Assessment of Treatment Response by ^{18}F-Fludeoxyglucose Positron Emission Tomography (FDG-PET) in Patients with Large Vessel Vasculitis (LVV)

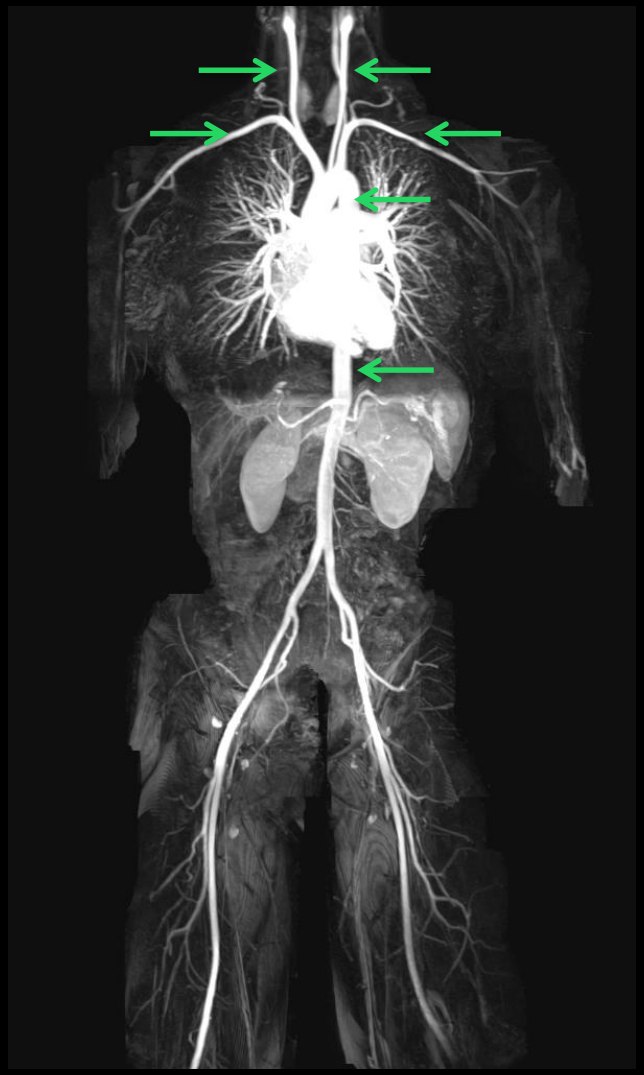
Shubhasree Banerjee[1], Sara Alehashemi[1], Mark A. Ahlman[2], Cahid Civelek[2], Elaine Novakovich[3], David A. Bluemke[2], Peter C. Grayson[3]

