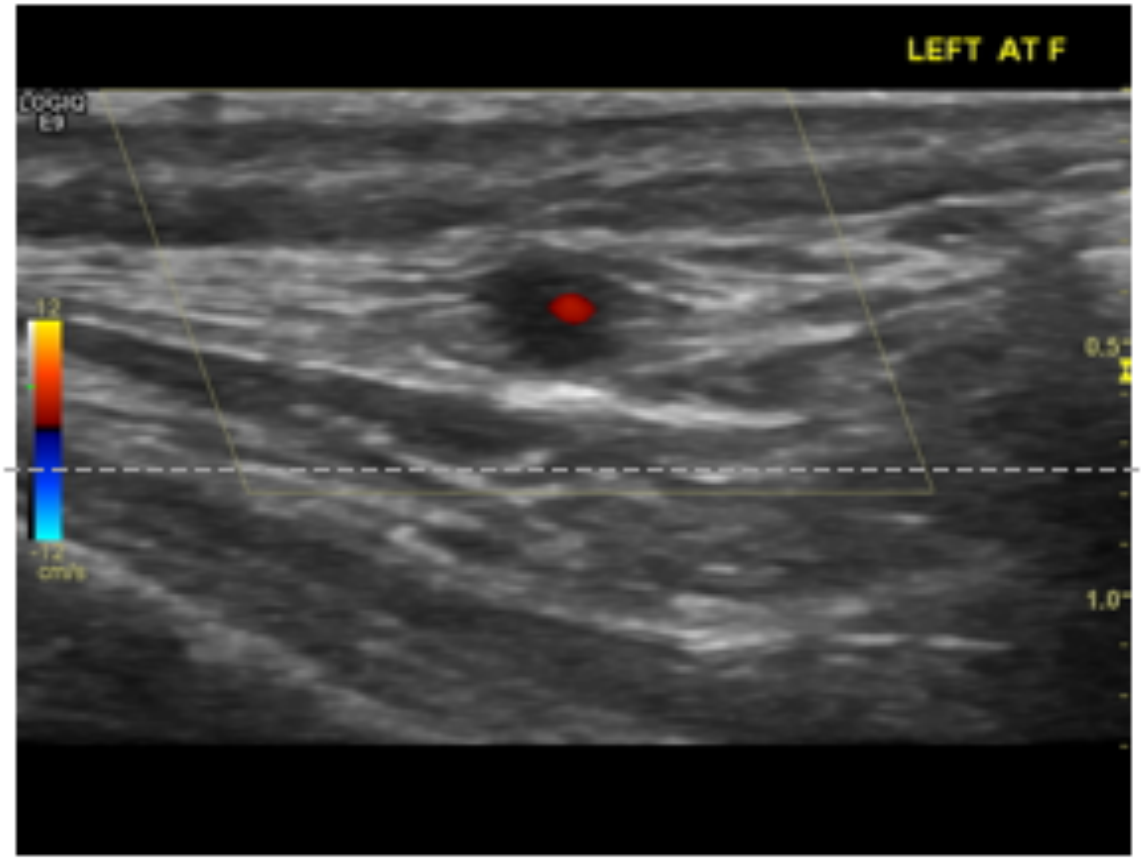


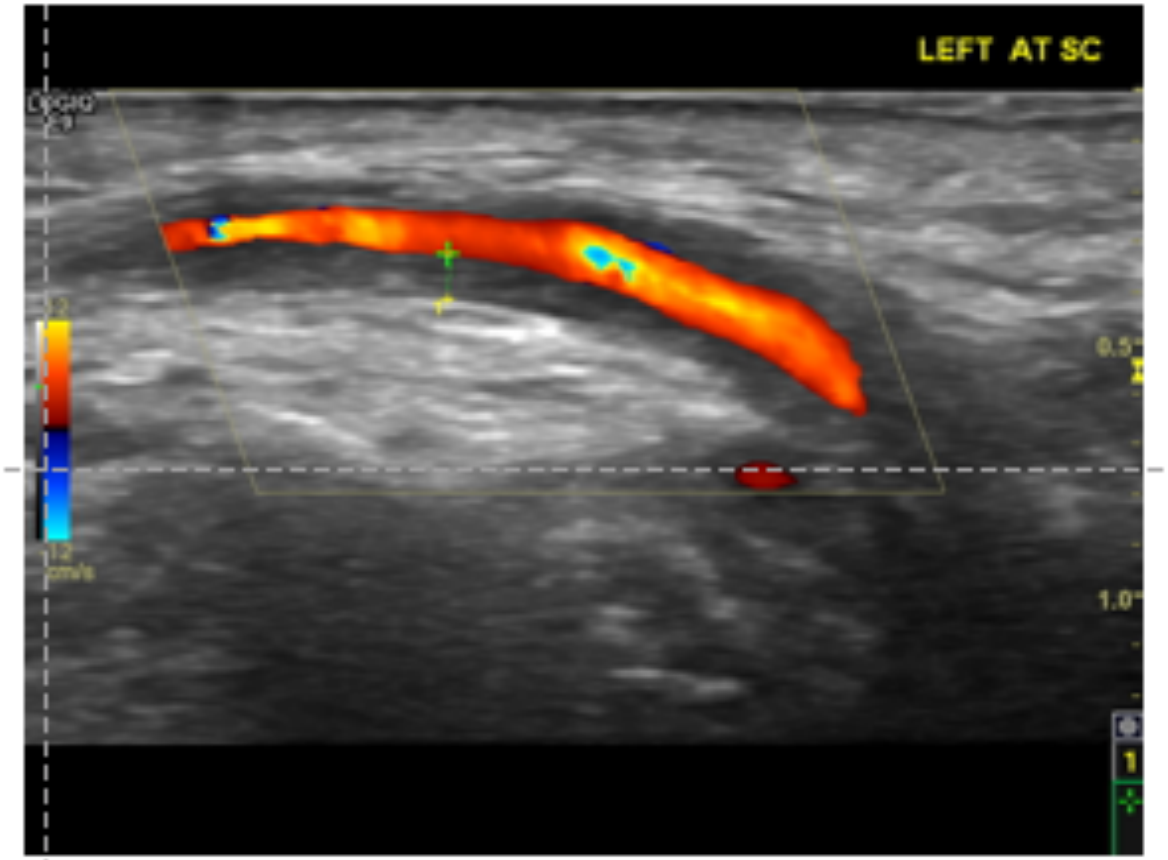
Gribbons et al A&R 2019

Vascular Imaging: Options

- Ultrasound
- Angiography
  - Catheter-based
  - Magnetic resonance imaging
  - Computed tomography
- Positron Emission Tomography (PET)

Temporal Artery Ultrasound in GCA





Courtesy of Dr. Cristina Ponte

Ultrasound

Advantages

- Cost effective
- No radiation
- At bedside
- Temporal, axillary, carotid, renal, iliofemoral arteries
- Fast track clinics

Disadvantages

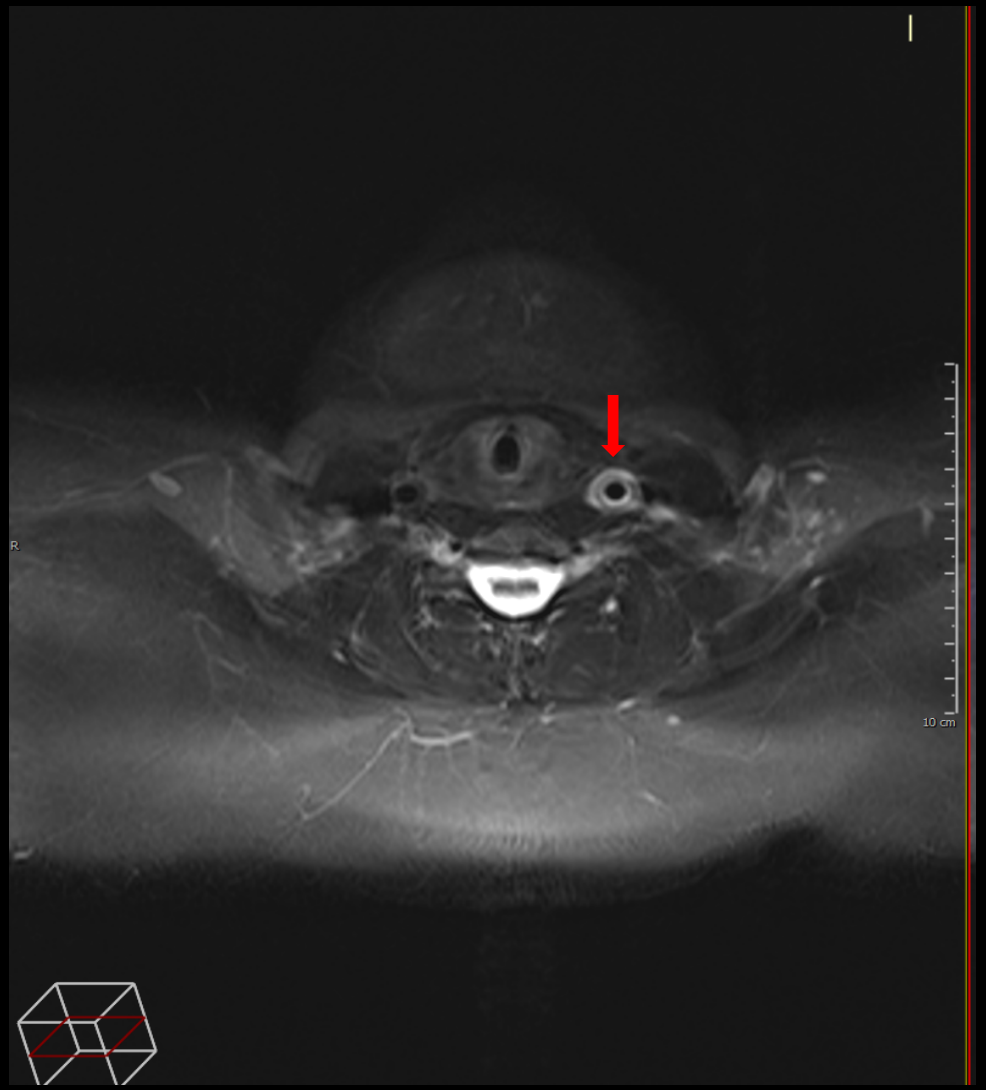
- Requires skills and training to perform and interpret
- Subclavian, vertebral, and aorta not as well covered
- Longitudinal monitoring not defined
- Does not align well with TAB findings in many studies

Type of angiography in TAK

- Computed tomographic and magnetic resonance angiography (CTA, MRA) are equivalent
- MRA preferred to avoid radiation
- Limited use of catheter-based angiography
  - Measurement of central artery pressures


< 105 - 1 >
Sag
A
I
L

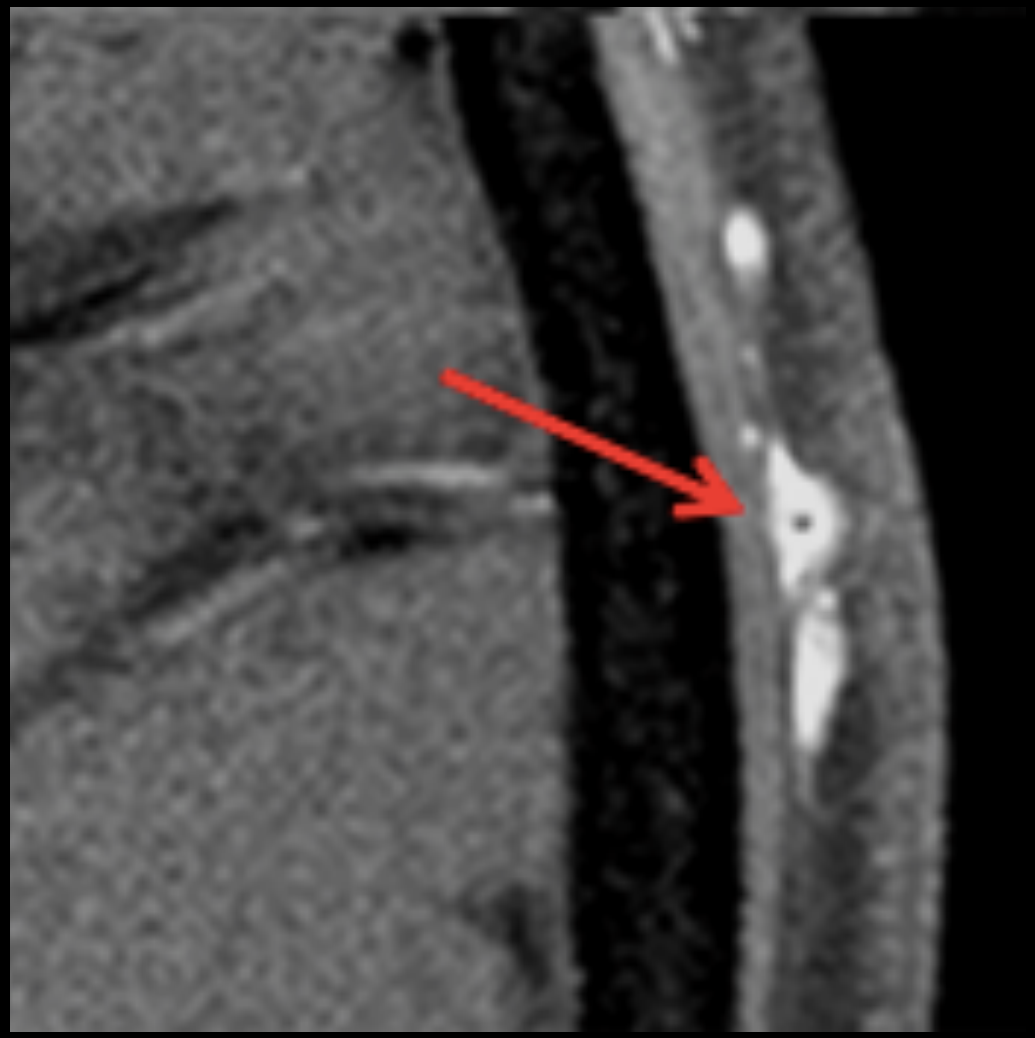
Magnetic Resonance Imaging



Vascular edema

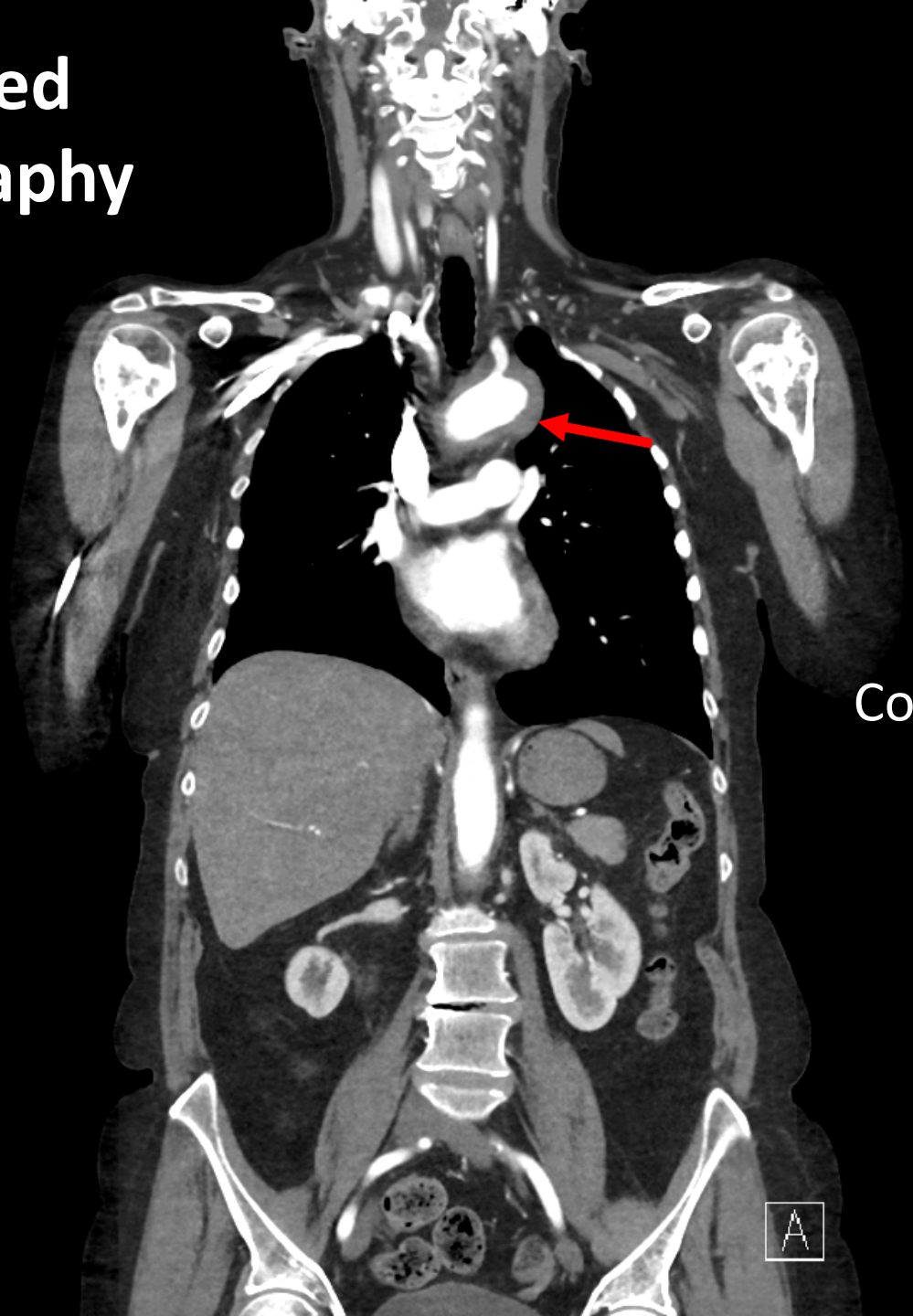
Quinn et al *ARD* 2018

High Resolution Scalp MRA



Rheaume et al *A&R* 2016

Computed Tomography



Contrast enhancement

Angiography

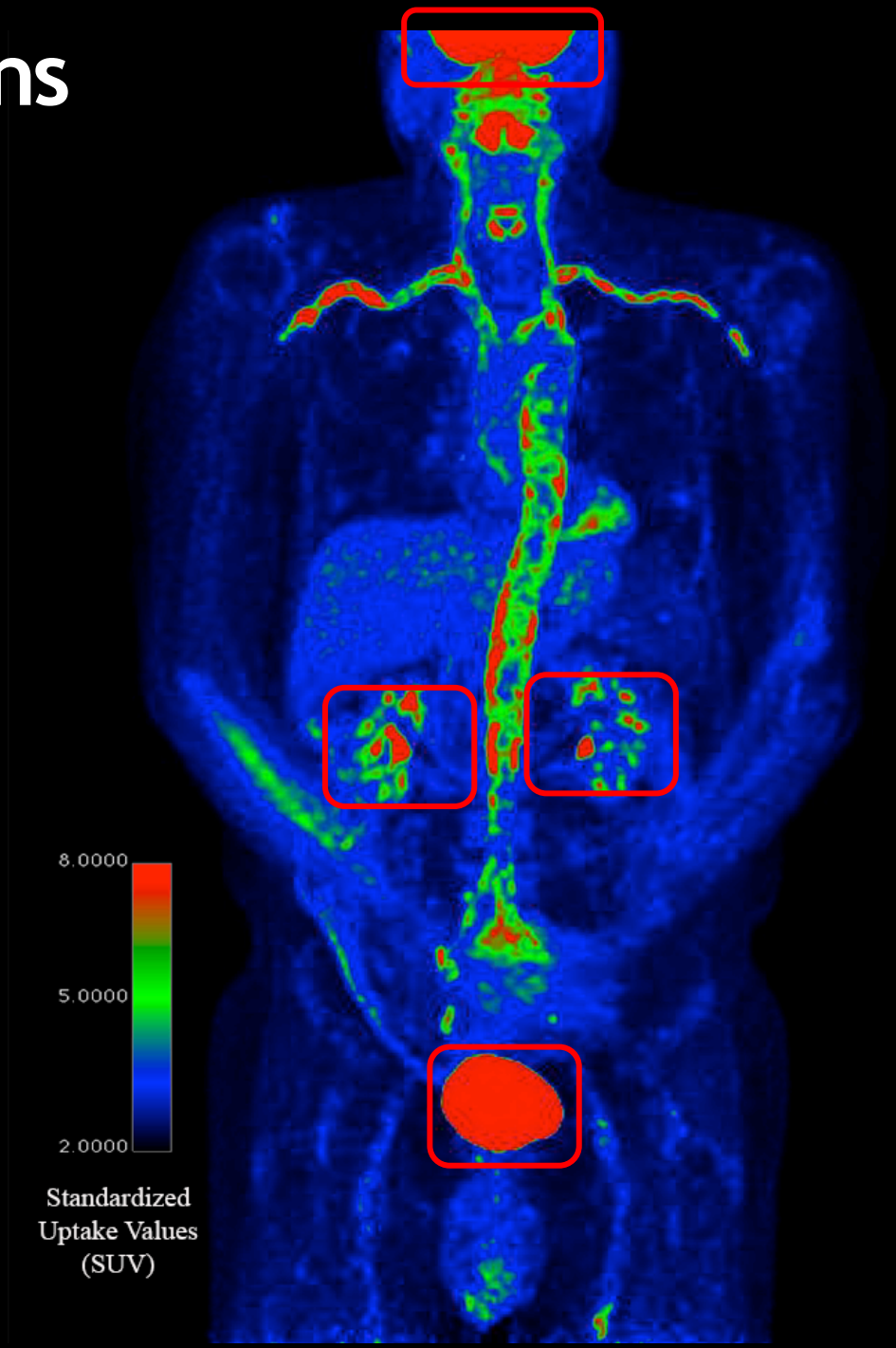
Advantages

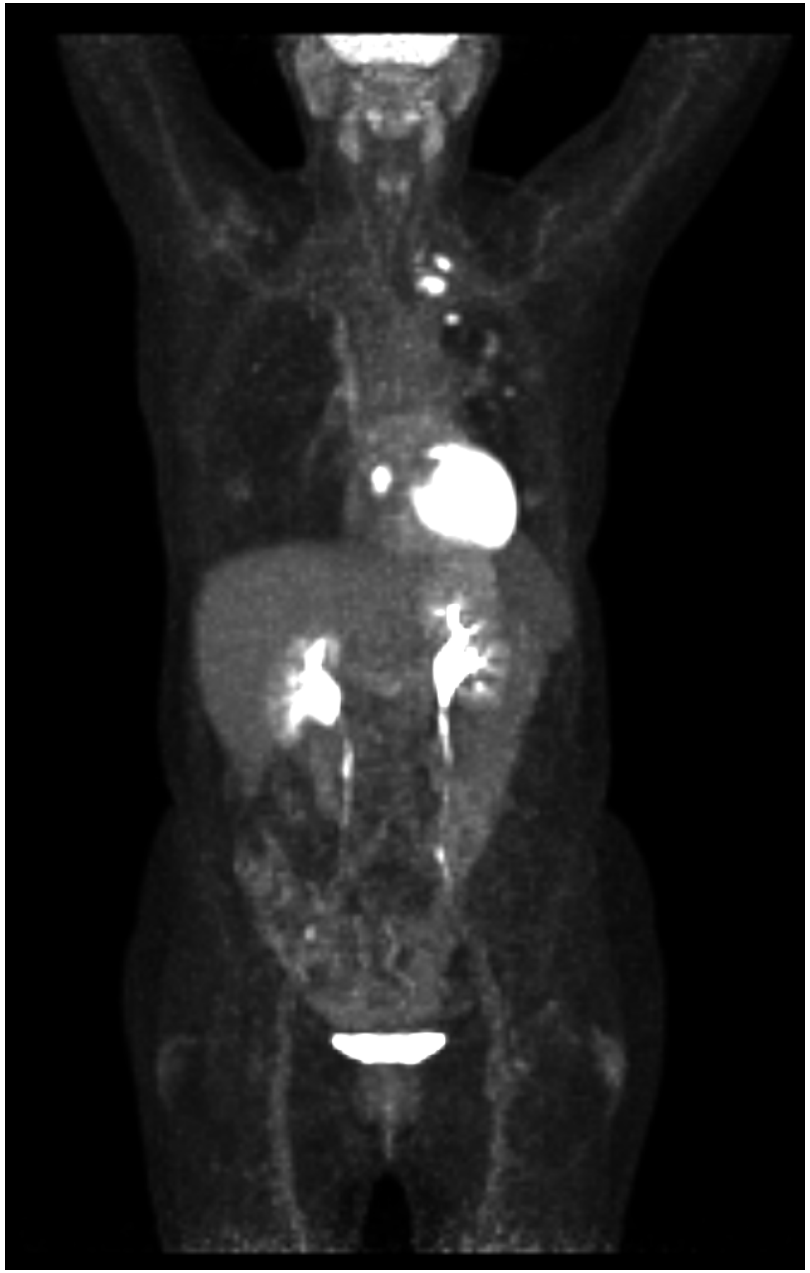
- Define luminal damage
- Assess wall morphology
- Profile aorta and branches
- Monitor progression of existing damage
- Monitor for new lesions

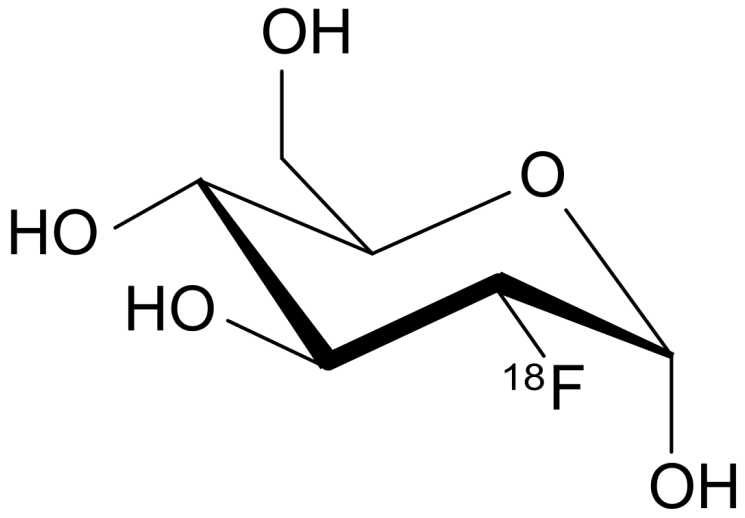
Disadvantages

- Technically challenging
- CTA with radiation
- Contrast exposure
  - Gadolinium retention
  - Iodinated contrast dye issues
- Cost
- Interpretation of wall morphology takes skill

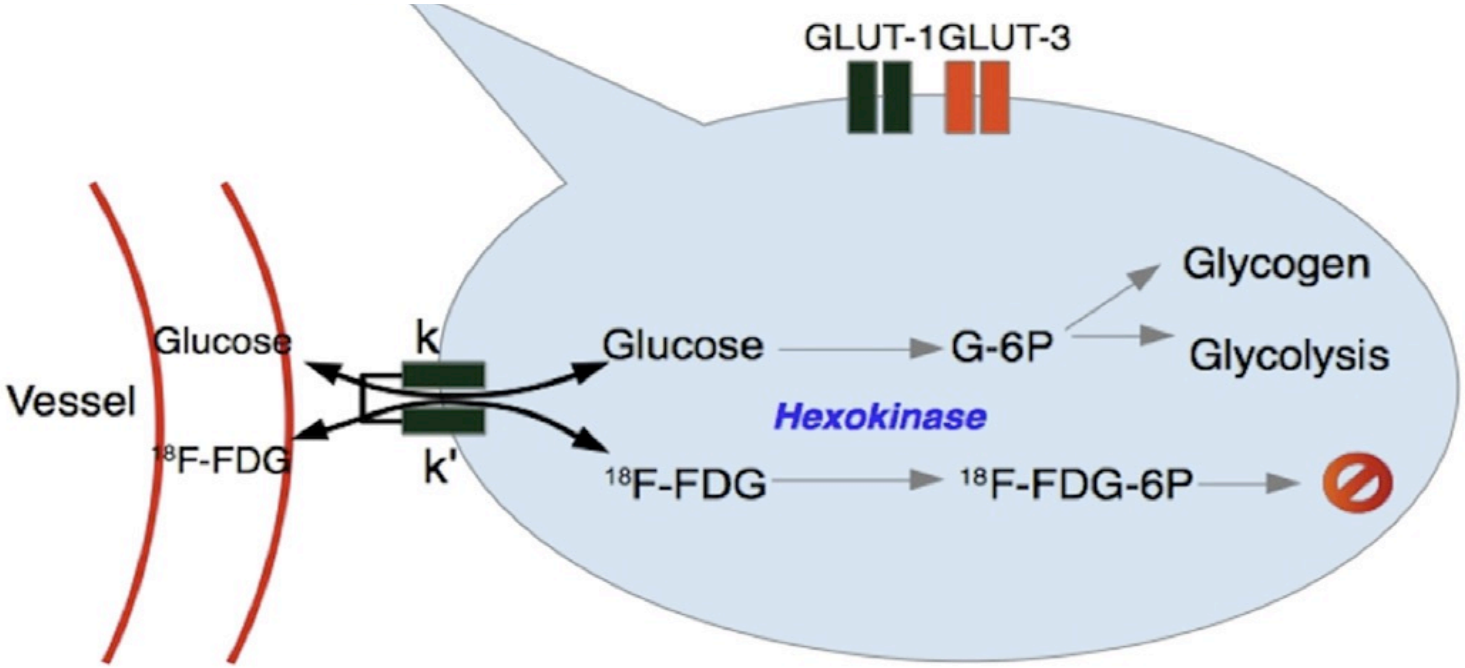
FDG-PET Scans

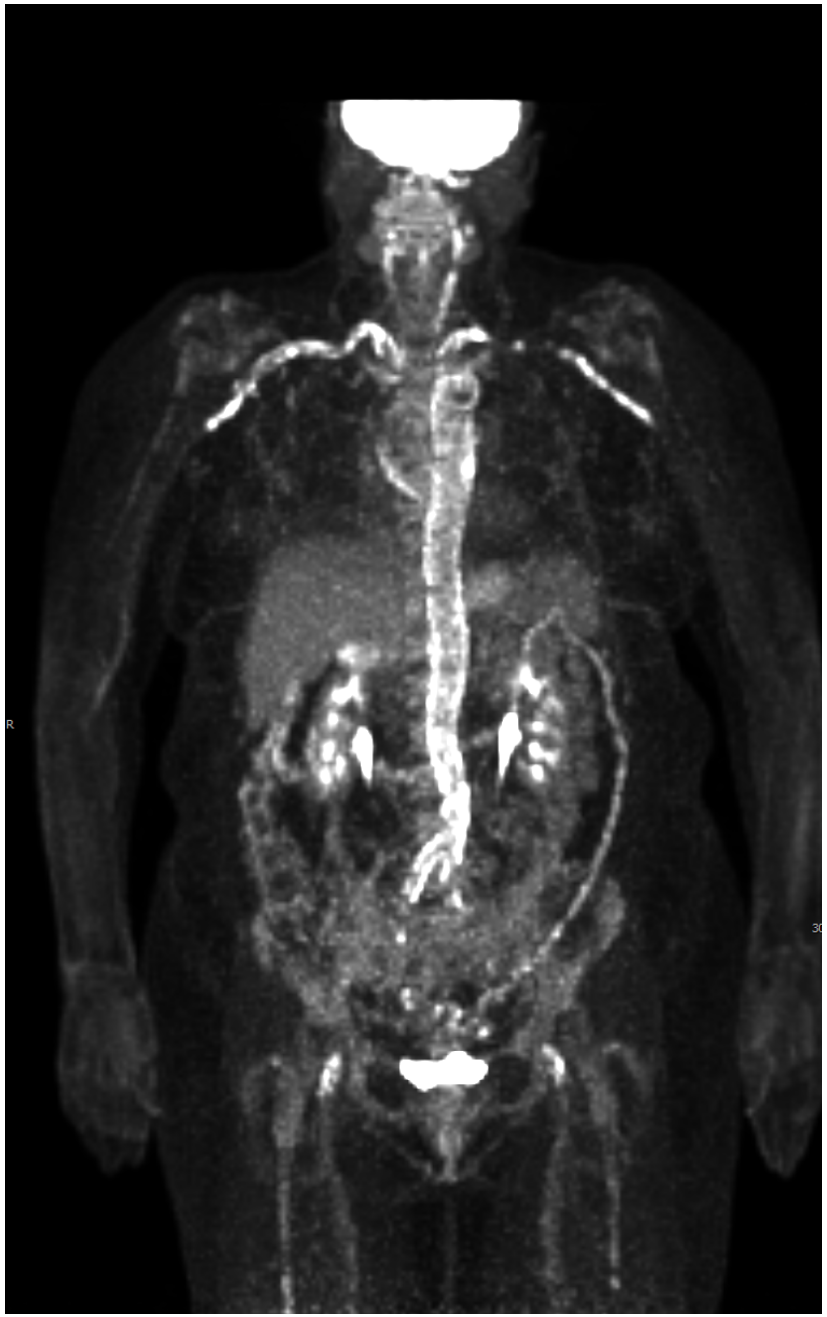


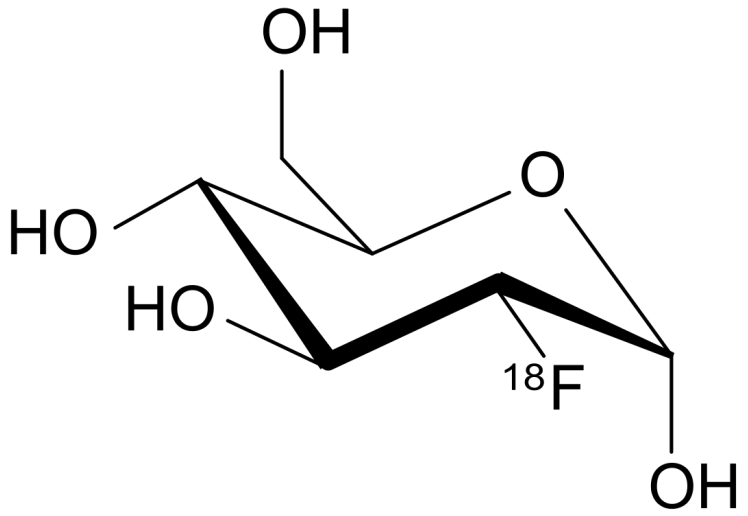



OH
O
HO
HO
18F
OH

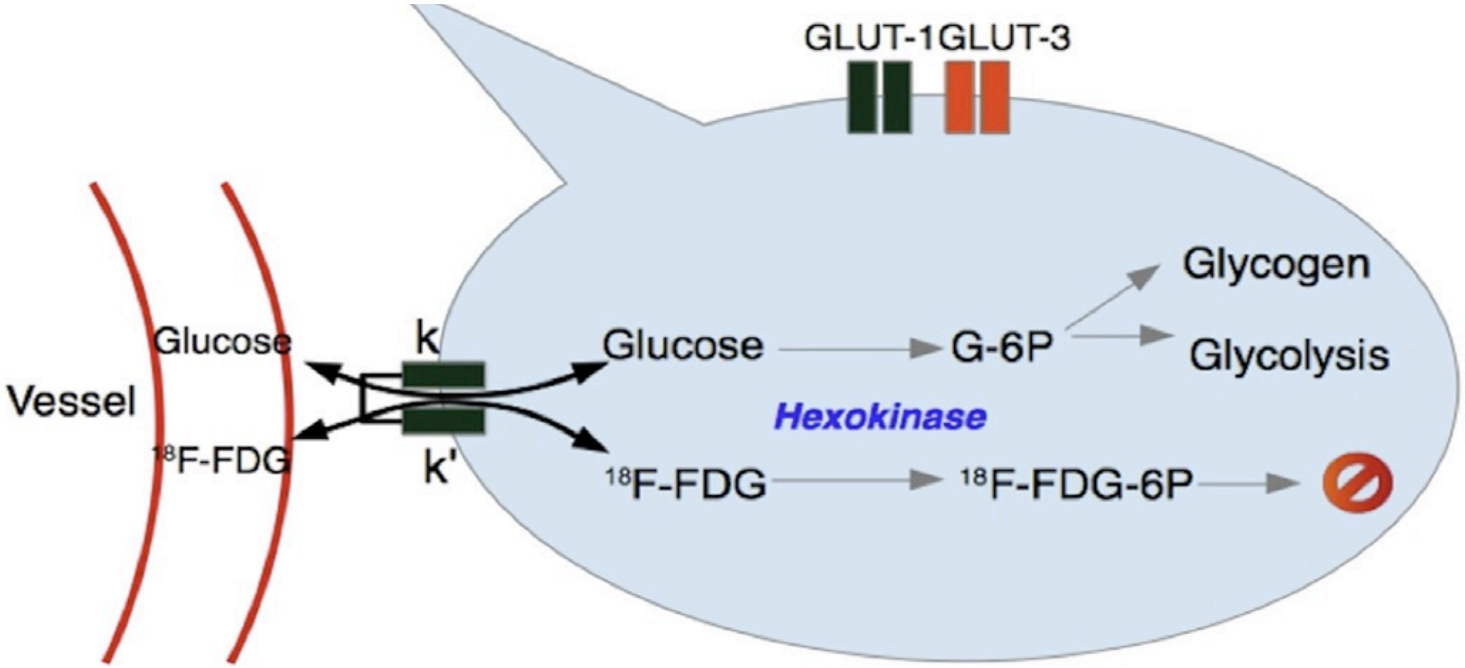
^{18}FDG


GLUT-1
GLUT-3
Glycogen
Glycolysis
Glucose
G-6P
Hexokinase
Glucose
k
Vessel
18F-FDG
k'
18F-FDG
18F-FDG-6P

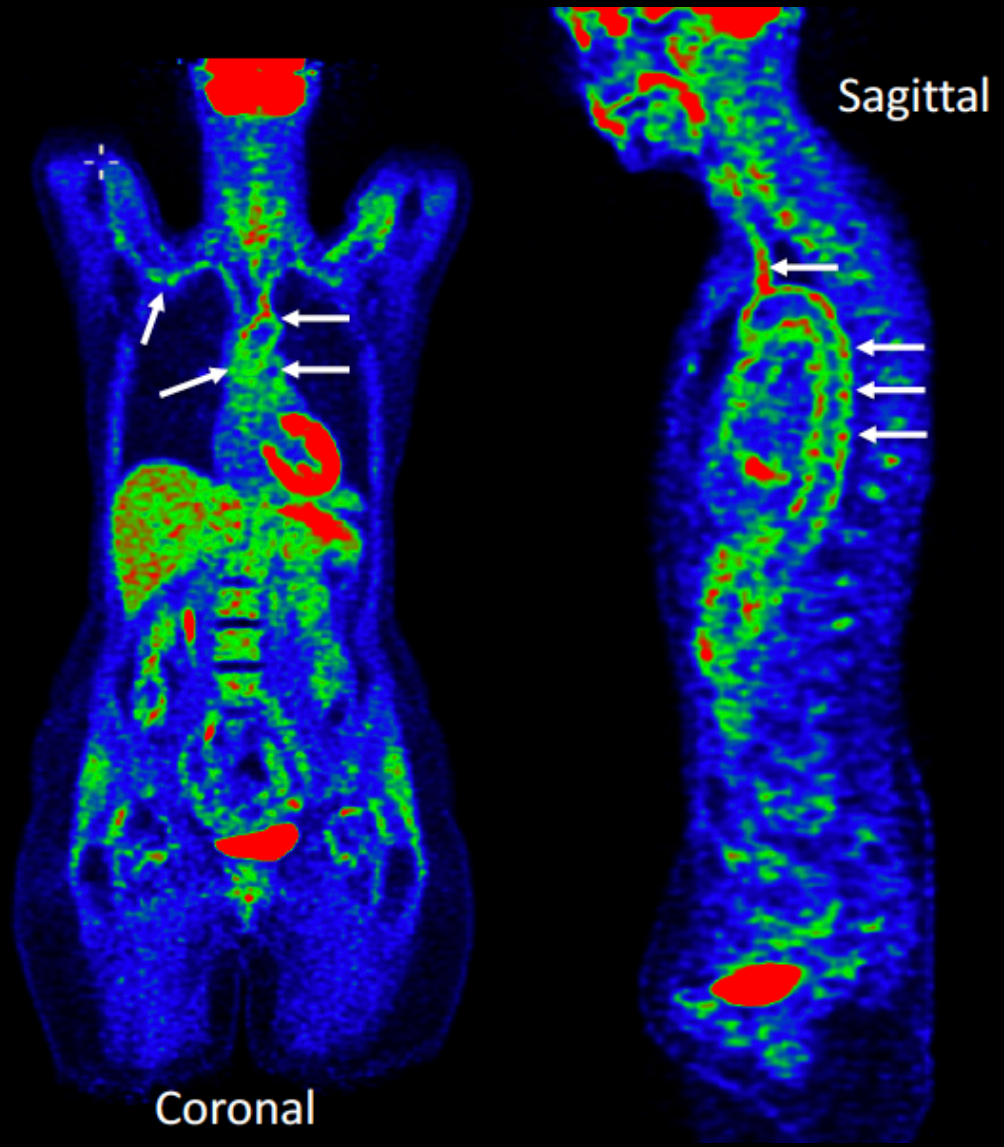



OH
O
HO
HO
18F
OH

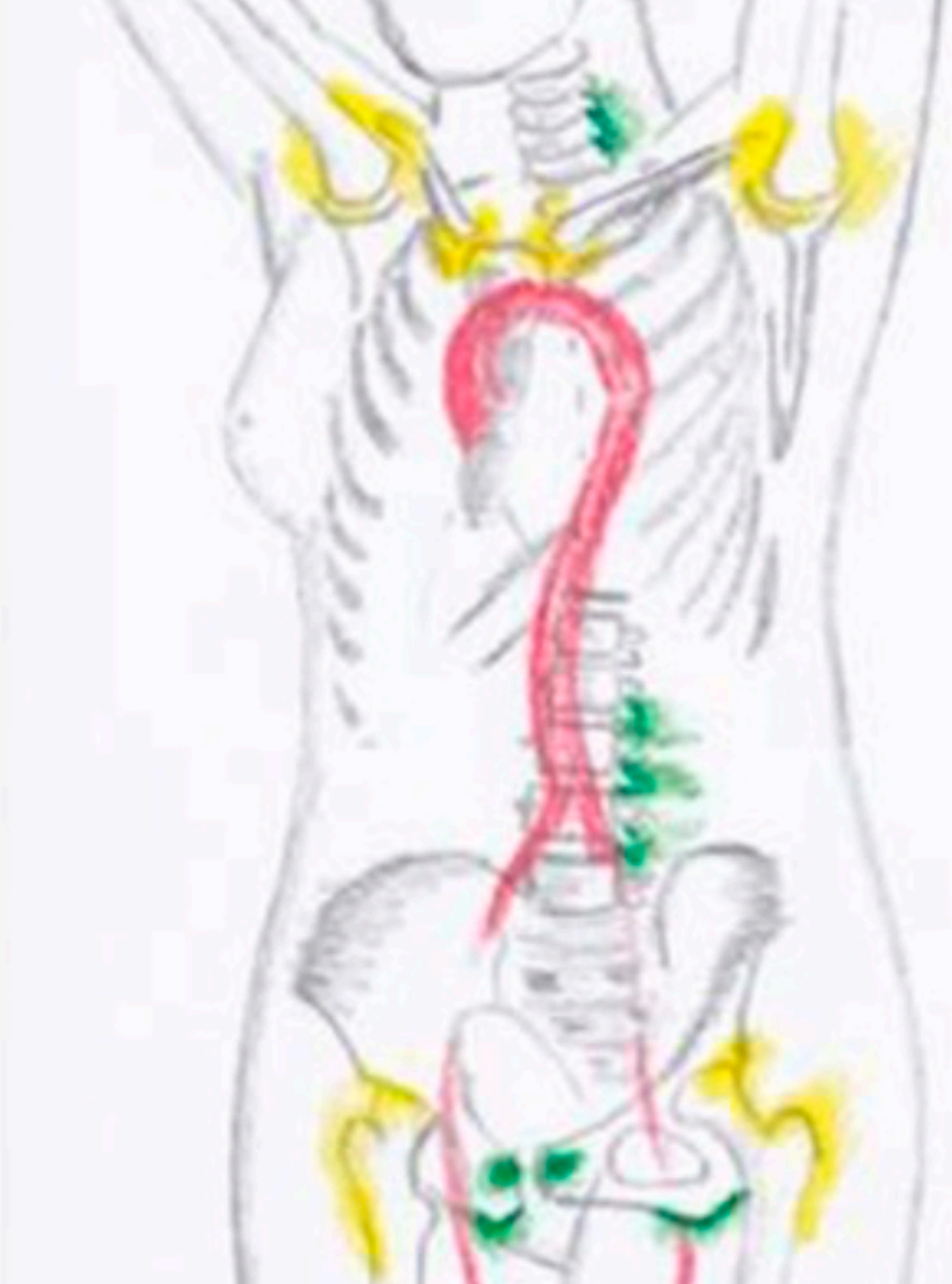
^{18}FDG


GLUT-1
GLUT-3
Glycogen
Glucose
G-6P
Glycolysis
k
Glucose
Vessel
Hexokinase
18F-FDG
k'
18F-FDG
18F-FDG-6P