[1] Rheumatology Fellowship and Training Branch, NIAMS, NIH

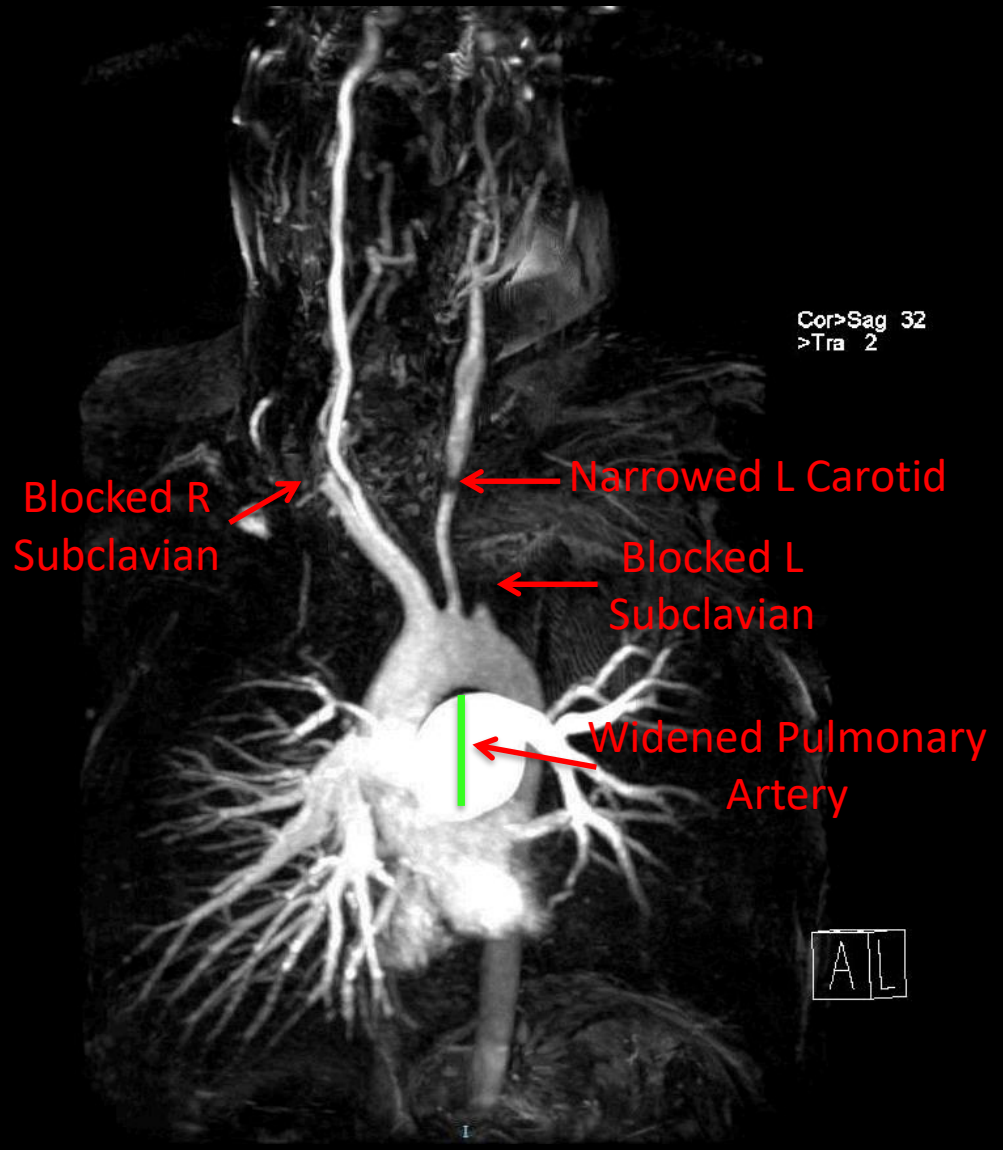
[2] Radiology and Imaging Sciences, Clinical Center, NIH

[3] Vasculitis Translational Research Program, NIAMS, NIH

Large Vessel Vasculitis

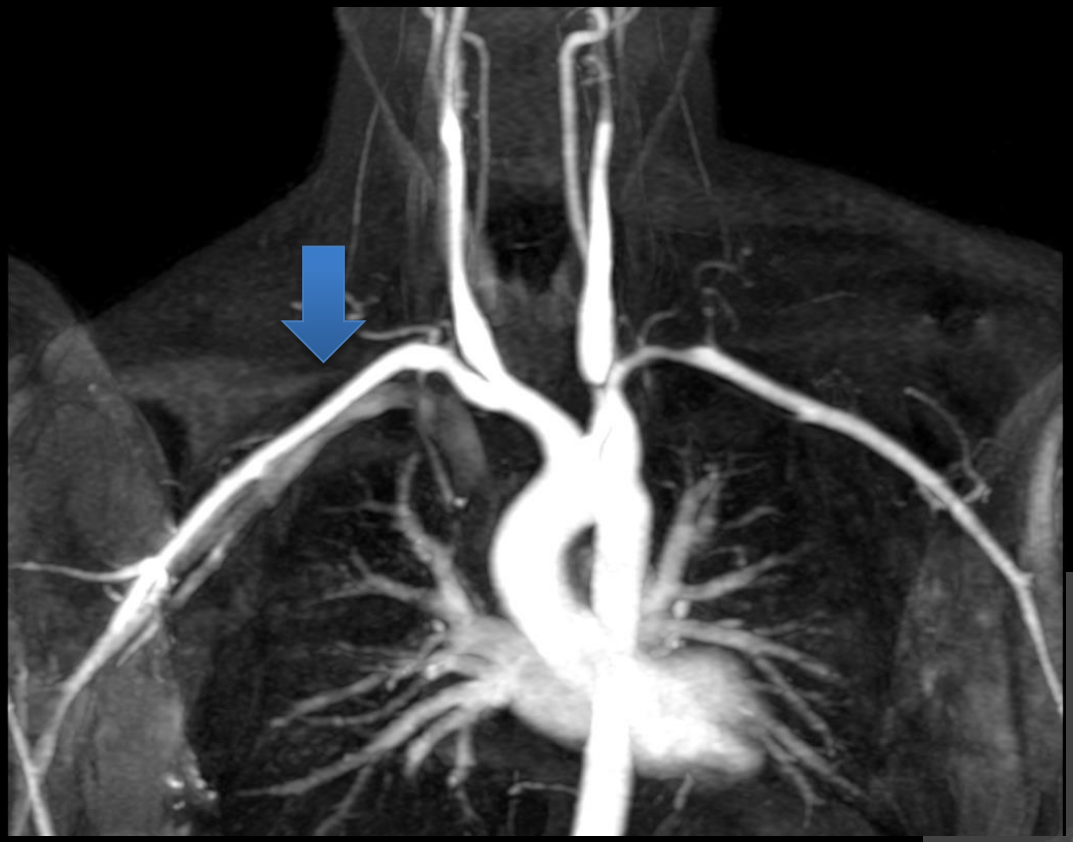


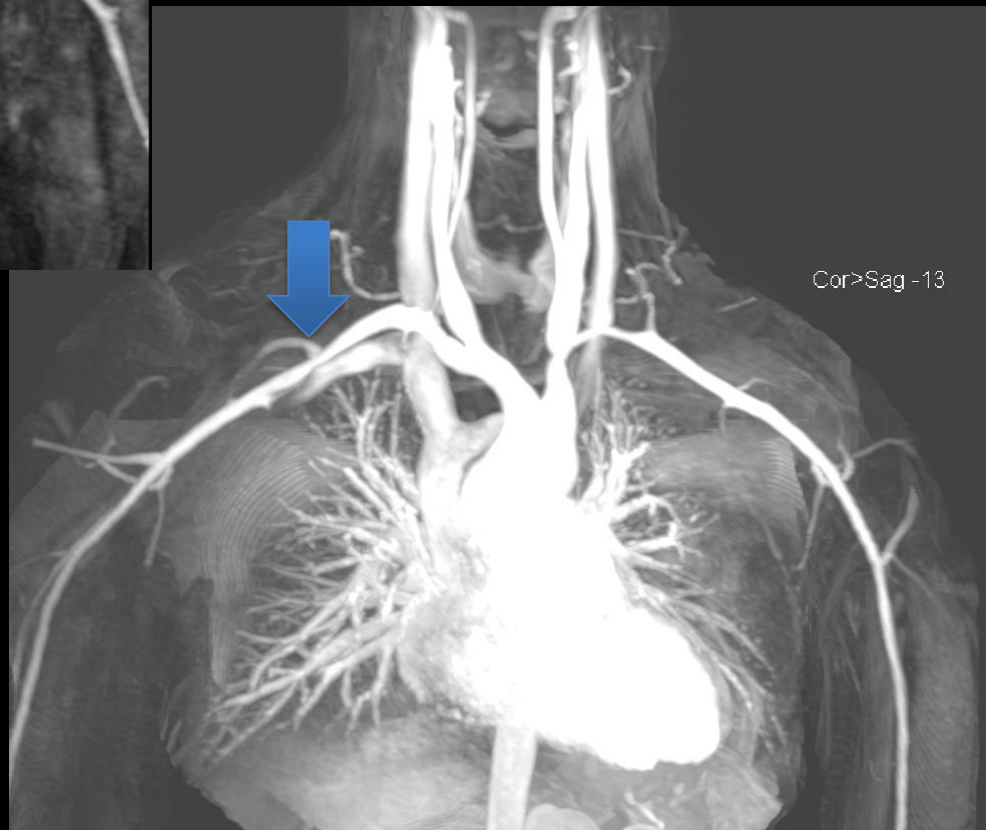
Healthy



Takayasu's arteritis

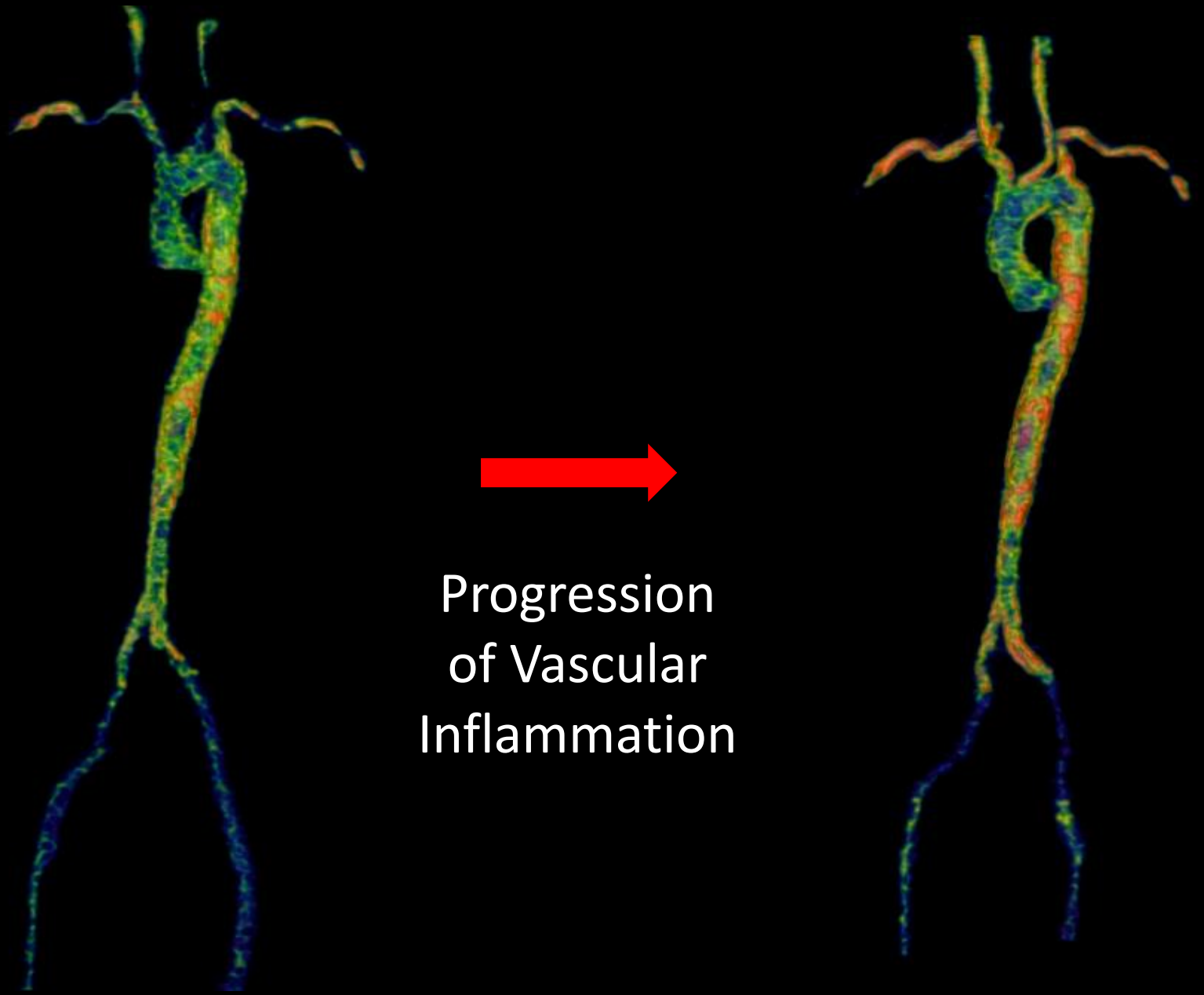
February 2016





September 2016

FDG-PET CT in Large Vessel Vasculitis



Progression
of Vascular
Inflammation

Study Objectives

- To study if change in treatment is associated with change in FDG-PET activity in LVV