Atherosclerosis



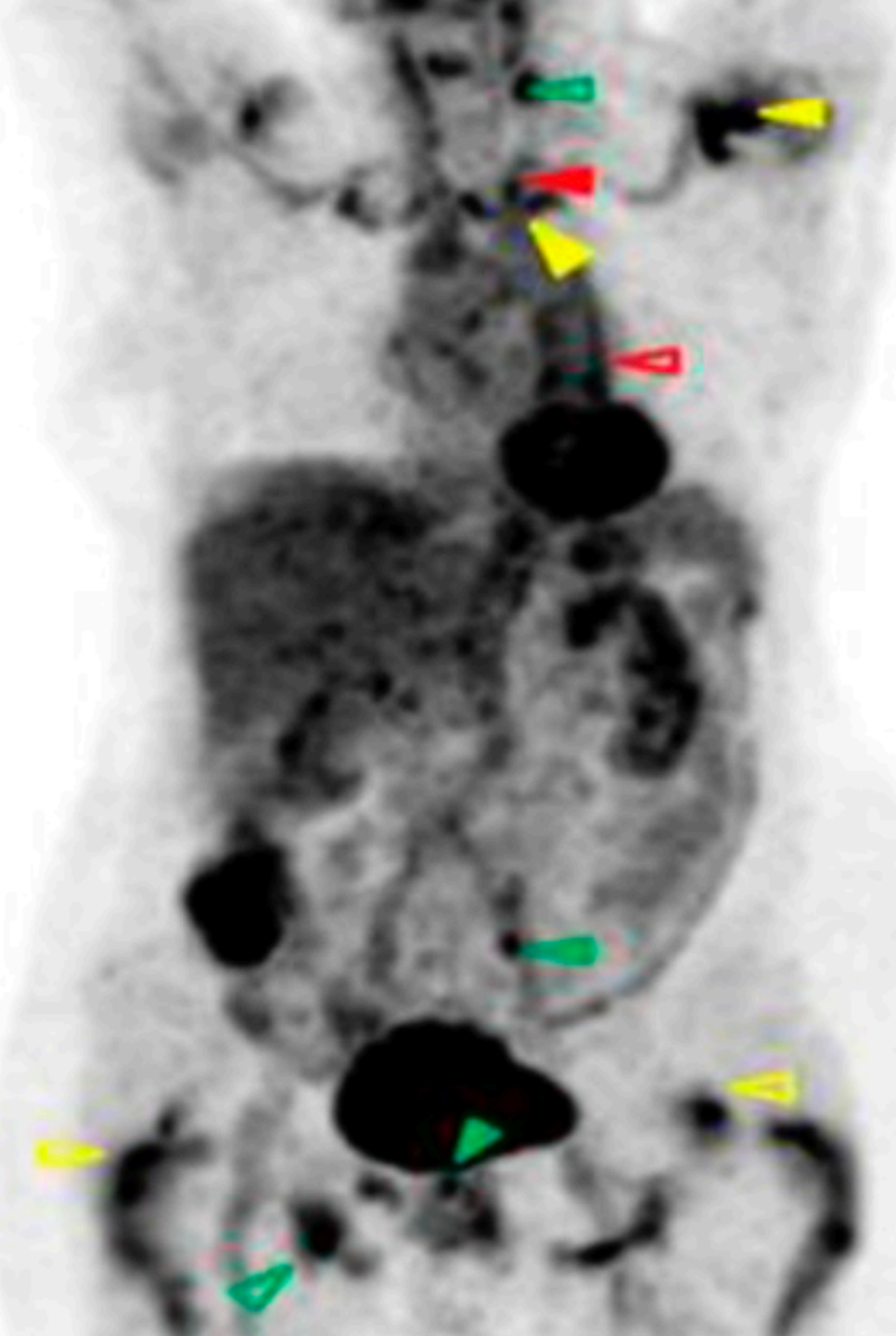
Grayson et al, A&R, 2018



PMR

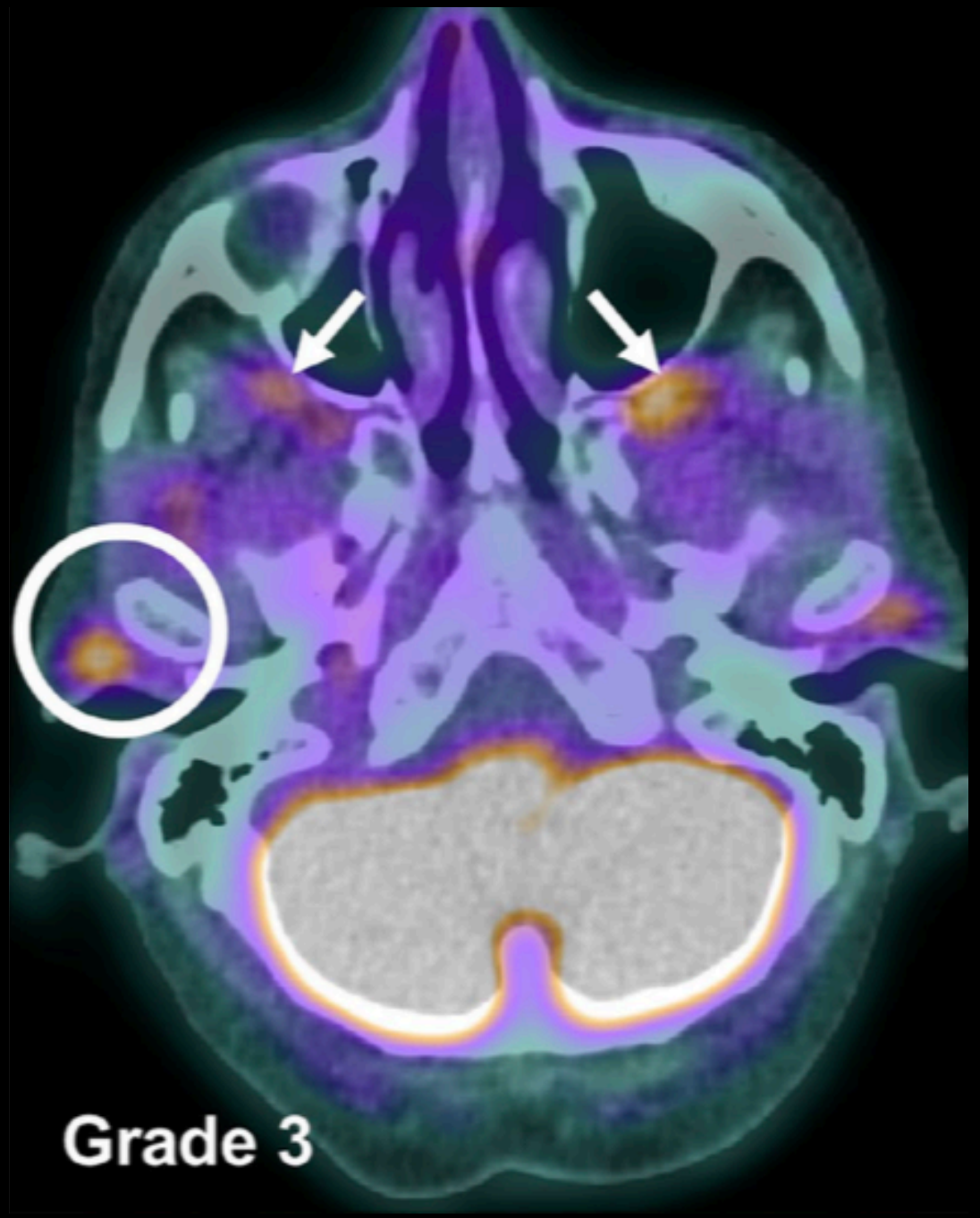
+

GCA



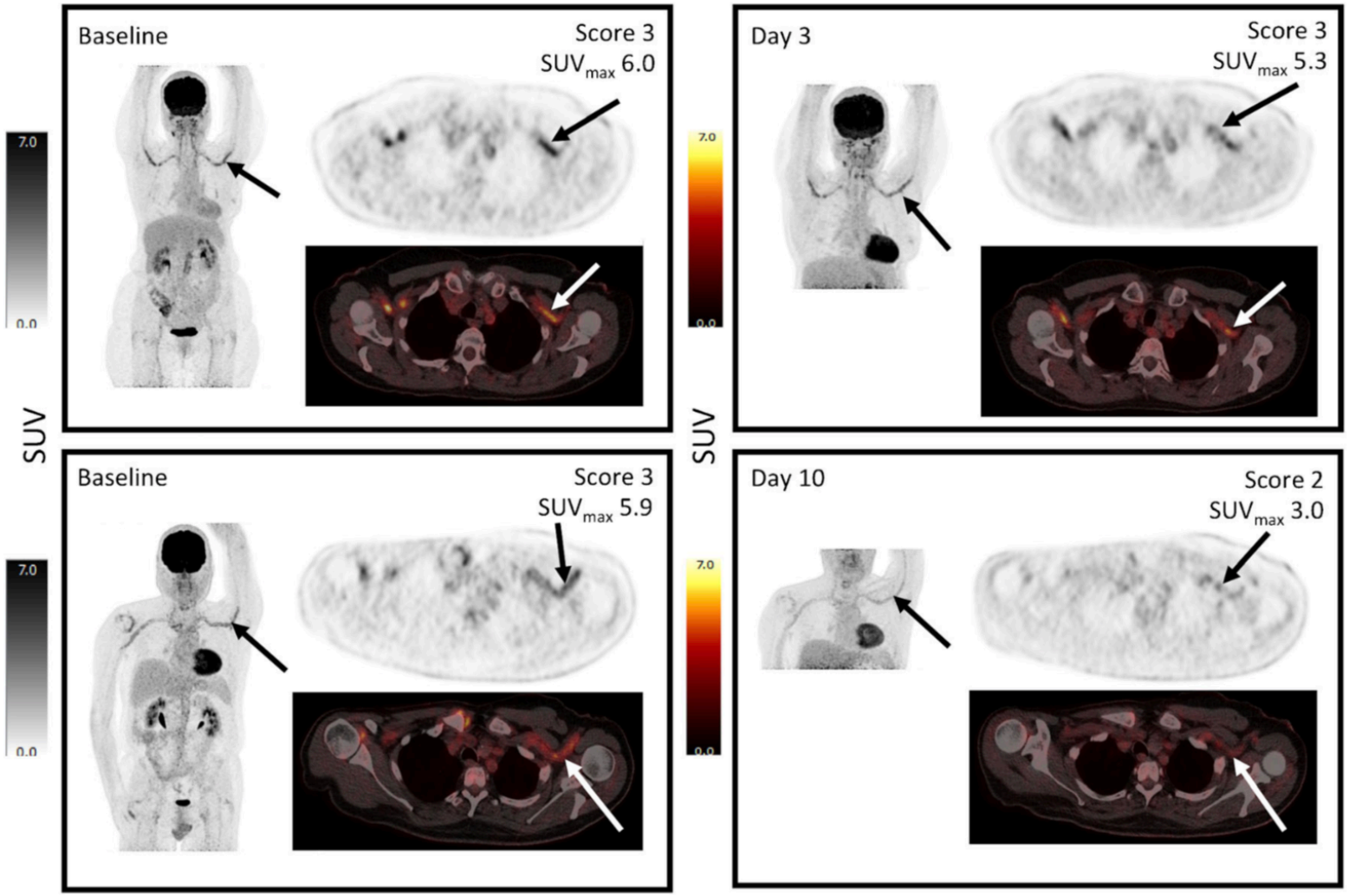
Blockmans *Br J Rad* 2017

FDG-PET Scanner Resolution is Improving



Sammel et al, A&R 2019
Nielsen et al, Eur J Nuc Med, 2018

Timing of FDG-PET Relative to GC Initiation



Randomized Trial

- Baseline FDG-PET
  - 24 active

↓

Prednisone 60mg/day

↓

- Repeat FDG-PET
  - Day 3: 10/10 active
  - Day 10: 5/14 active

Nielsen et al 2019

Positron Emission Tomography

Advantages

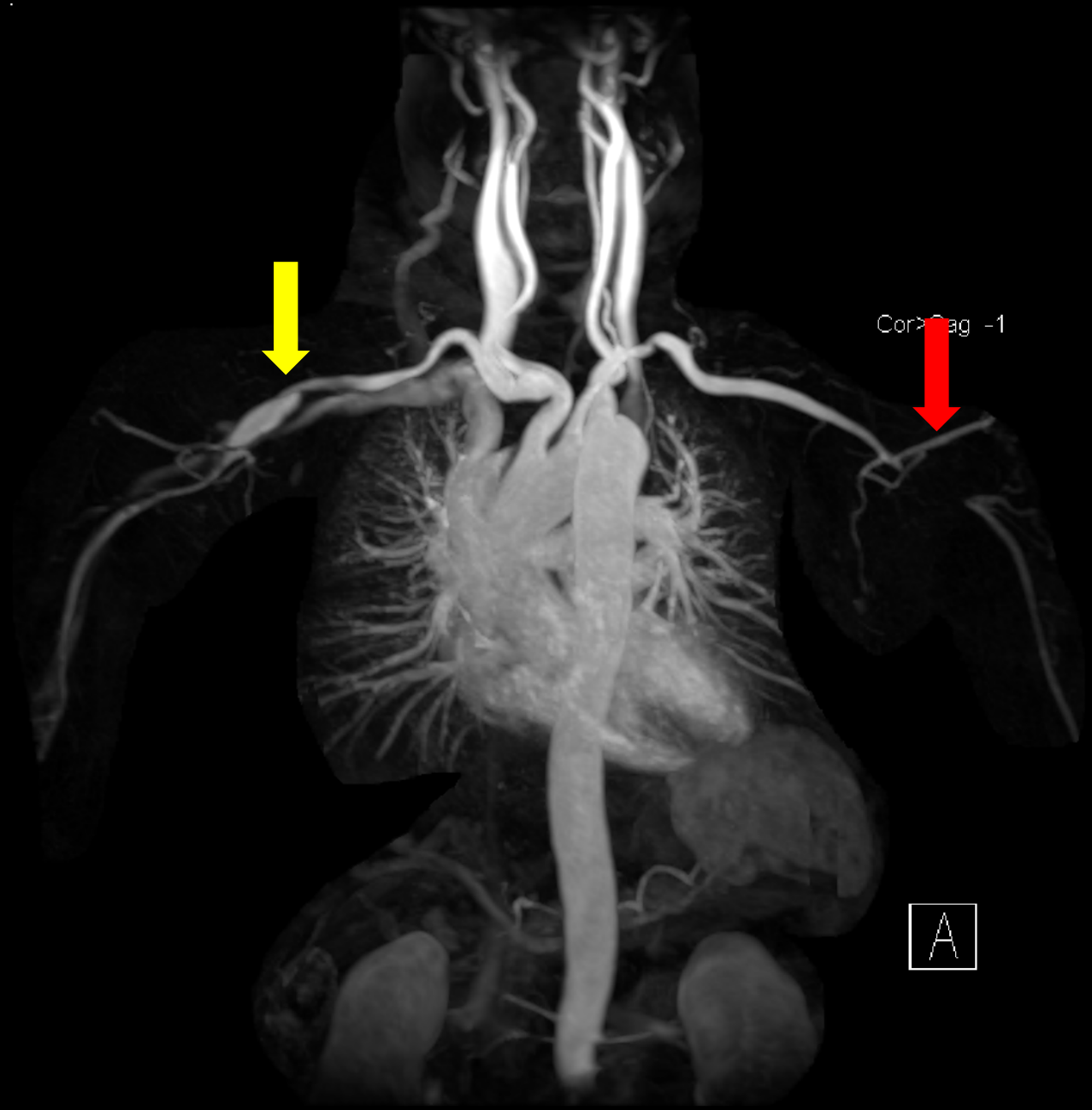
- Comprehensive assessment
- Vascular inflammation readout
- Compliments angiography
- Diagnostic test
- Clarify unusual symptoms
- Monitor treatment response

Disadvantages

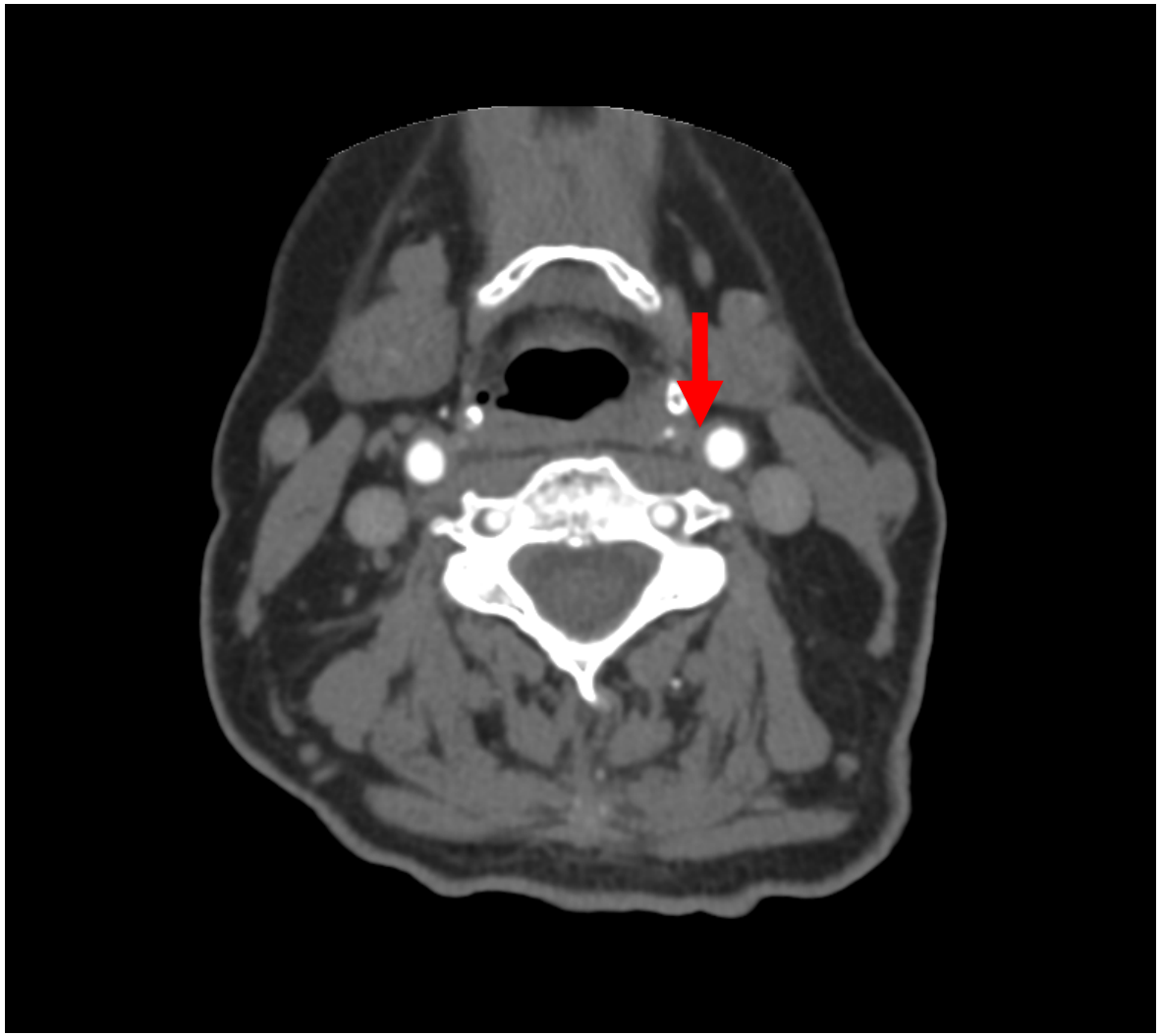
- Cost
- Radiation
- Interpretation
- Glucocorticoid effect
- Insurance approval
- Subclinical inflammation
- Longitudinal data lacking

Our case…

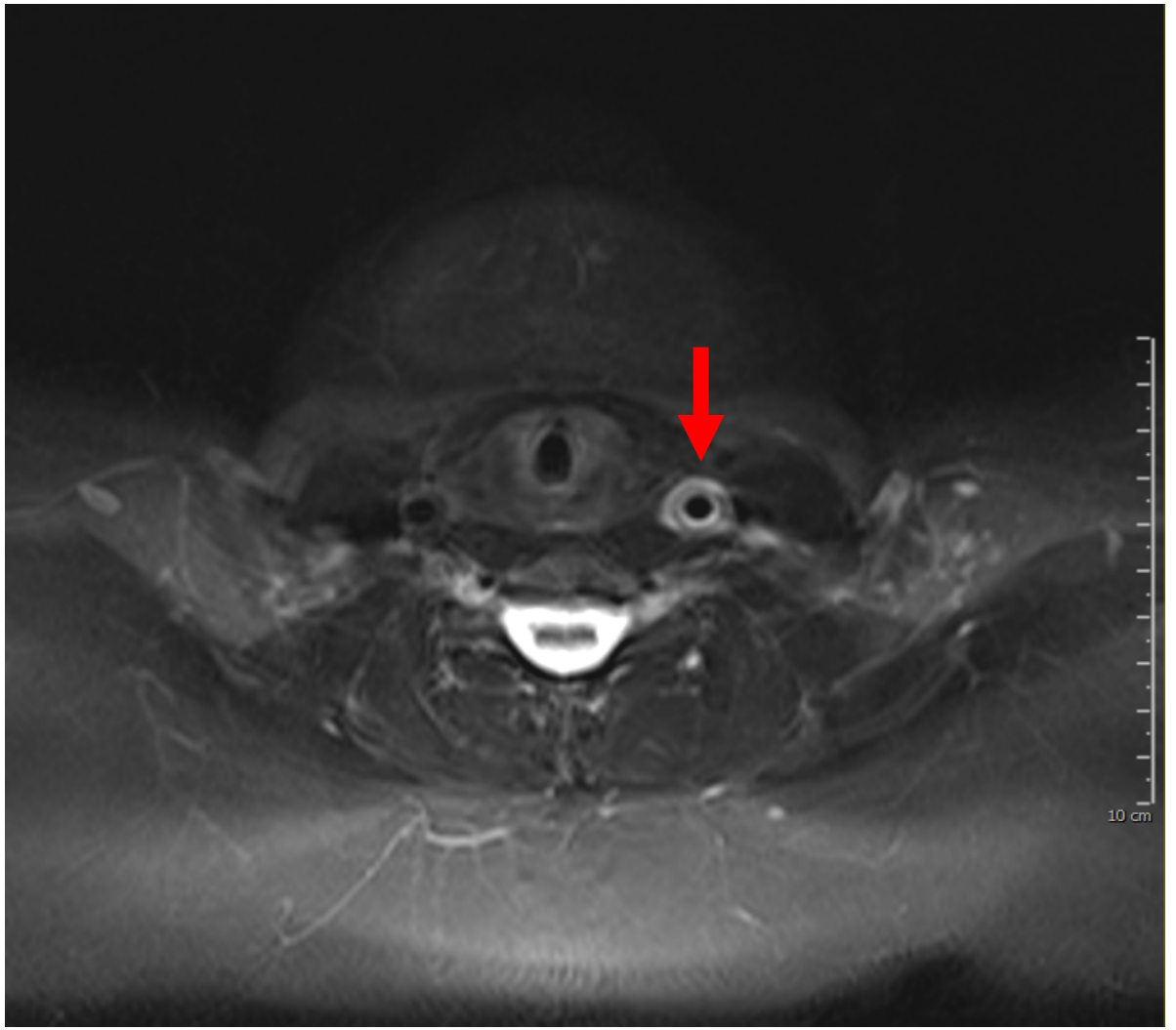
- 69-year-old woman referred to the NIH from a local hospital for suspected vasculitis. She was diagnosed with an inflammatory arthritis five years ago and treated with glucocorticoids and TNF inhibitor therapy.
- She did well for a number of years until she developed a rise in acute phase reactants followed by left arm claudication. She was noted to have decreased left radial pulse. She subsequently developed claudication in the right arm. She reports chronic right sided headaches.
- On physical examination there was reduced radial pulses bilaterally and a left subclavian bruit. BP was 111/68 in the right arm and unobtainable in the left arm. ESR 88 mm/hr and CRP 55 mg/L.