- To determine if specific therapies for LVV impact vascular FDG uptake

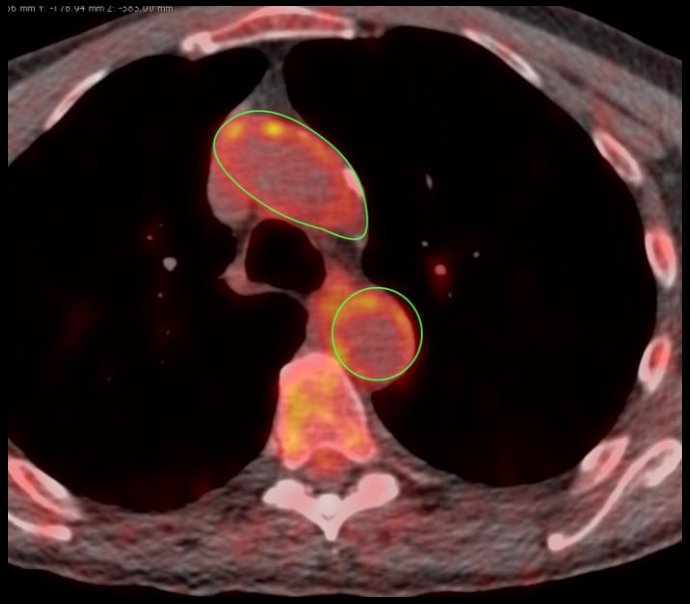
Methods

- Patients with giant cell arteritis (GCA) or Takayasu's arteritis (TAK) recruited into prospective, observational cohort of LVV

- FDG-PET/CT at 6-month intervals (256 matrix, 3mm slice, 2 hour uptake time)

Standardized Uptake Values (SUVs)

- Semi-quantitative analysis of vascular FDG uptake



- Limitations of SUV as measure of vascular FDG uptake
  - Values are machine specific
  - Cannot be compared longitudinally

Target to background ratio (TBR)

- TBR= SUV_{max} Aorta Region / SUV_{mean} Liver
- Standardized uptake values (SUVs):
  - Ascending aorta and arch
  - Descending aorta
  - Liver (background)
- Change in TBR in each aortic region calculated between interval visits