A

Computed Tomography (CT)

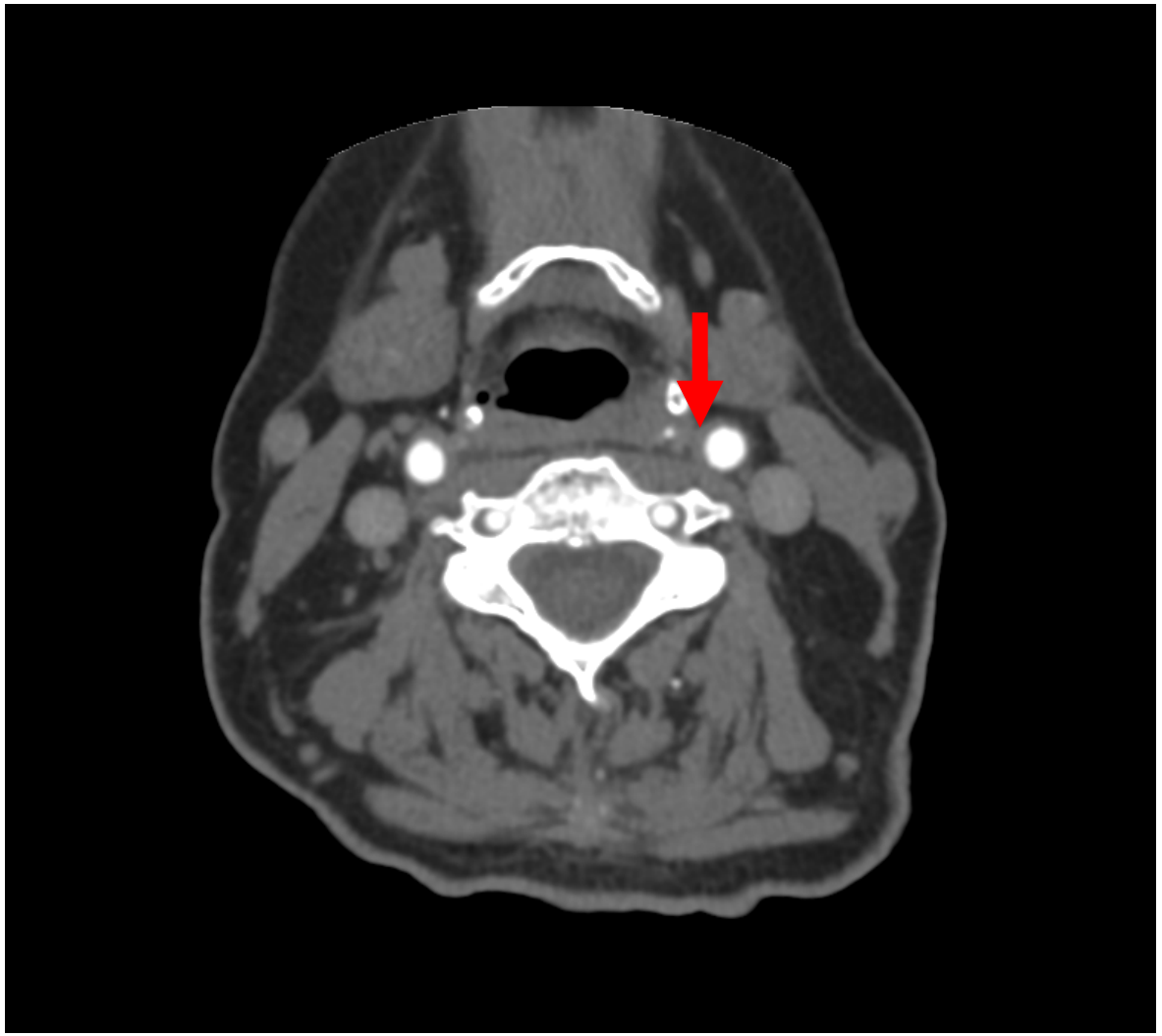


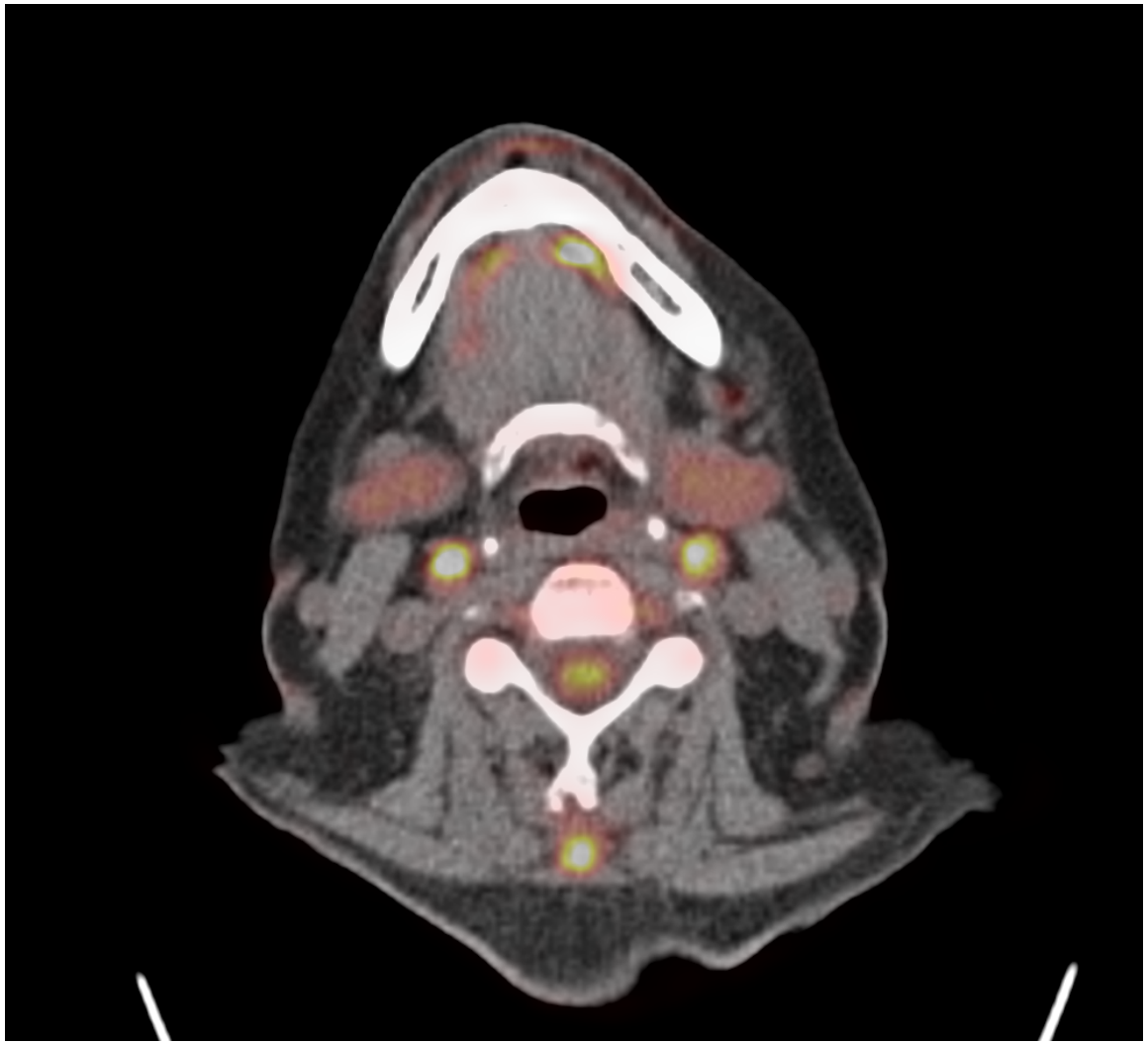
MRI – Wall Edema Imaging



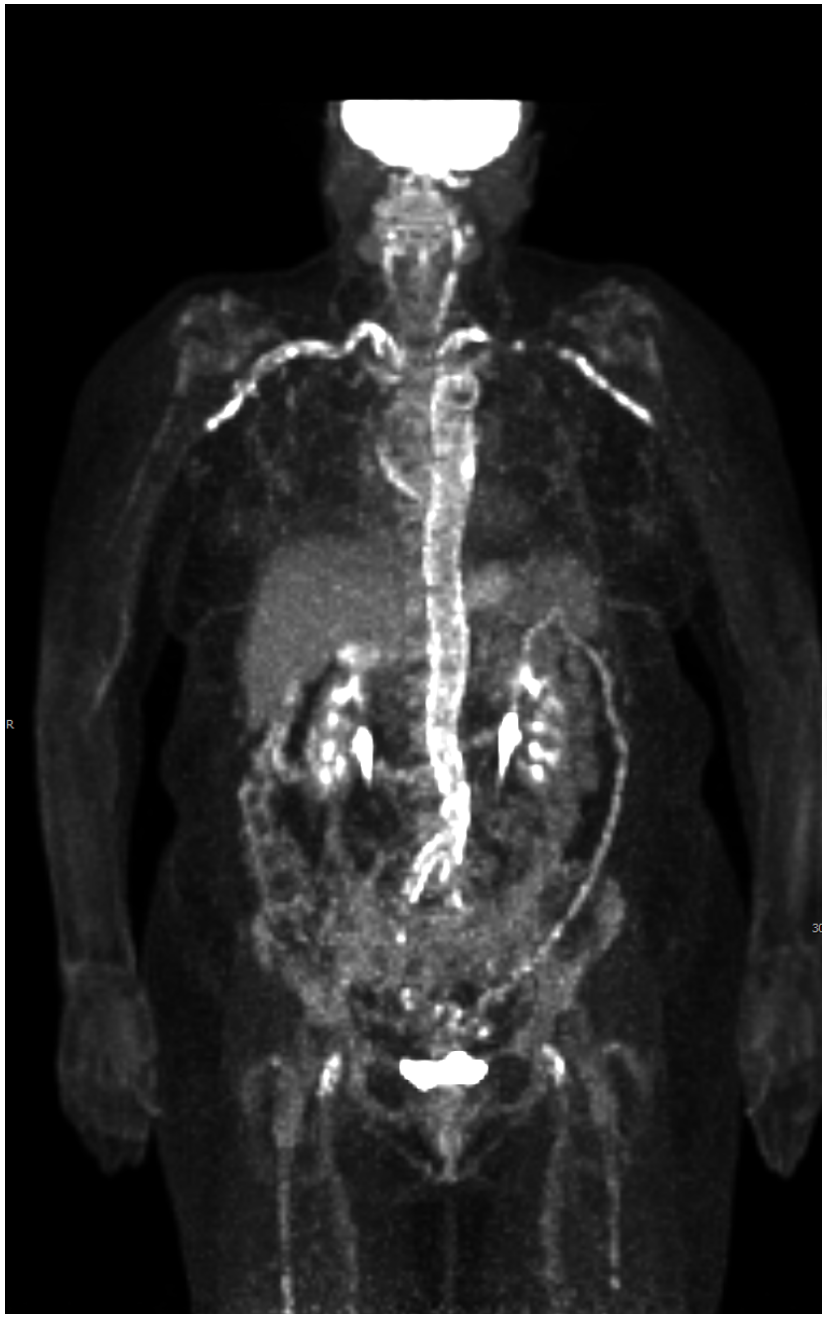
Computed Tomography (CT)

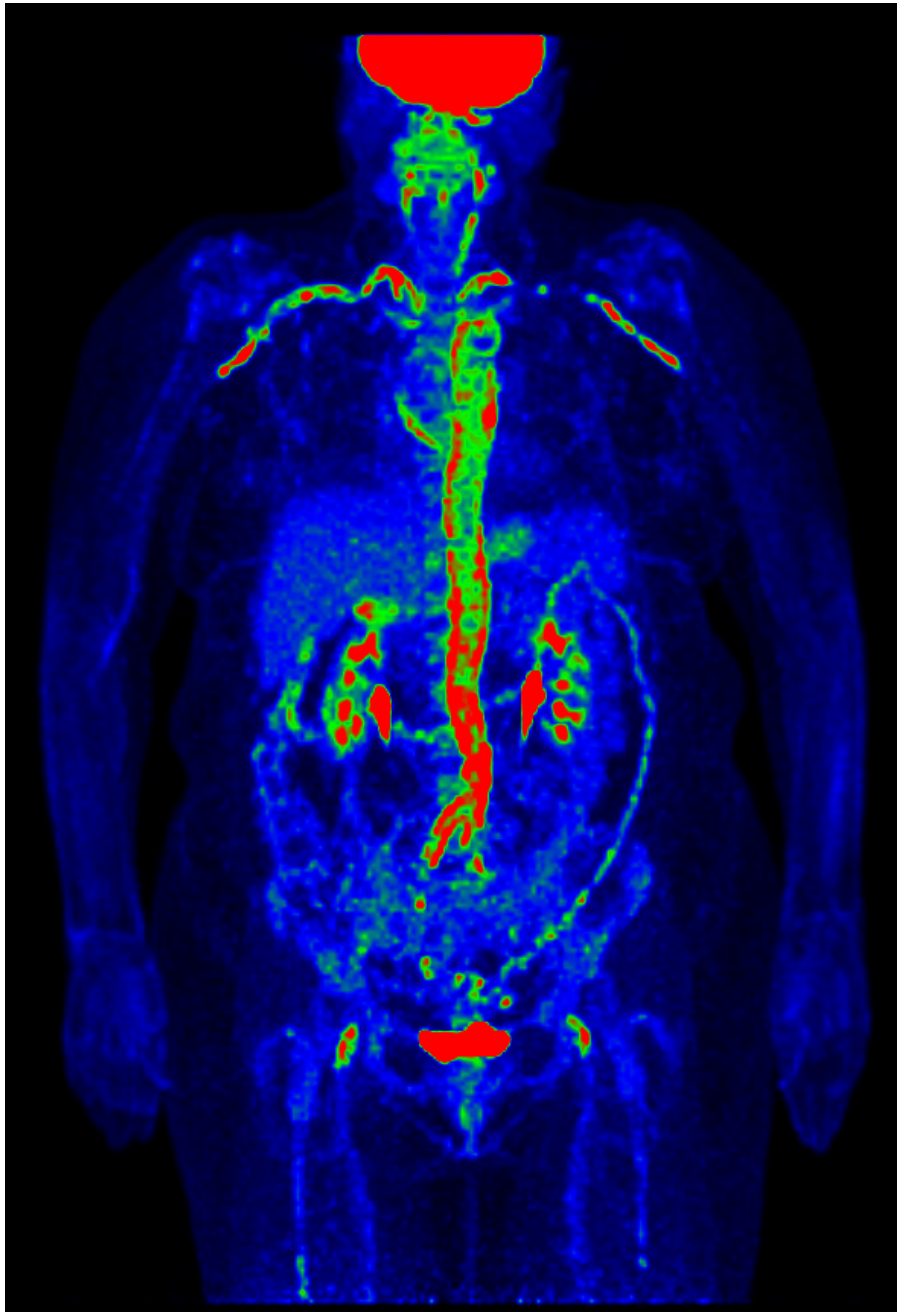
^{18}F Fluorodeoxyglucose (FDG)





Positron Emission Tomography (PET)

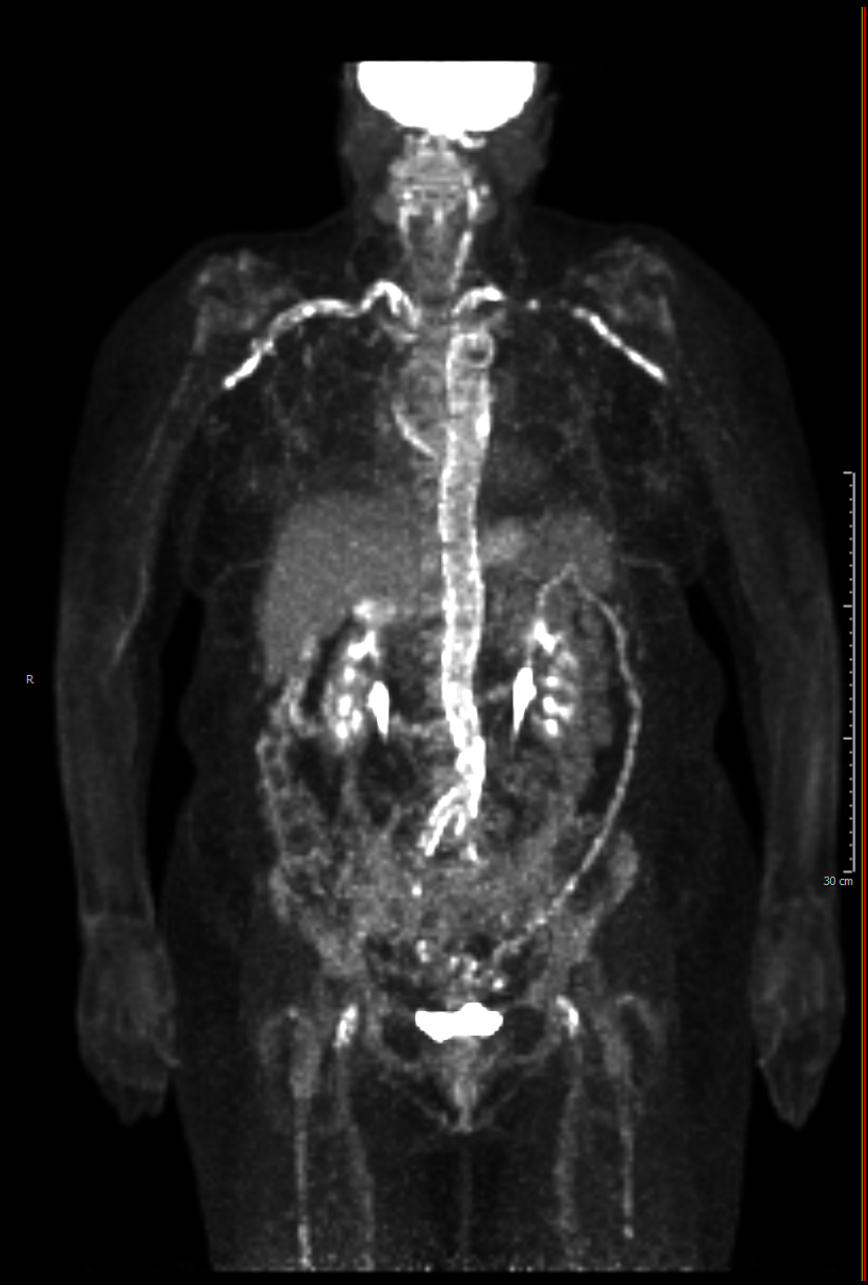




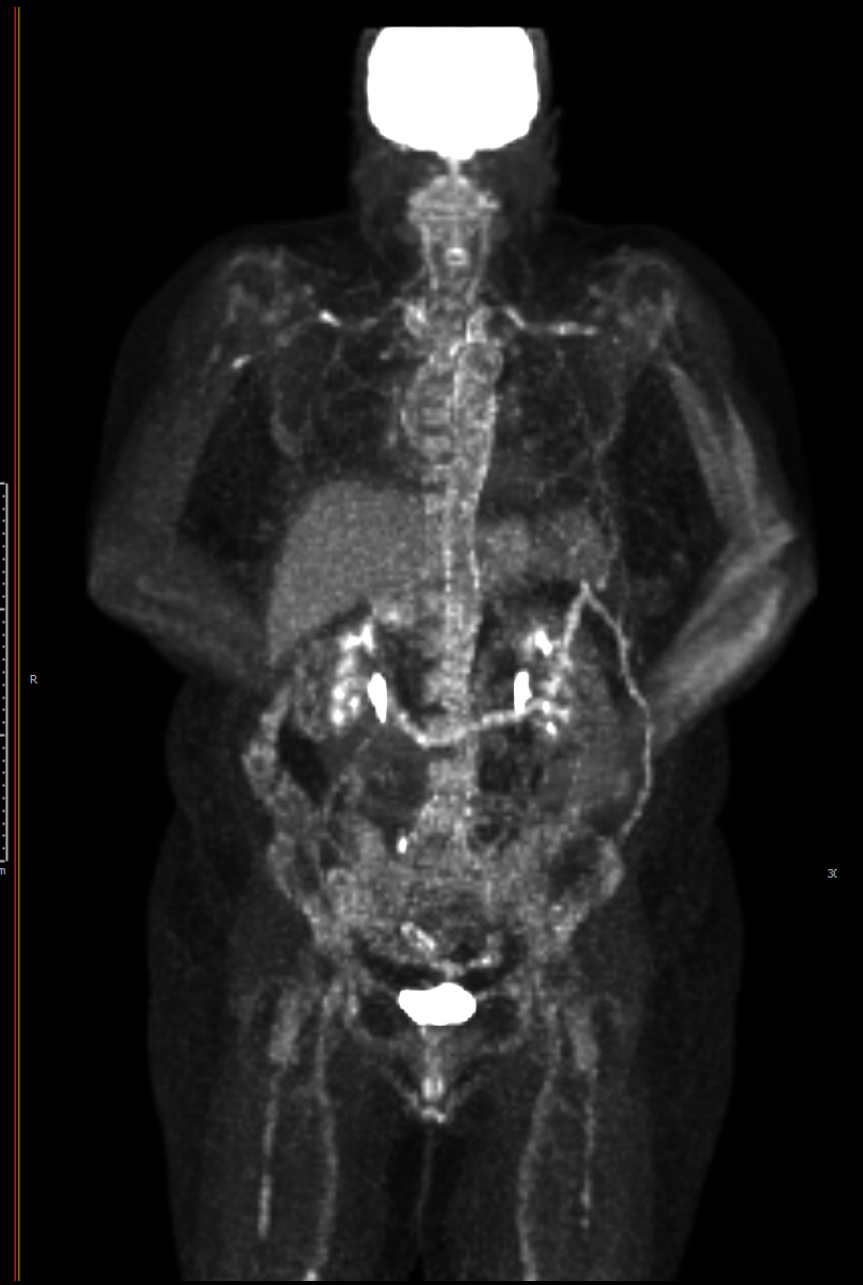
Patient was treated successfully for one year…