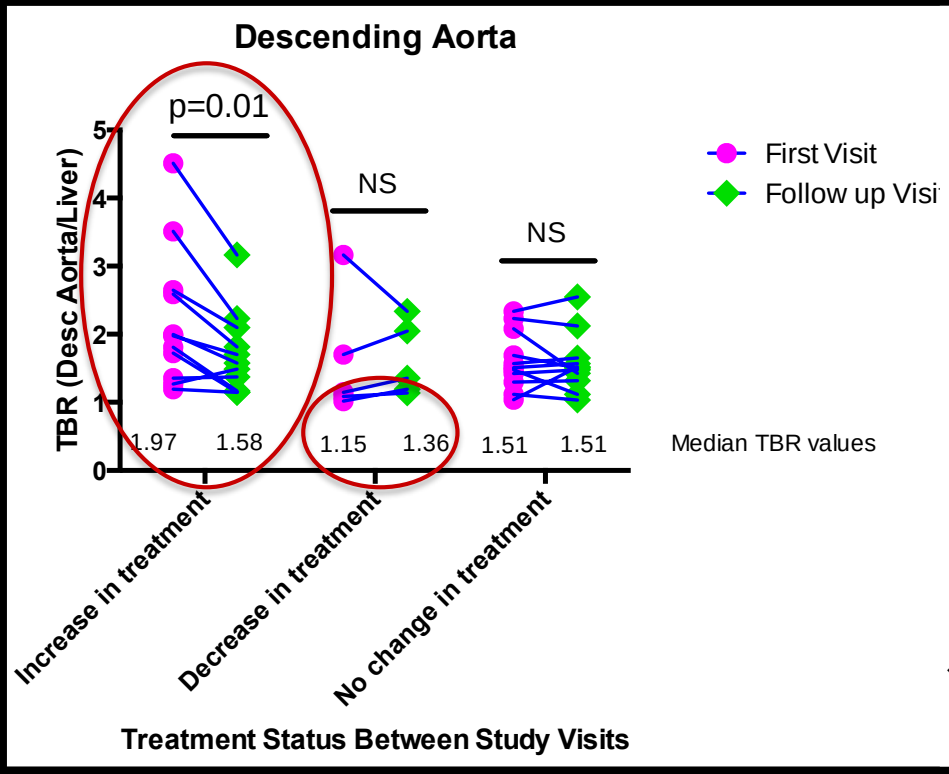
Treatment Status between Interval Visits	Criteria for Treatment Status Classification		
Increased	Increase in average daily prednisone over past 7 days by≥ 5 mg	≥50% increased dose of DMARD/ biologic from baseline	Addition of new DMARD or biologic agent
Decreased	Decrease in average daily prednisone over past 7 days by≥ 5 mg	≥50% reduction from baseline dose of DMARD/ biologic	
Unchanged	Change in average daily prednisone over past 7 days by< 5 mg	<50% change from baseline dose of DMARD/ biologic	