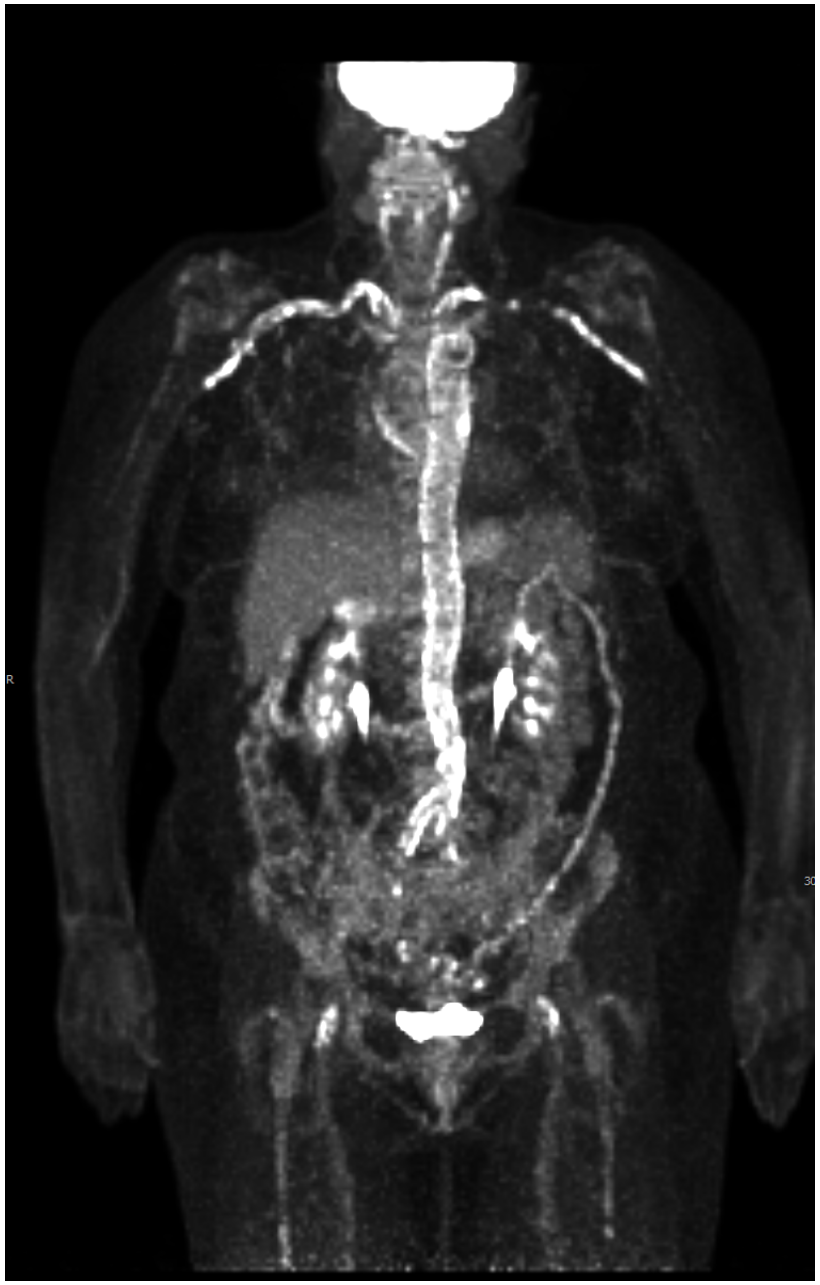
What happens to imaging findings over time?

Angiogram Unchanged in First of Treatment

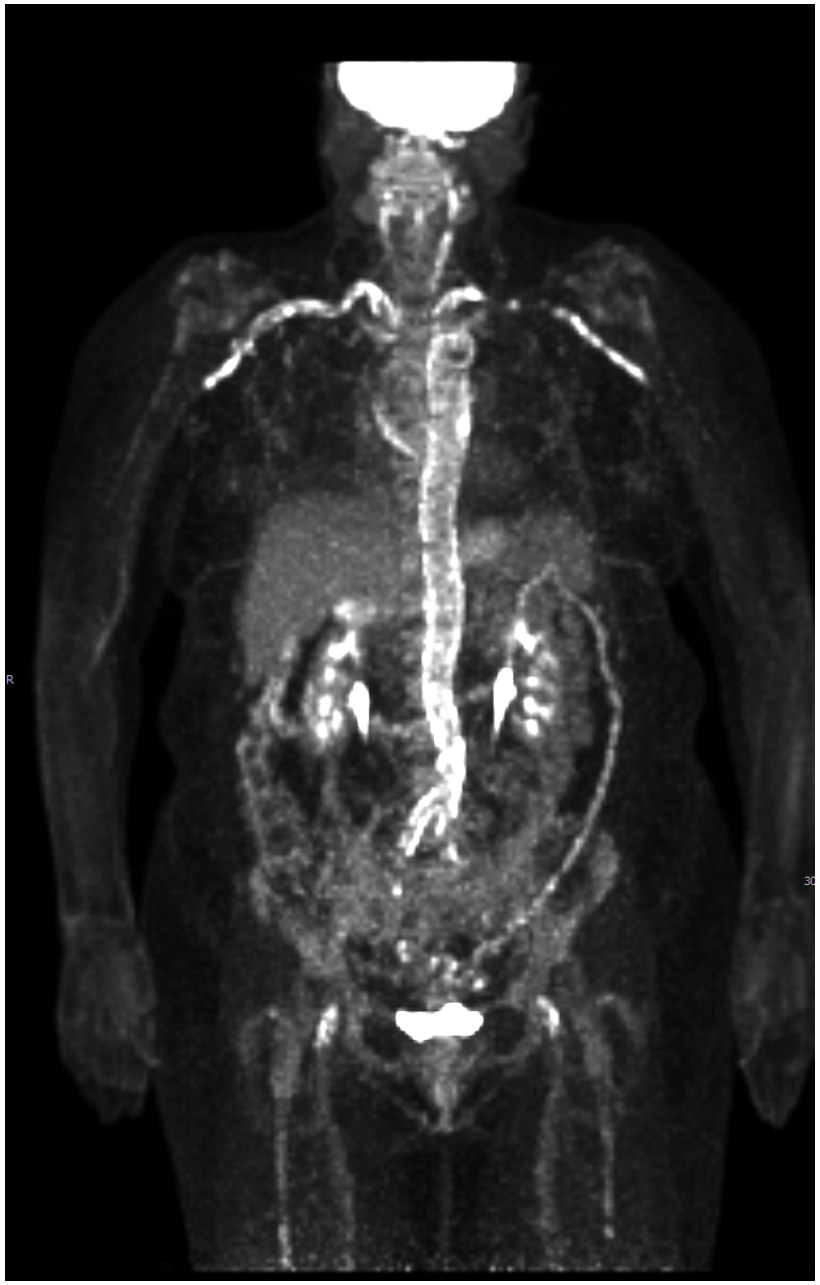

R
30 cm


R


R
30 cm



	Early	Mid	Late
Inflammation	↑↑	↑	↑
Wall Thickening	↑↓	↑	↑
Wall Edema	↑↓	↑	↑
Stenosis	↑↓	↑	↑↑
Symptoms	↑↓	↑↓	↑↓



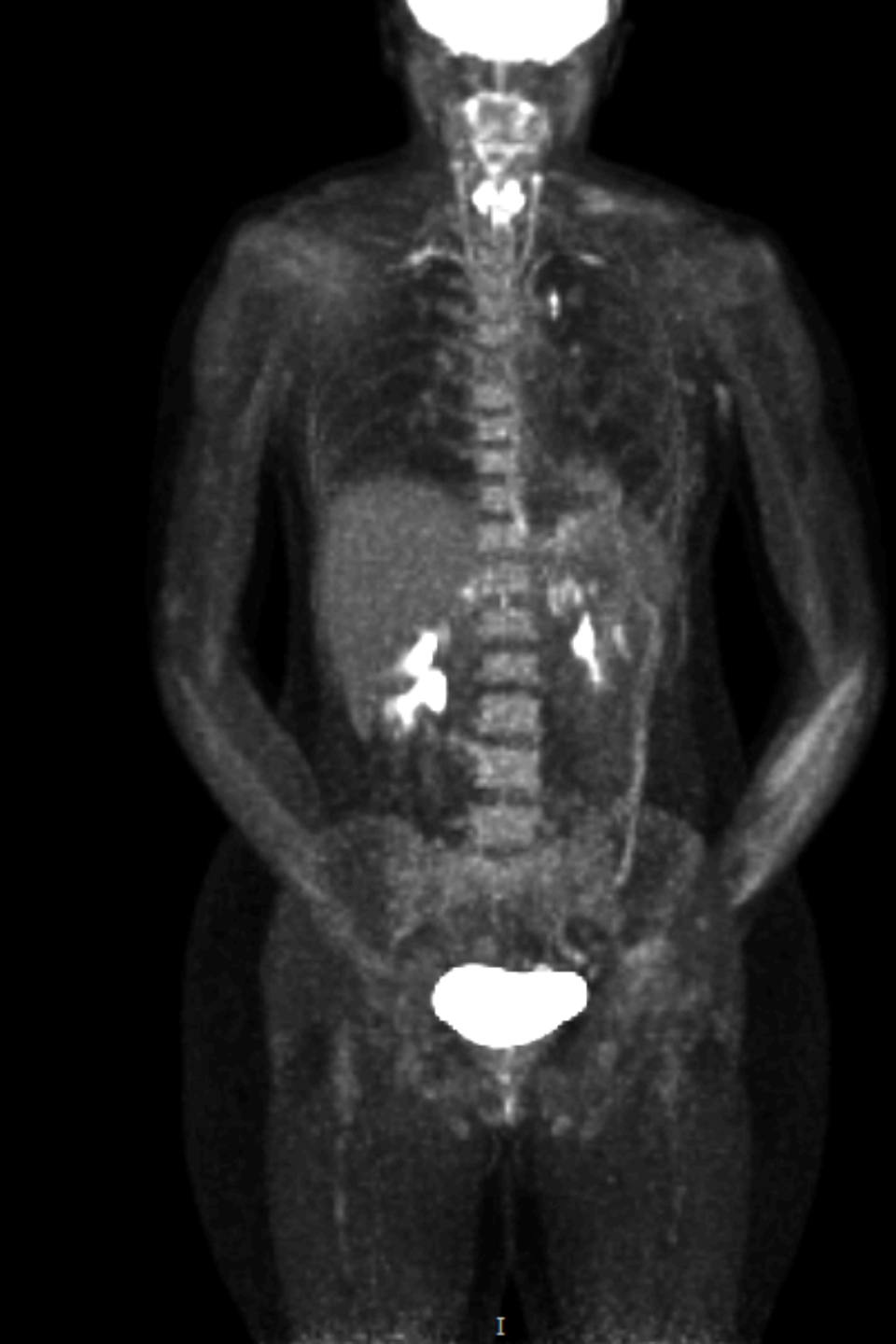
	Early	Mid	Late
Inflammation	⇑		
Wall Thickening			
Wall Edema			⇑
Stenosis			

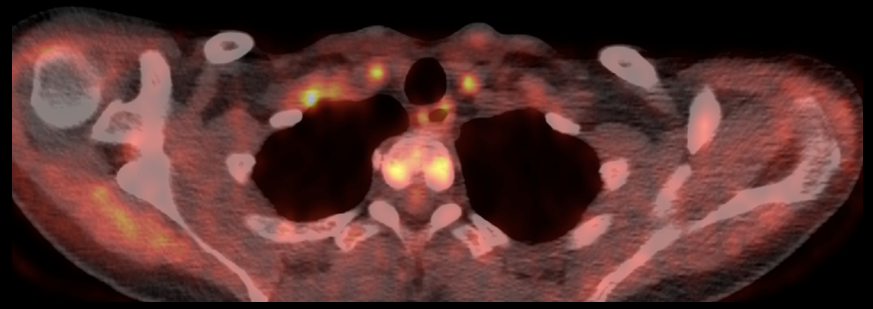
Our next case…

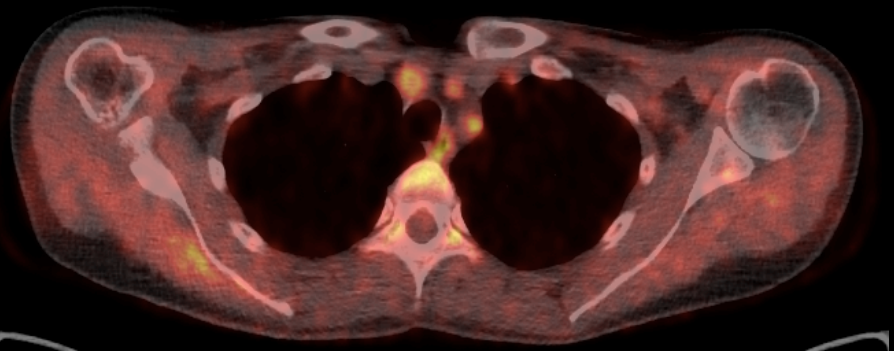
- 42-year-old woman referred to the NIH from a local hospital with newly diagnosed Takayasu's arteritis for help with clinical management
- She describes a month of profound fatigue approximately one year ago that eventually resolved.
- Over the last six months she reports ongoing frontal and occipital headaches and episodes of vision loss. The episodes are sporadic and last up to 30 seconds. She also reports jaw and arm claudication.
- She is not sure if symptoms are getting worse but think they have been relatively stable for several months.
- She has absent radial pulse and unobtainable blood pressures in both arms. Carotid pulses are diminished with a right carotid bruit.
- She has not received any treatment for her condition.

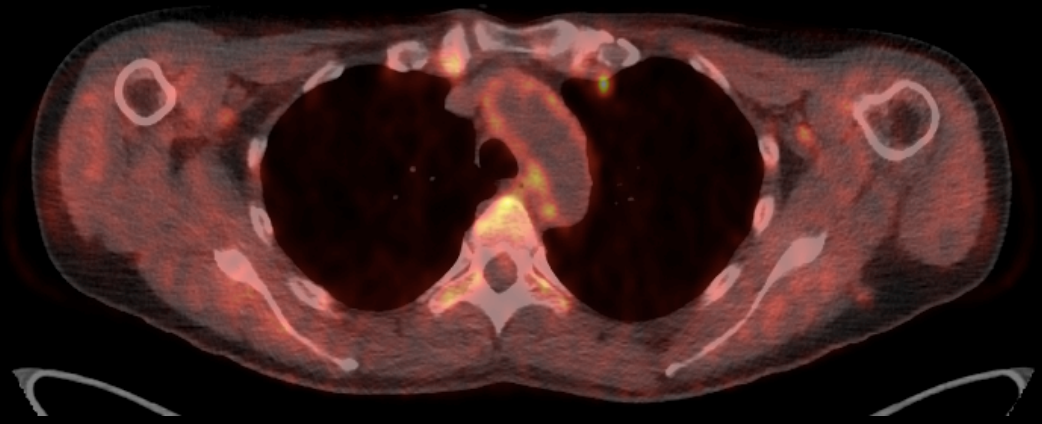
CRP 3.7 mg/L
ESR 42 mm/hr

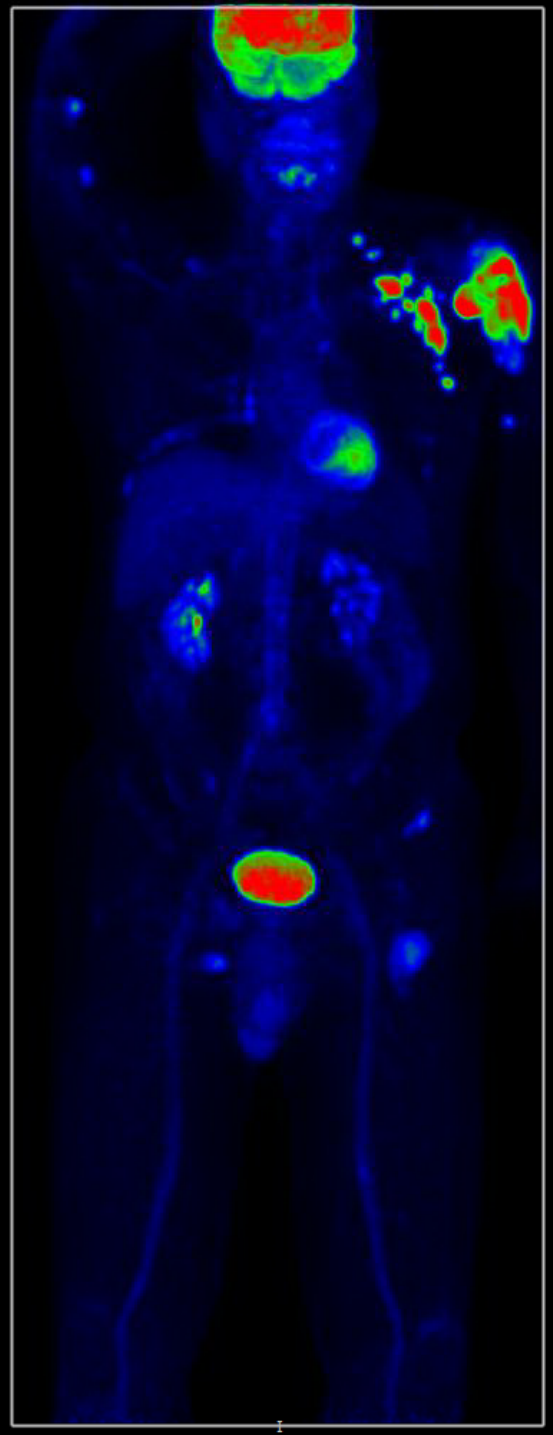
A new case of 42 yo woman…







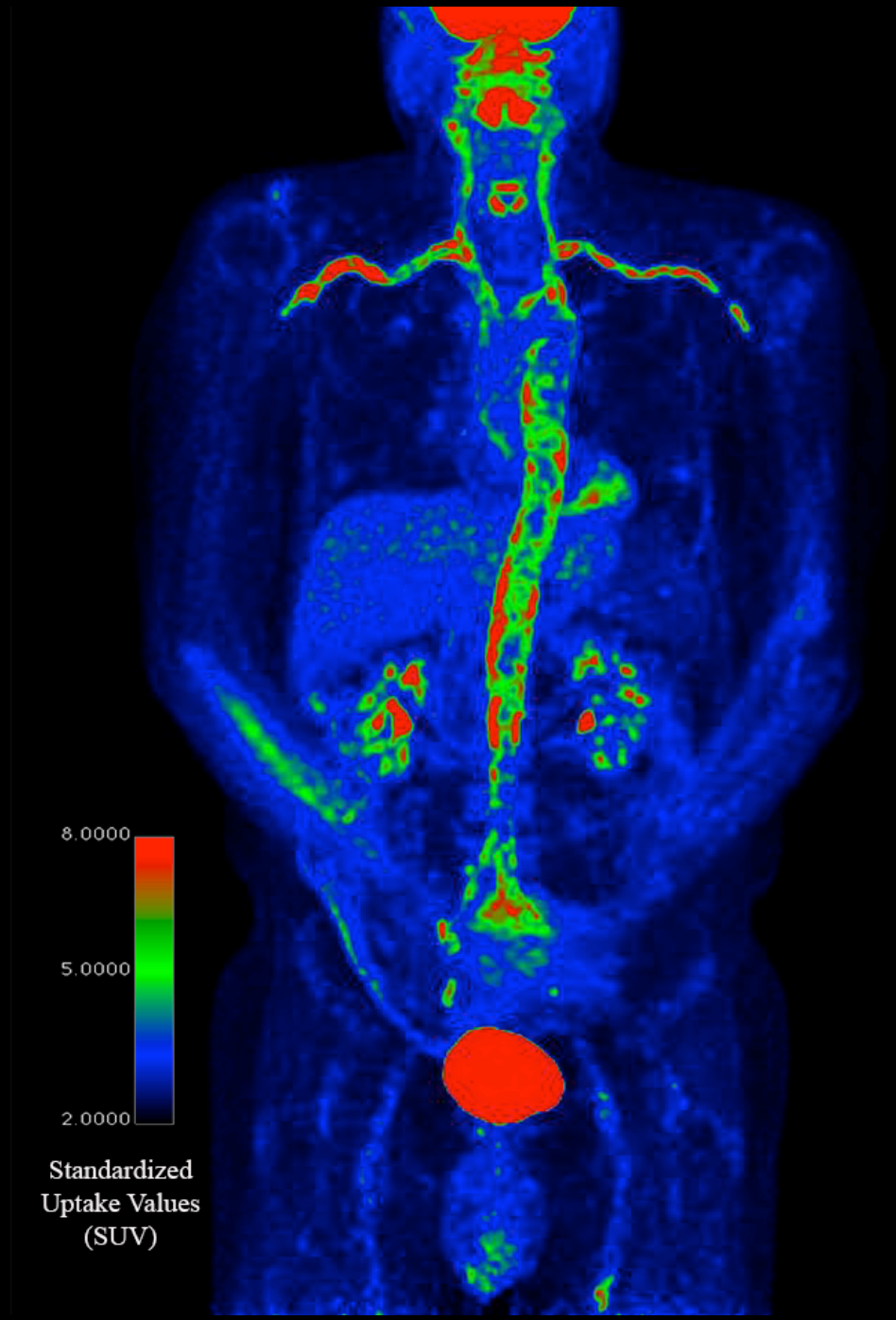




71-yearold male
presents with pathologic
left humerus fracture

Our Case…

- Biopsy of left humeral mass was diagnostic for diffuse large B-cell lymphoma
- Mutation in c-myc oncogene
- Treated with 6 cycles of R-EPOCH (Rituximab, Etoposide, Prednisone, Vincristine, Cyclophosphamide, Doxorubicin)
- No radiation therapy was given