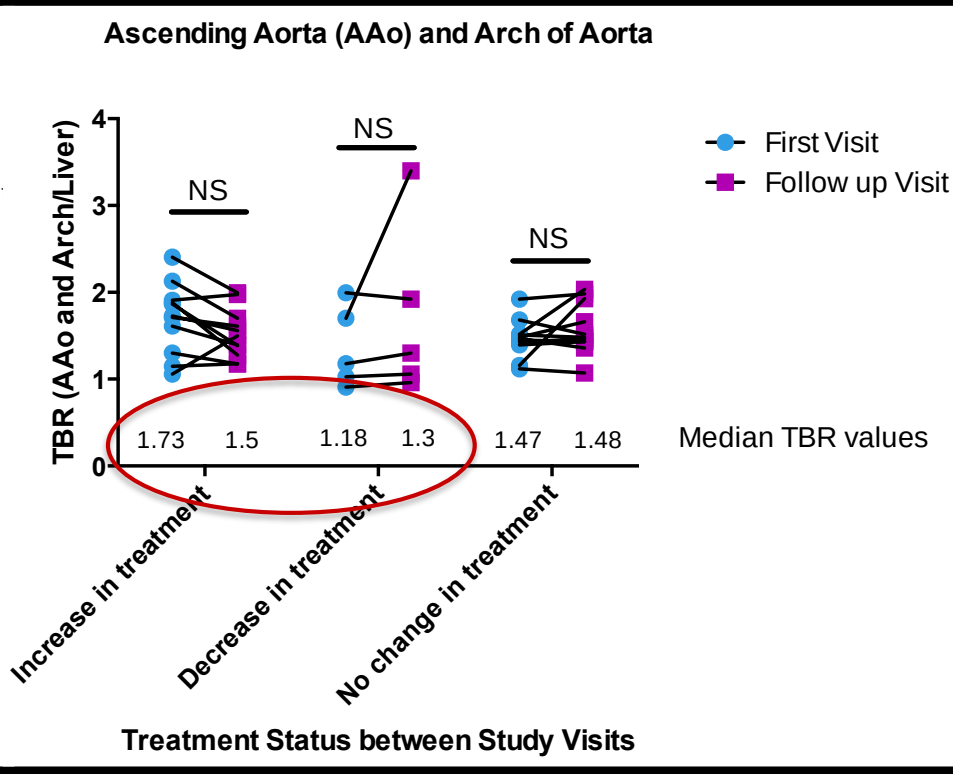
Results

Total number of patients	**20**
GCA and TAK	14 and 6
Total number of visits	49
Patients treated with Glucocorticoids (GC)	15 (75%)
Patients treated with methotrexate (MTX)	10 (50%)
Patients treated with other DMARD/ biologic	8 (40%)
Increased treatment	11 visit intervals
Decreased treatment	5 visit intervals
No change in treatment	11 visit intervals

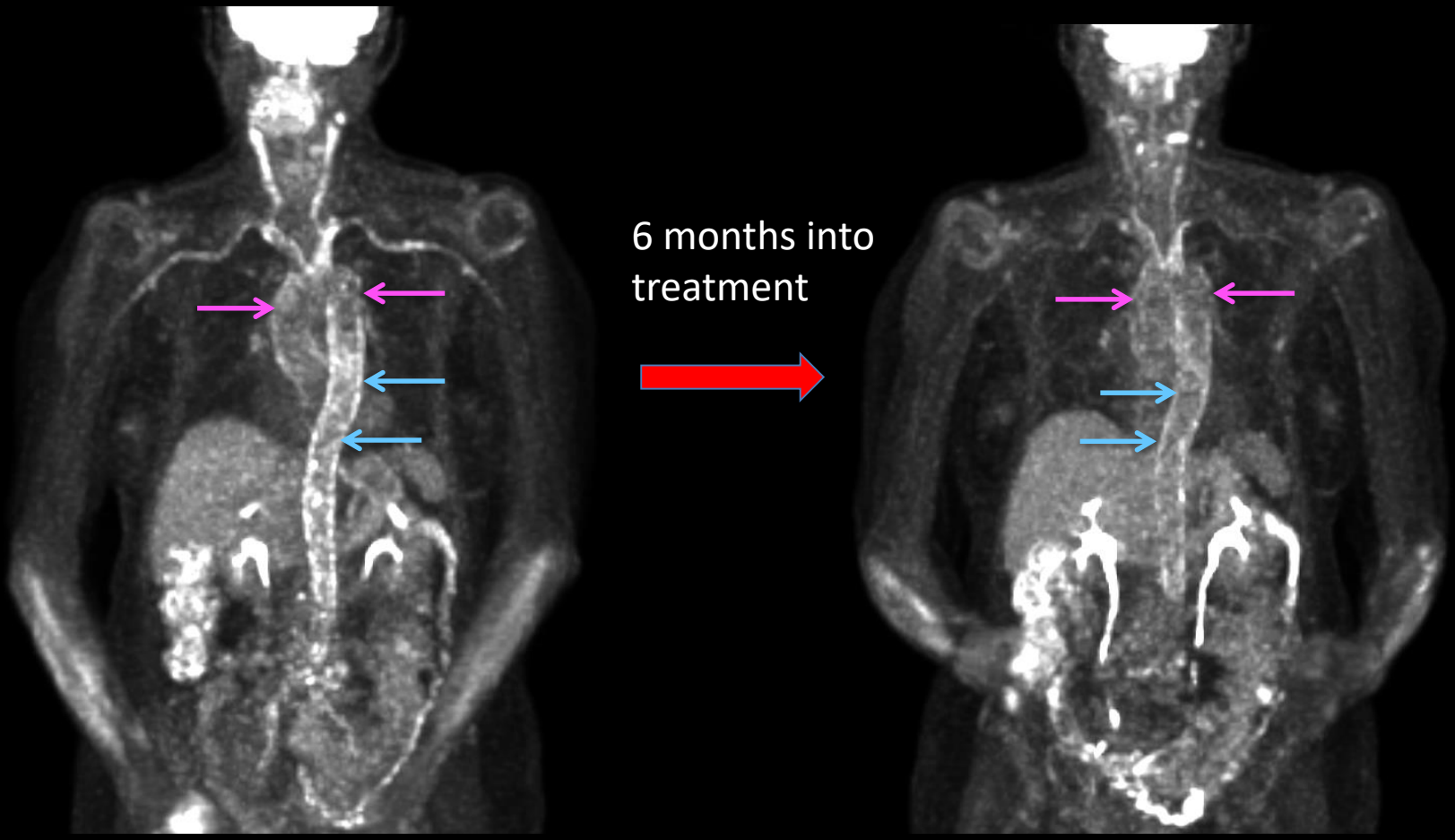
*Simultaneous decrease in GC with increase of DMARD over 2 treatment intervals excluded from analysis.