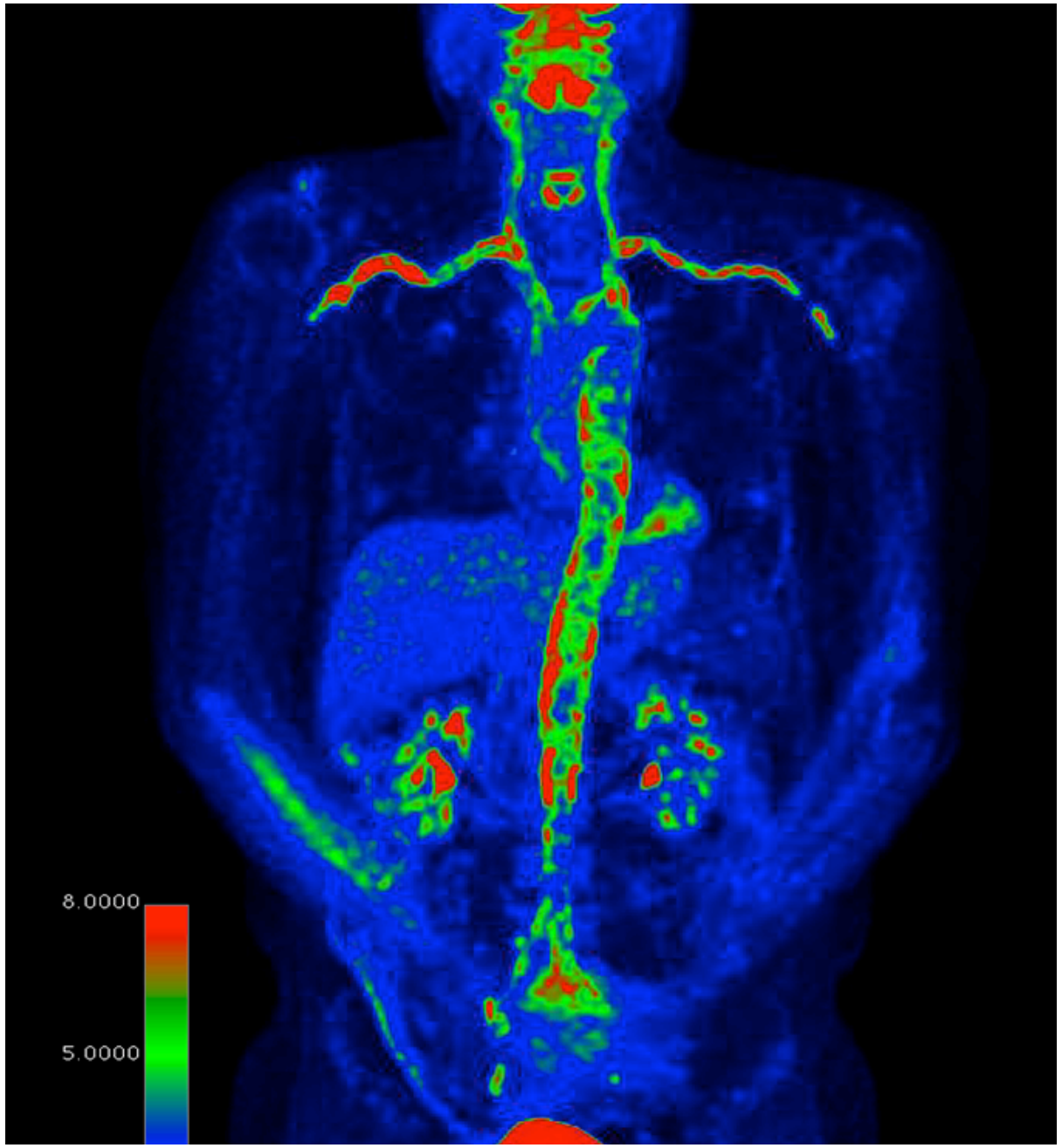

8.0000
5.0000
2.0000
Standardized
Uptake Values
(SUV)

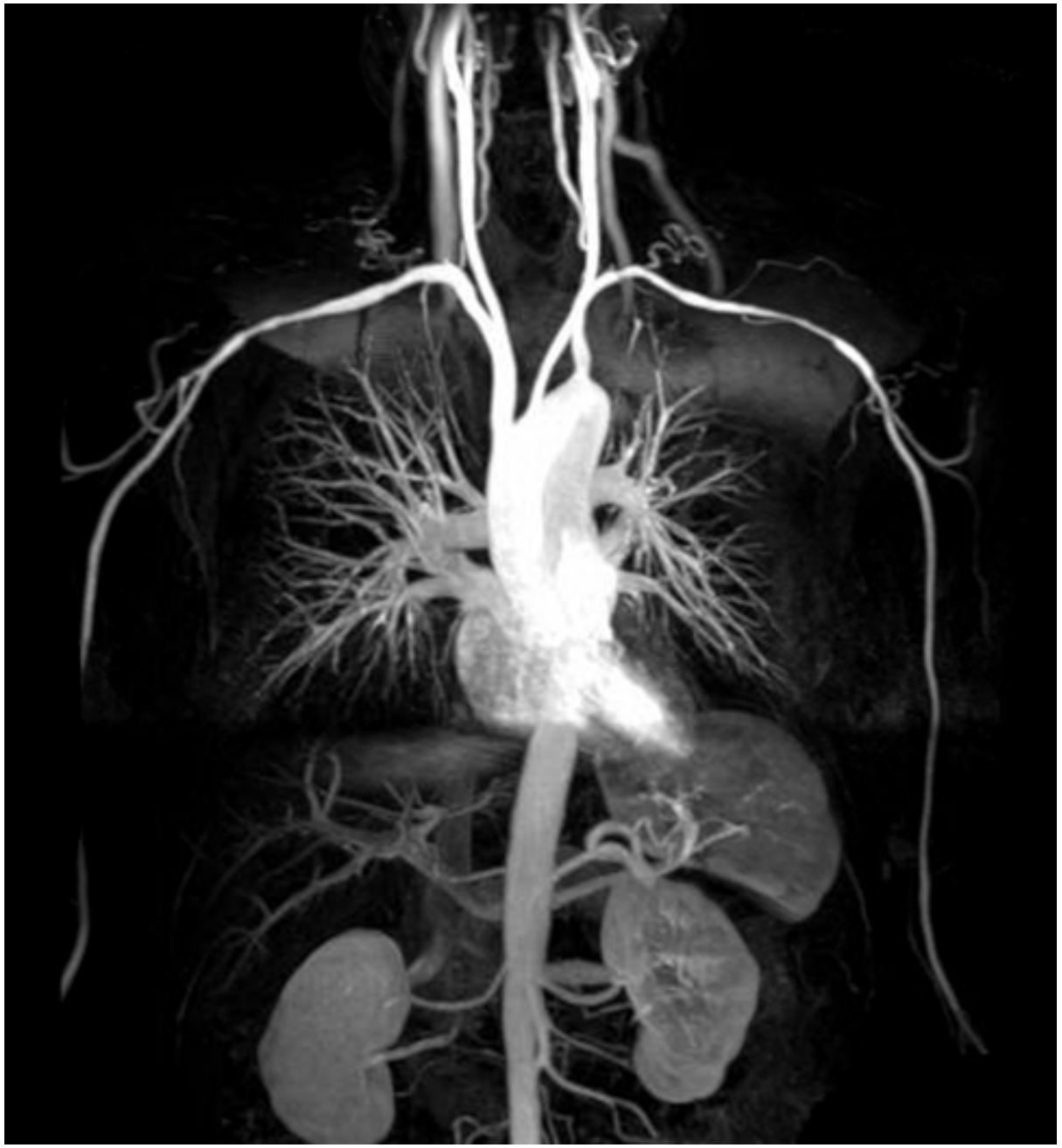
Rheumatology Assessment

- **Patient was completely asymptomatic**
  - Denied headaches, jaw or limb claudication, scalp tenderness, constitutional symptoms, vision loss, shoulder or hip discomfort.

- **Vascular exam was normal**
  - BP equal in all 4 extremities. Temporal arteries were not tender or nodular. Peripheral pulses present and 2+ in all arteries. No bruits.

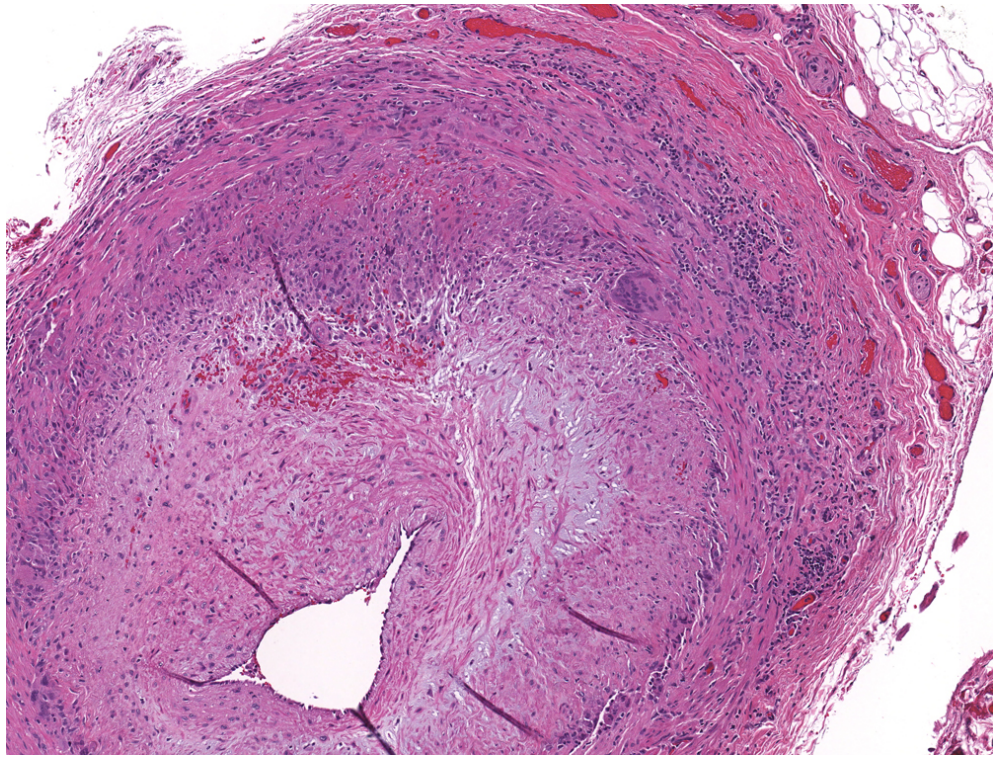
- **Inflammatory markers were not elevated**
  - ESR 16 mm/h, CRP 3.9 mg/L
  - WBC 5.2, H/H 14.9/42.3, Plt 215



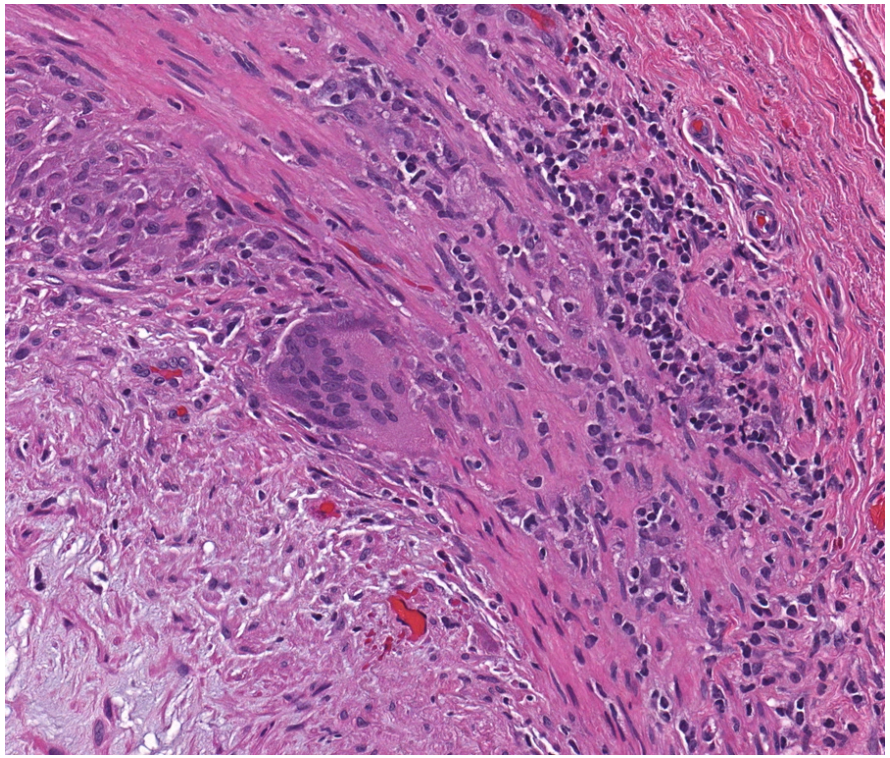


Newman et al ARD 2018

Temporal artery biopsy findings



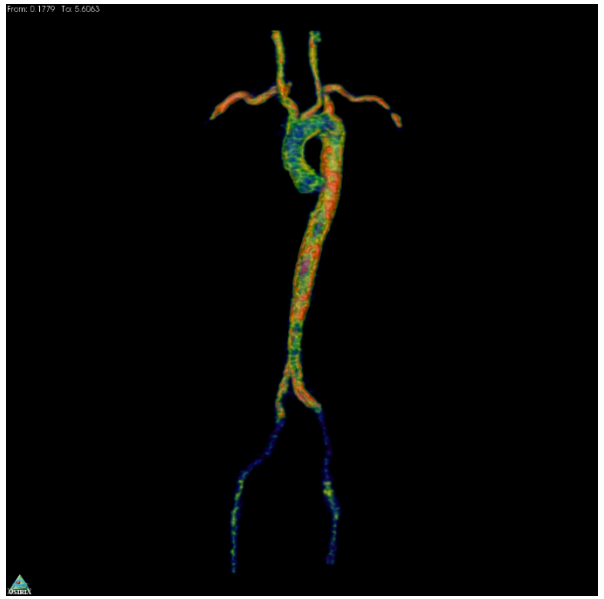
Transmural inflammation



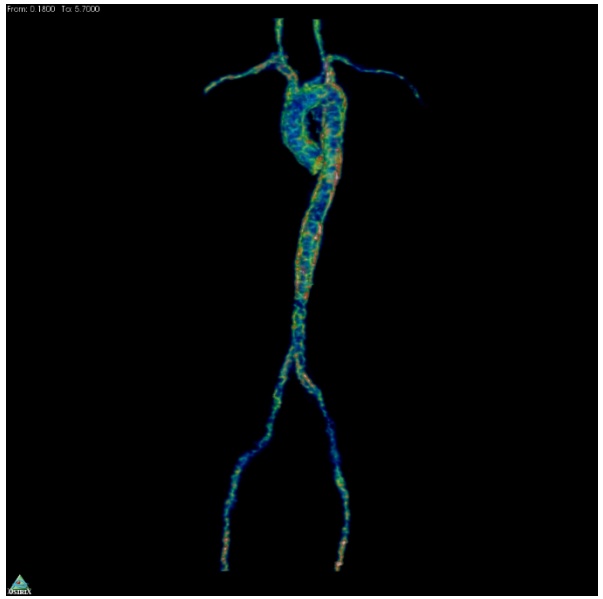
Giant Cells

Progression of disease

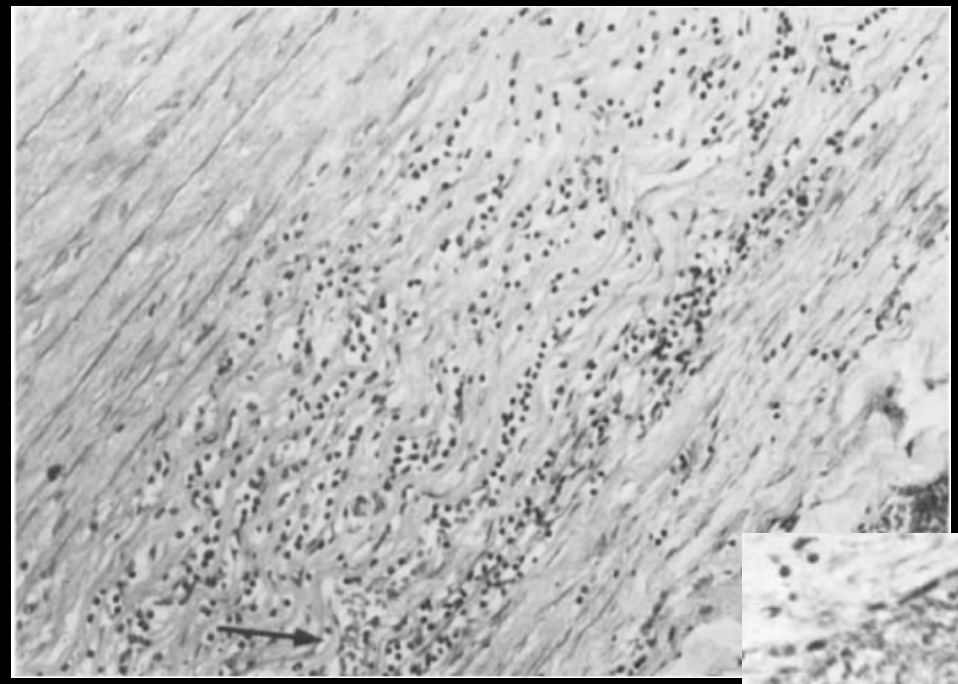
Baseline FDG-PET scan in patient with possible vasculitis



Worsening, untreated disease in same patient 6 months after baseline scan



Improved vascular inflammation 8 months into treatment

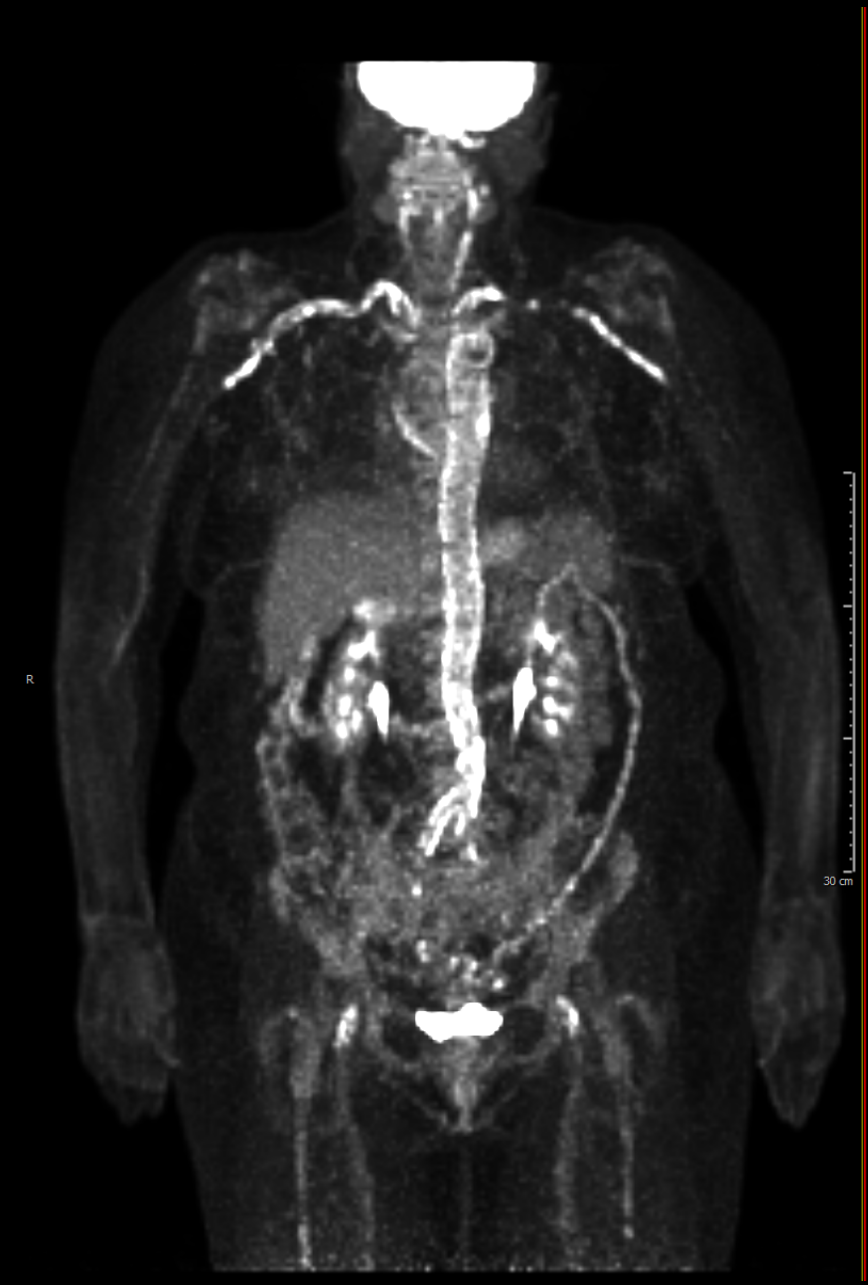


The lesions seemed to be of varying age with active necrosis and inflammation occurring besides healing with fibrosis in one and the same case, suggesting that the arteritis is a chronic and migrating disease.
Ostberg 1972

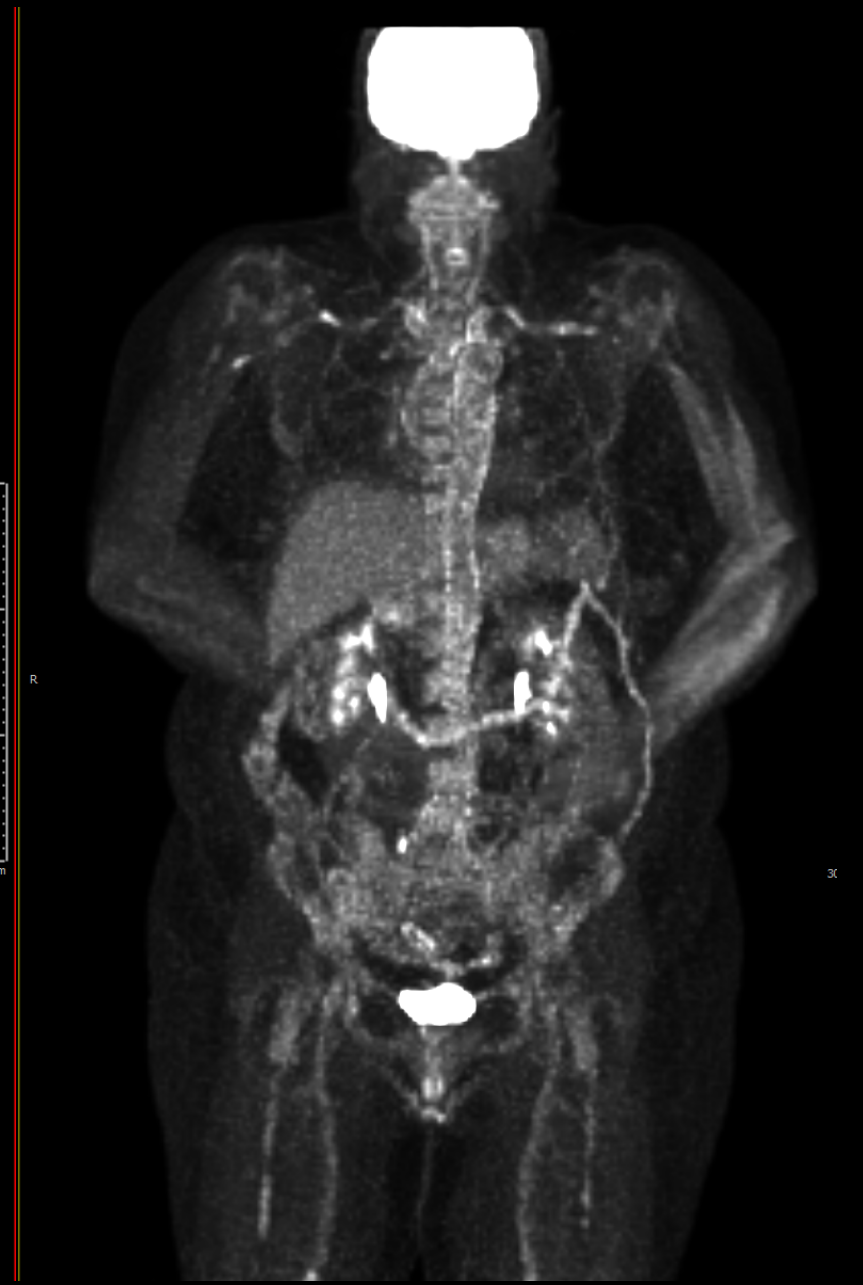
Utility as a Imaging Biomarker of Disease Activity

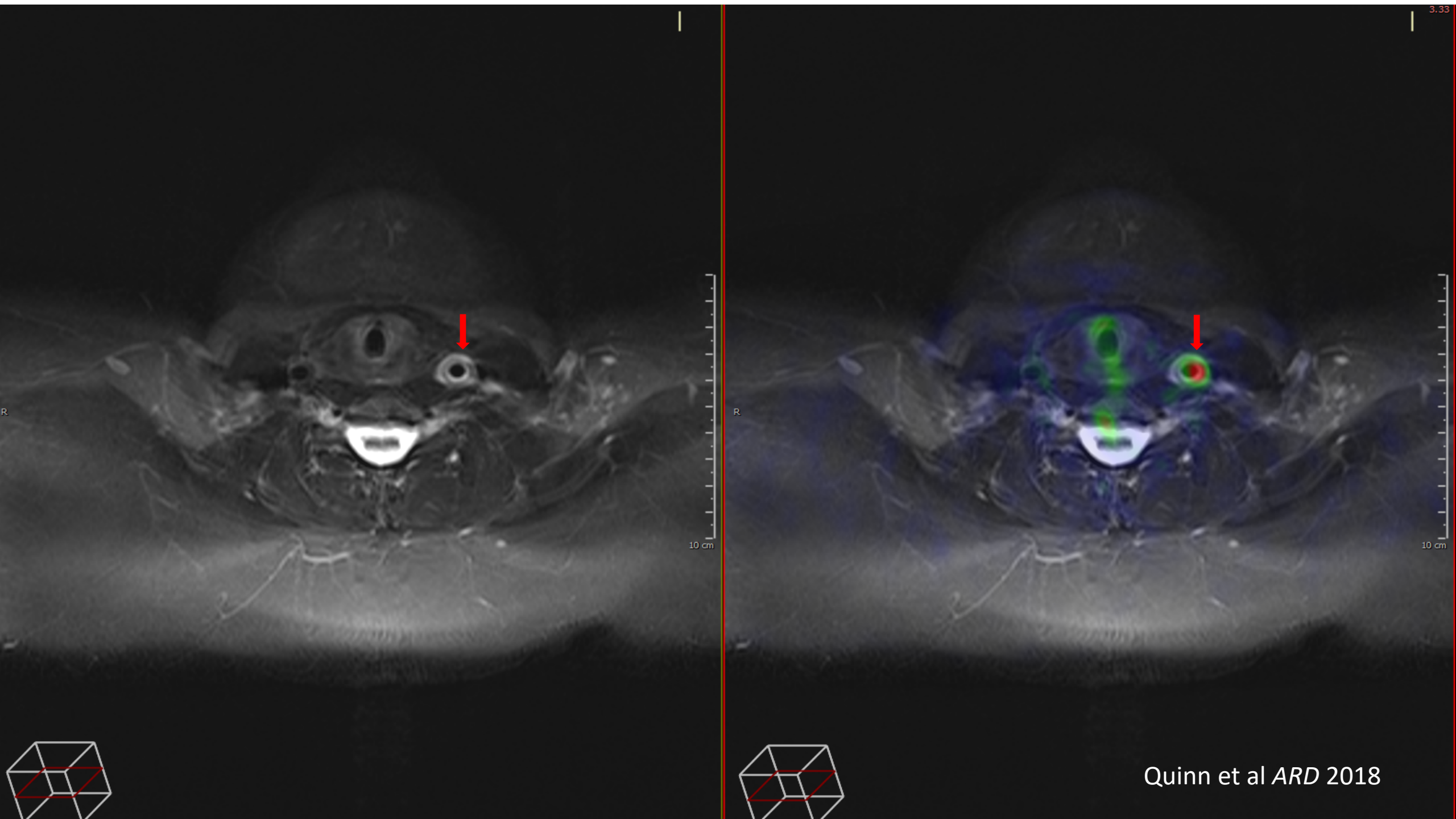
	Clinically Active	Clinical Remission	Total
Abnormal PET	33	41	74
Normal PET	6	30	34
Total	39	71	108

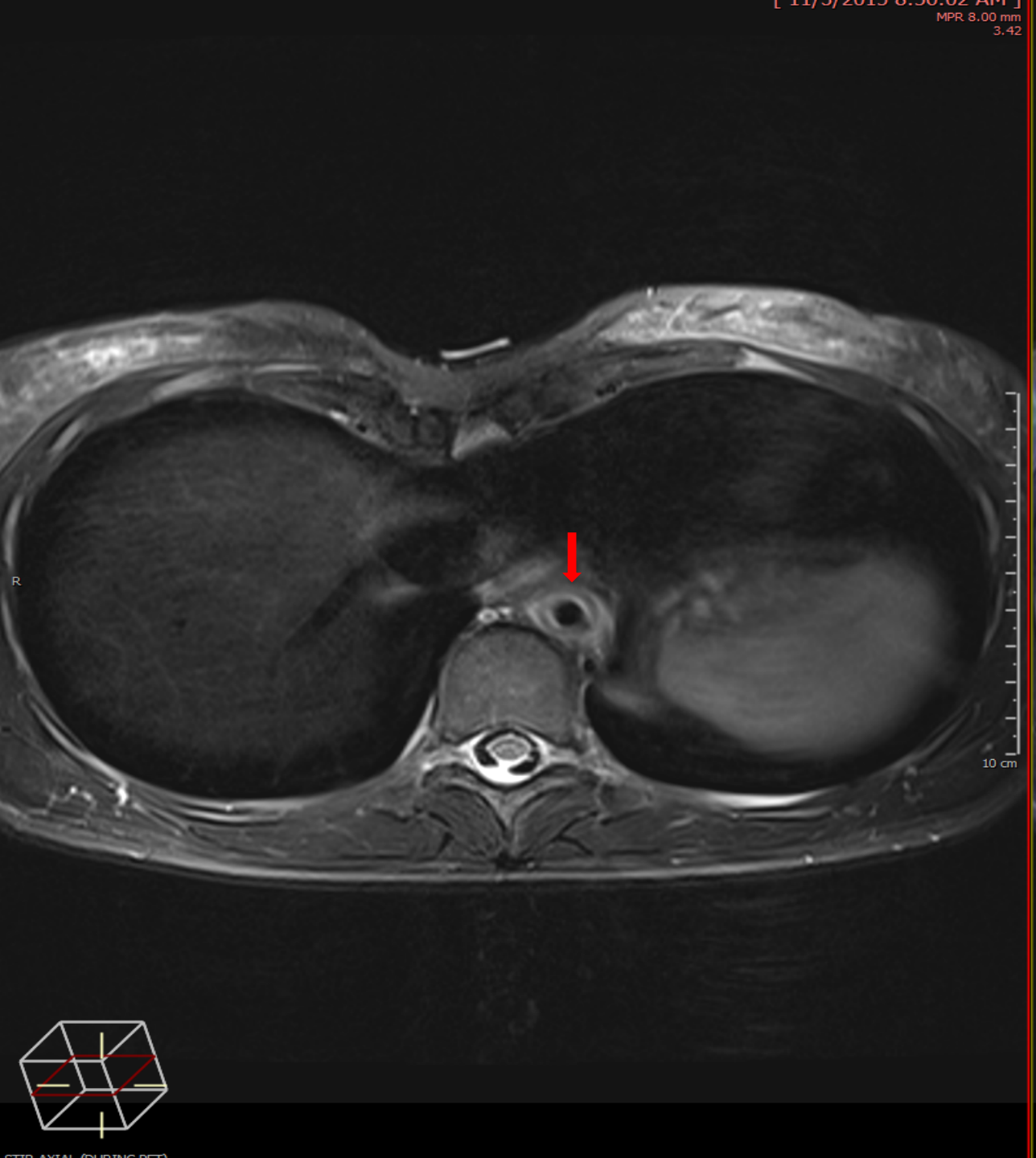
Grayson et al *A&R* 2018

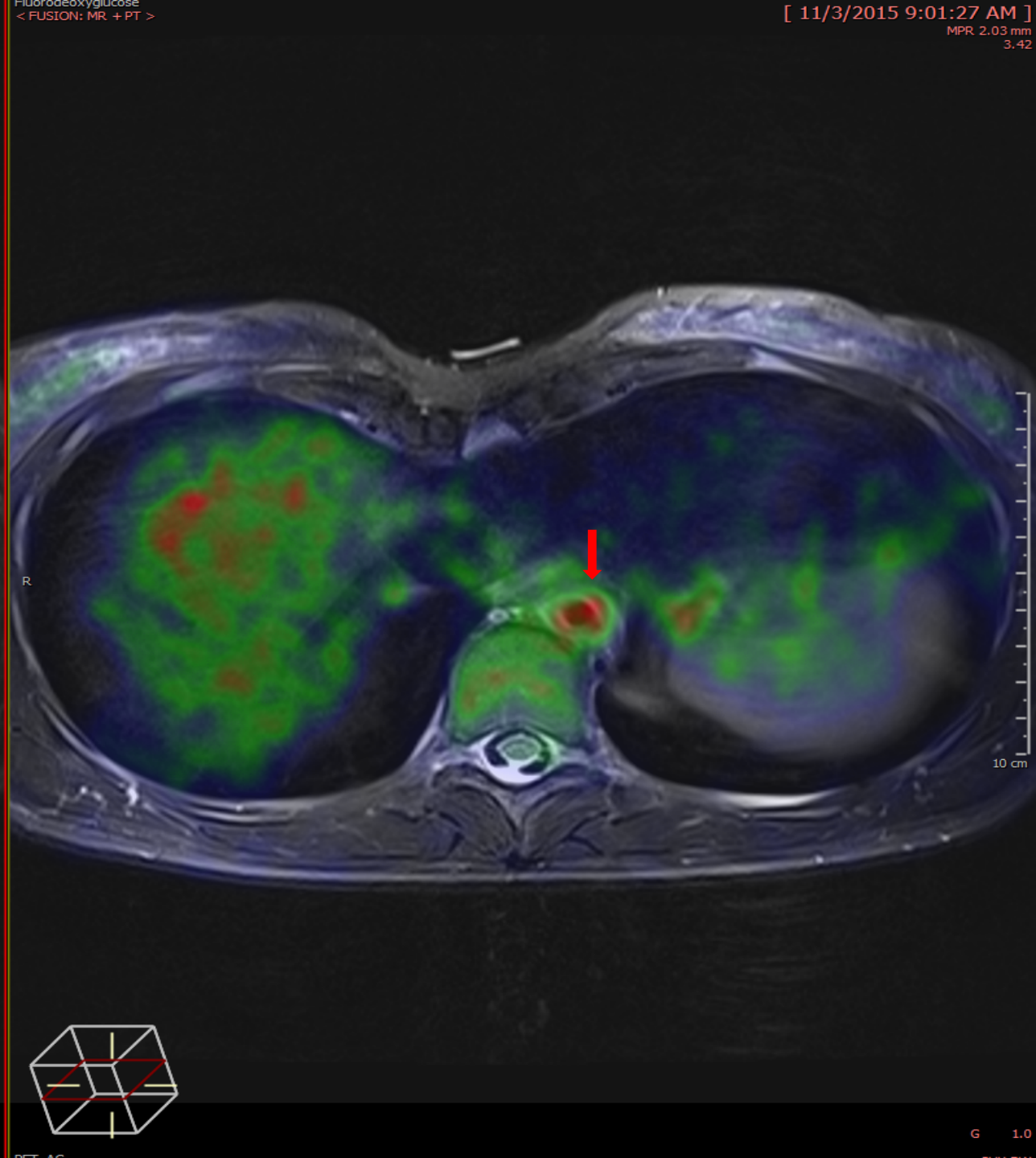

R
30 cm

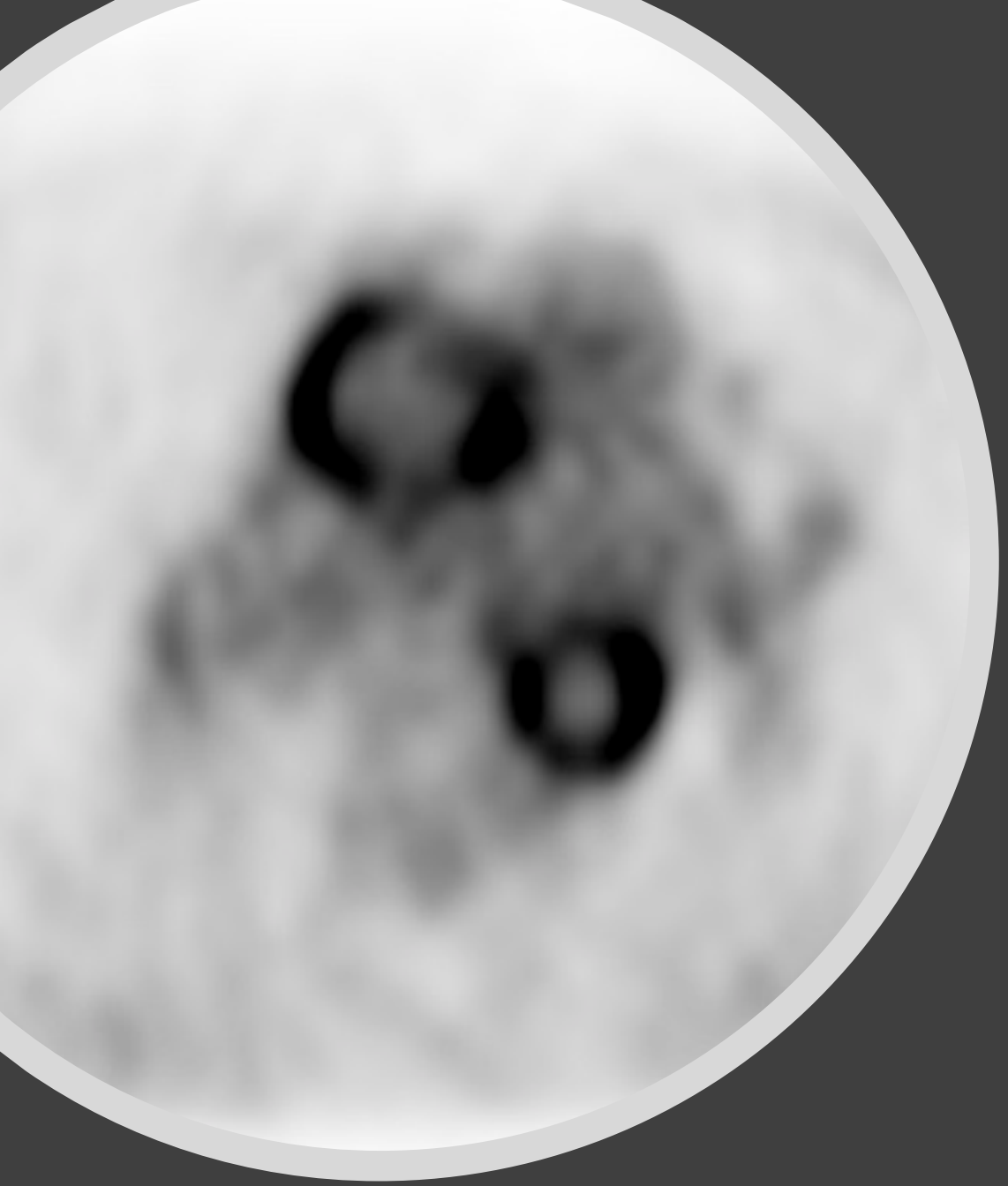

R


R
30 cm


R
10 cm
R
10 cm
Quinn et al *ARD* 2018


MPR 8.00 mm
3.42
R
10 cm


Fluorodeoxyglucose
< FUSION: MR + PT >
[11/3/2015 9:01:27 AM]
MPR 2.03 mm
3.42
R
10 cm
G 1.0

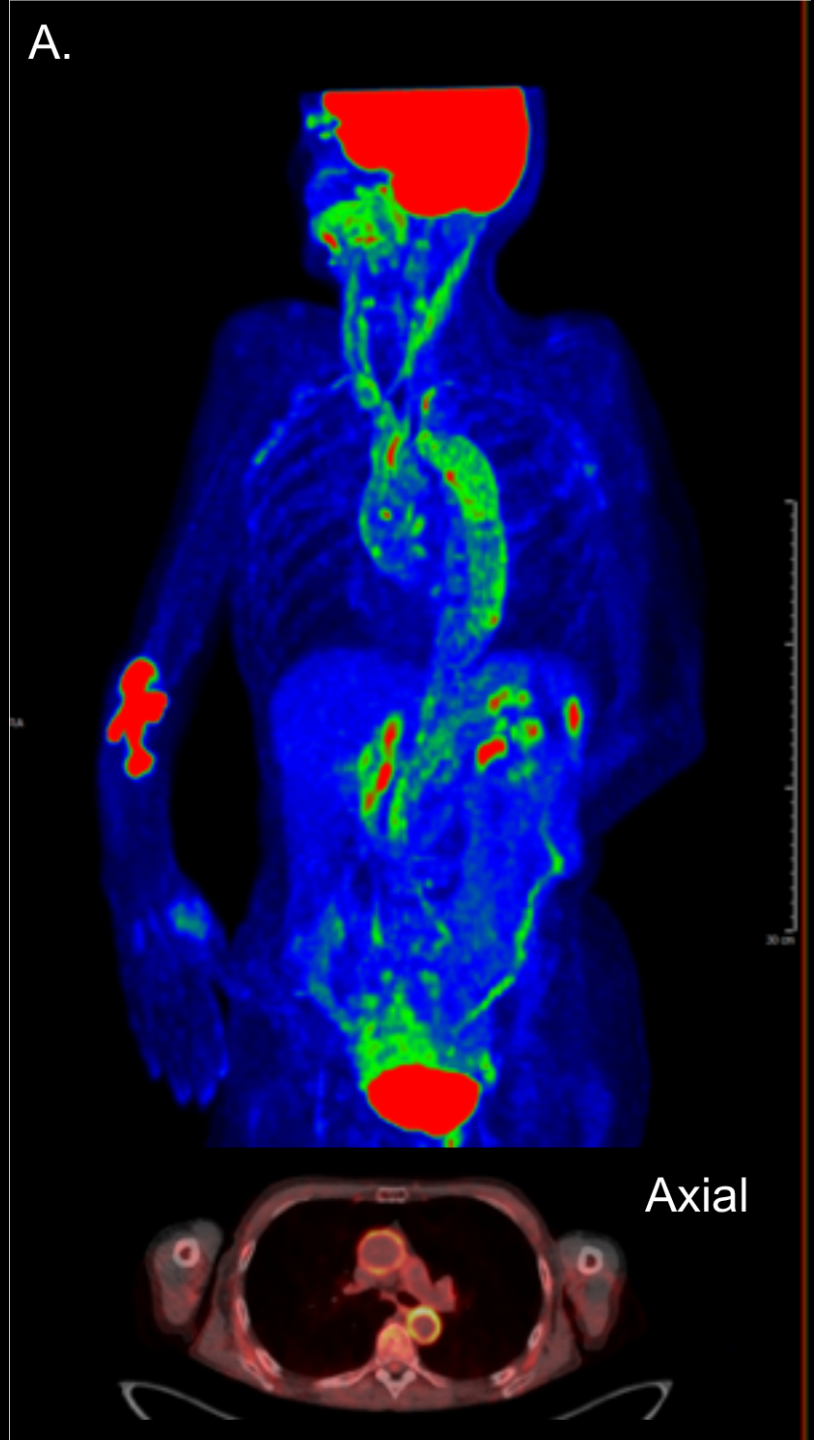


Subclinical inflammation is common in patients with large-vessel vasculitis and can be detected by FDG-PET

We can quantify vascular inflammation

Baseline Study

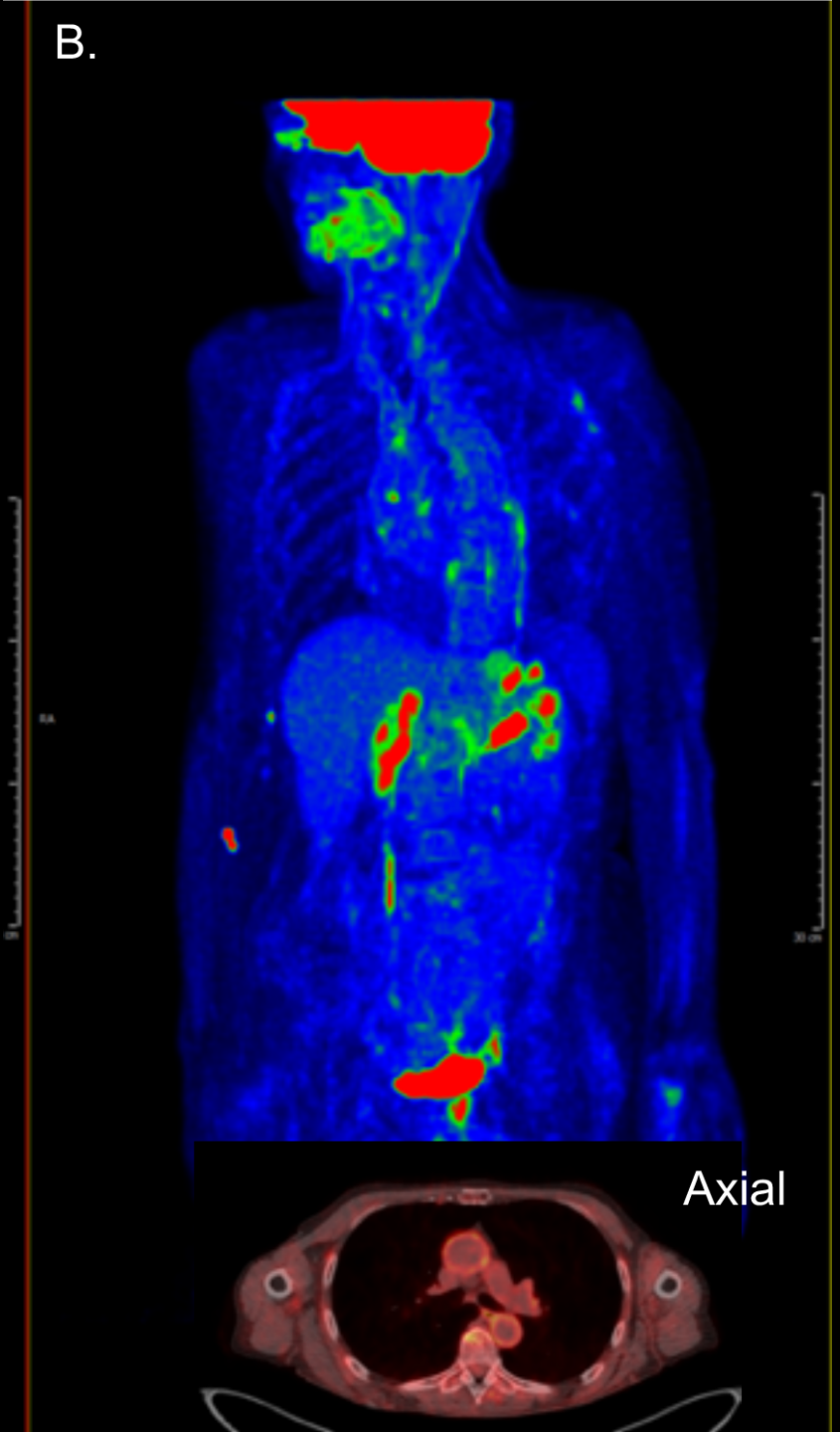
A.



Axial

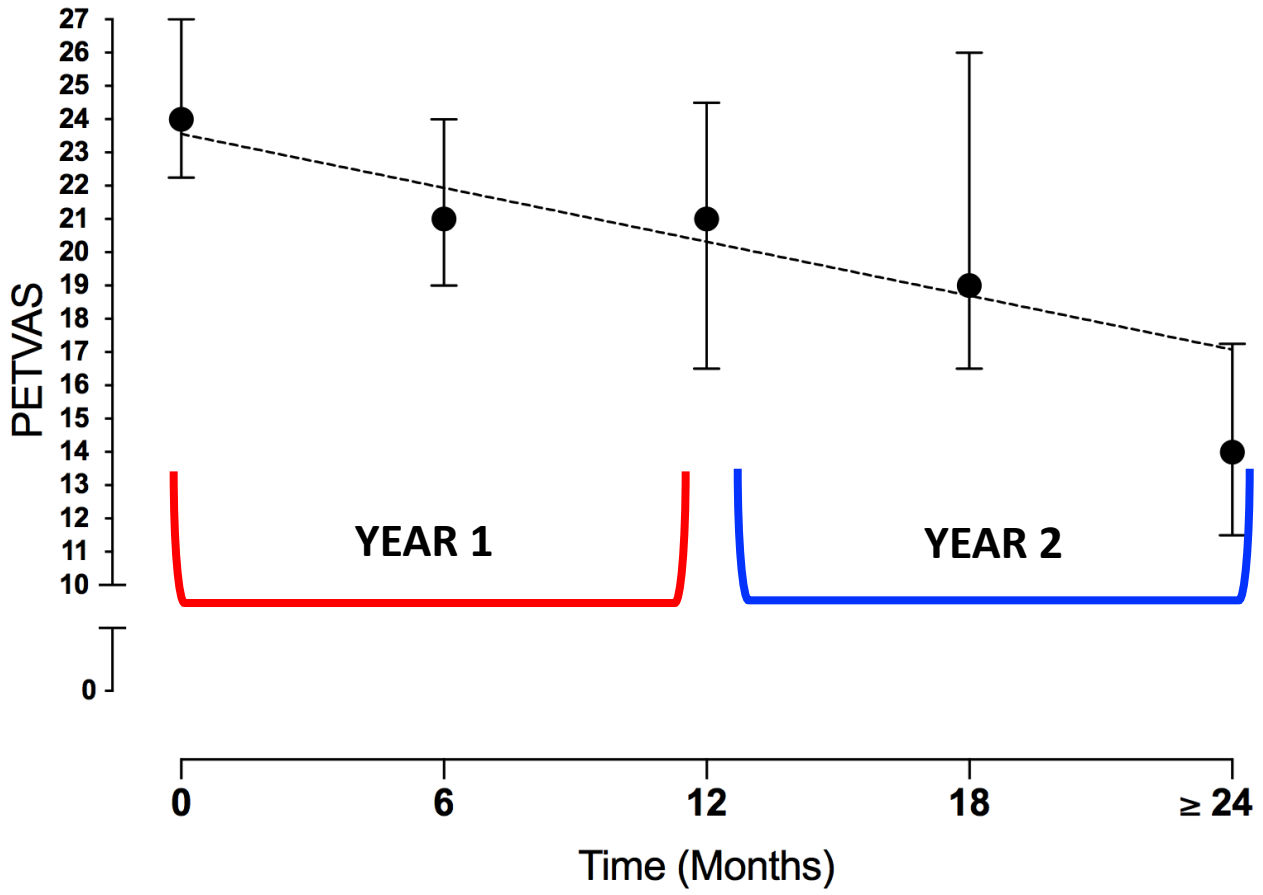
6 Months Later
- Tocilizumab

B.



Axial

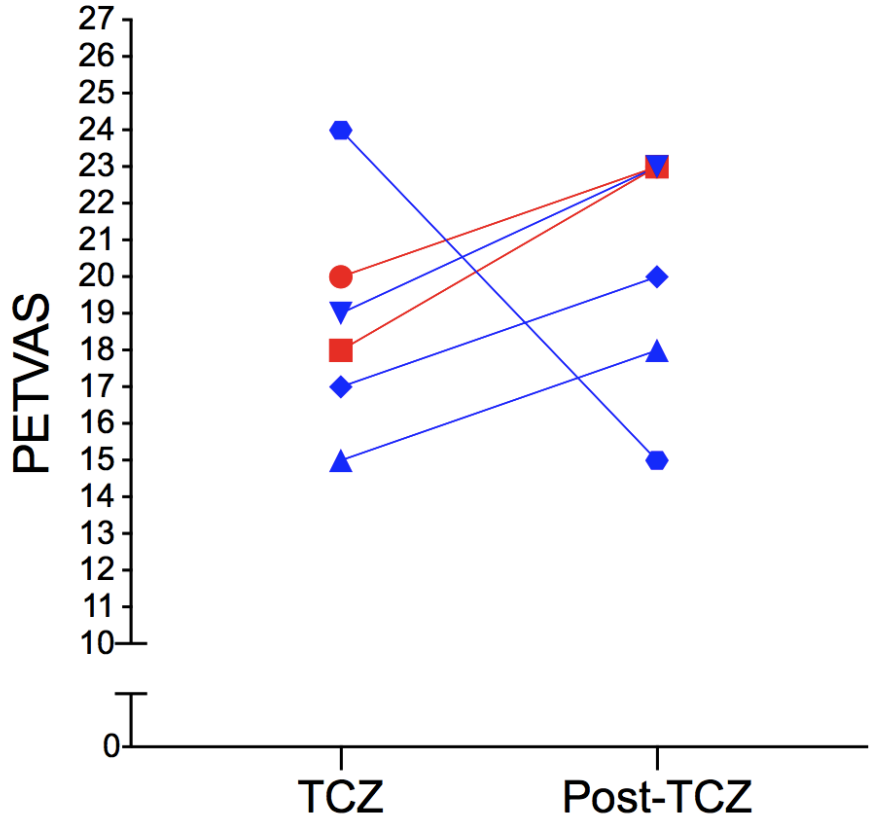
FDG-PET to Monitor Treatment Response to Tocilizumab in GCA

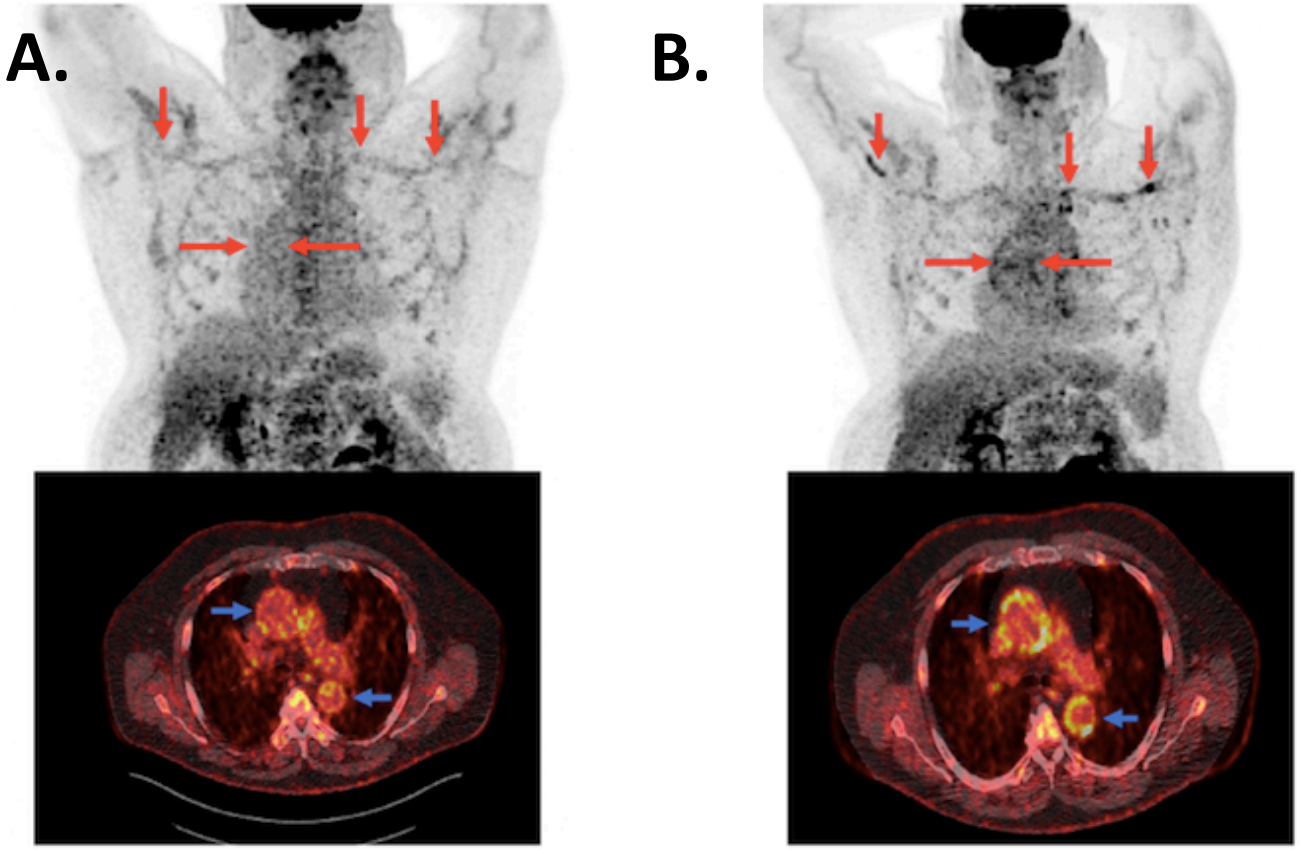


N = 25 patients

Quinn, KA et al. *Rheumatology (Oxford). 2020*

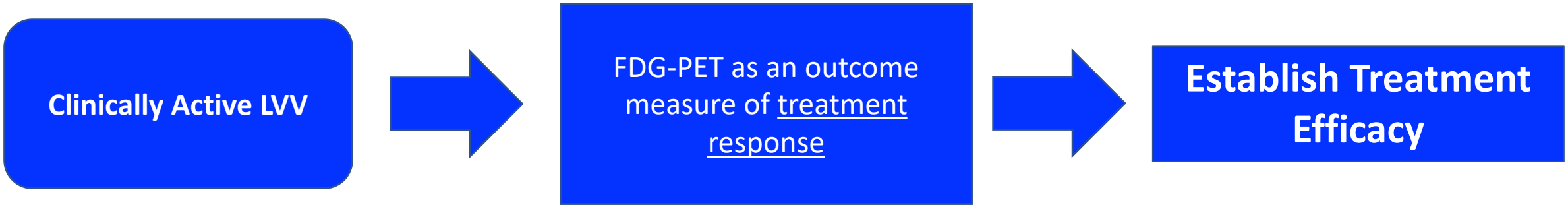
Rebound of PET activity upon tocilizumab discontinuation



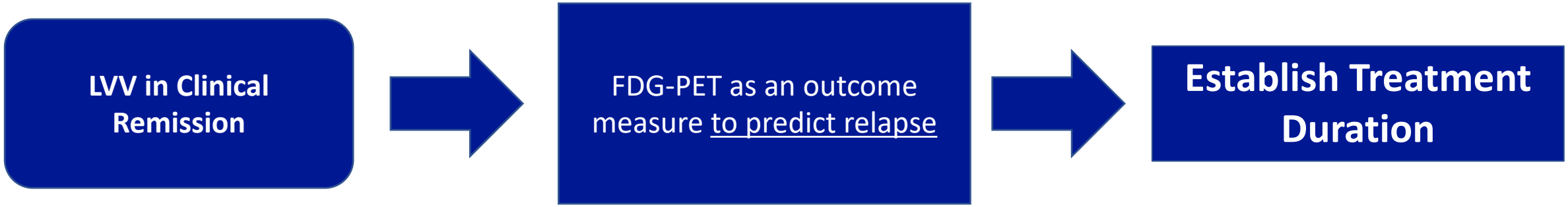


Trials of the Future in LVV

1. Randomized Placebo Controlled Trial:



2. Randomized Withdrawal Trial:



FDG-PET can be useful to monitor vascular inflammation in response to treatment

Does FDG-PET Predict Angiographic Progression of Disease?

- Aortic aneurysms and dissections are feared events in LVV
  - Typically occur 5-10 years into the course of disease
  - 17x increased risk for thoracic aorta aneurysms in GCA

Evans et al *Ann Int Med* 1995

Diagnostic Imaging Guidelines for GCA

American College of Rheumatology

- *In patients with suspected GCA, we conditionally recommend temporal artery biopsy over temporal artery ultrasound for diagnosis of GCA*
- *In patients with suspected GCA and a negative temporal artery biopsy (or biopsies), we conditionally recommend non-invasive vascular imaging of the large vessels with clinical assessment to aid in diagnosis over clinical assessment alone*
- *In patients with newly diagnosed GCA, we conditionally recommend obtaining non-invasive vascular imaging to evaluate for large vessel involvement*

Diagnostic Imaging Guidelines for GCA

EULAR

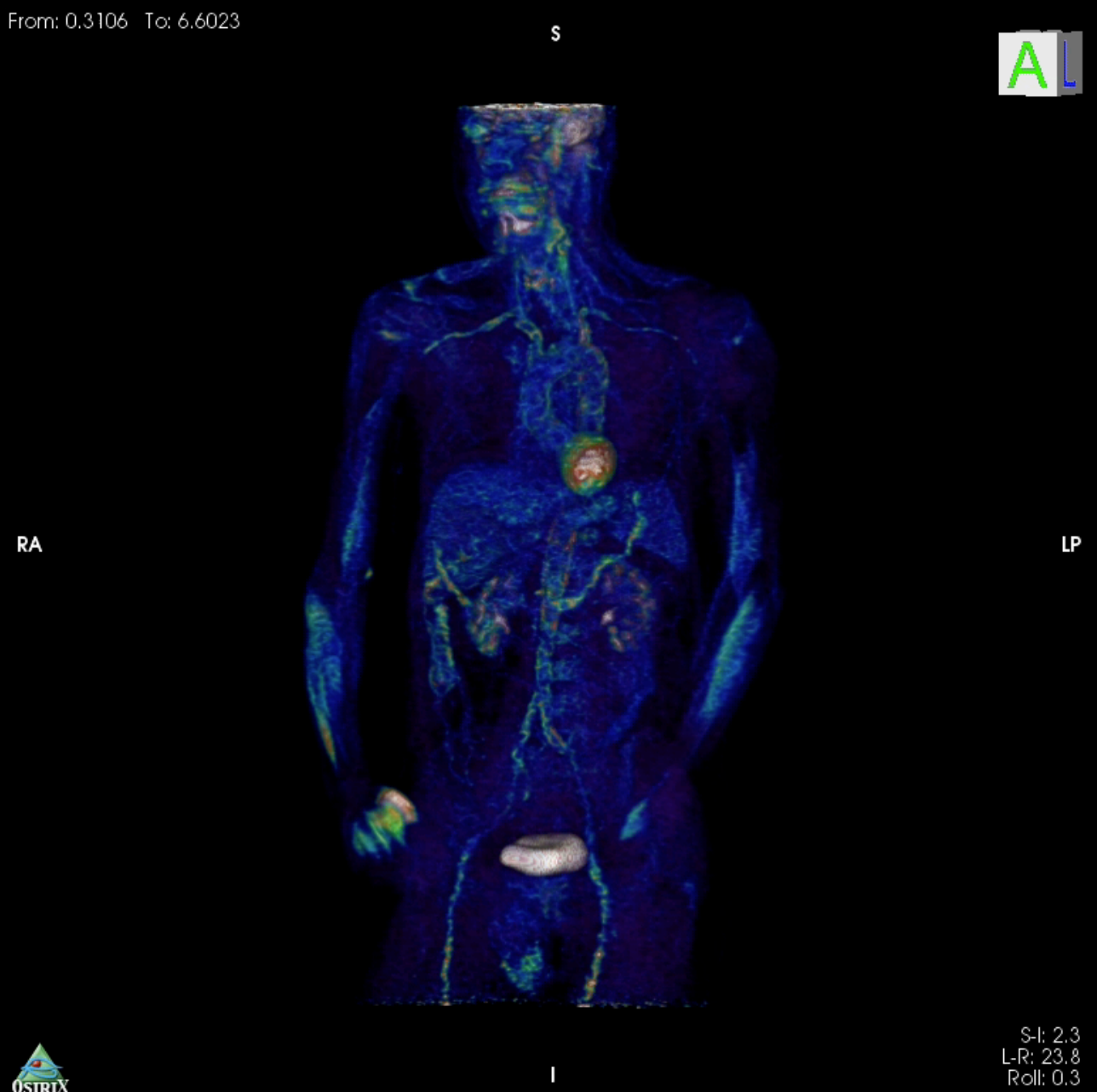
- *An early imaging test is recommended to complement the clinical criteria for diagnosing GCA*
- *In patients in whom there is a high clinical suspicion of GCA and a positive imaging test, the diagnosis of GCA may be made without an additional test (biopsy or further imaging)*
- *MRA and FDG-PET have diagnostic value in cases of large artery involvement*

Personalize your approach

Know your institutional capabilities!

- Discuss with your radiology and nuclear medicine department
  - Directly review your imaging studies with them
- Acquire skills in ultrasound
- Consider imaging as a diagnostic surrogate in appropriate cases
  - High probability
  - Contraindication to biopsy
  - Biopsy negative cases
- When monitoring patients, match imaging findings to patient history, physical exam, and labs

Exciting Times in LVV Management



Thanks to these people!

NIAMS Vasculitis Translational Research Program

Kaitlin Quinn, Marcela Ferrada, Elaine Novakovich, Wendy Goodspeed, Bates Gribbons, Joel Rosenblum, Casey Rimland, Emily Rose, Kristina Wells, Himanshu Dashora

Radiology Department NIH Clinical Center

Jaime Marko, Ashkan Malayeri, Cheryl Beegle, Rob Evers, Elizabeth Jones, Hadi Bagheri, David Bluemke, Cahid Civelek

NIAMS

Mariana Kaplan, John O'Shea, Robert Colbert, Jim Katz, Robert Carter

Thanks for your attention!

peter.grayson@nih.gov
301-827-9187
@petercgrayson