Change in TBR of Aorta Among the 3 Treatment Categories





Regional Differences in Vascular FDG uptake with Treatment

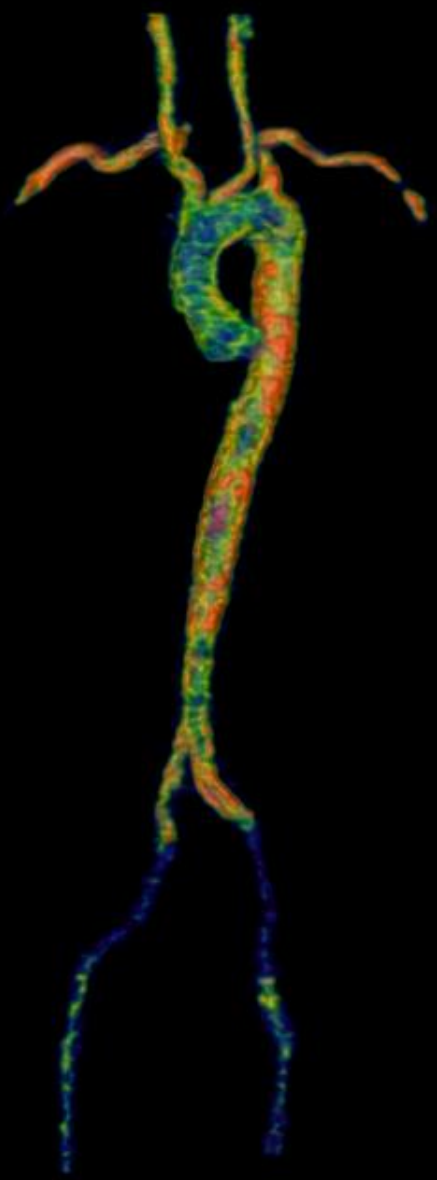


Treatment with Methotrexate and Glucocorticoids is Associated with Reduced FDG-PET Vascular Activity

TBR in specific aortic region	Variables	Correlation Coefficient	P Value
Descending Aorta	MTX	-0.67	0.01
Descending Aorta	GCs	-0.40	0.03
Ascending Aorta and Arch	MTX	-0.42	0.16
Ascending Aorta and Arch	GCs	-0.22	0.25

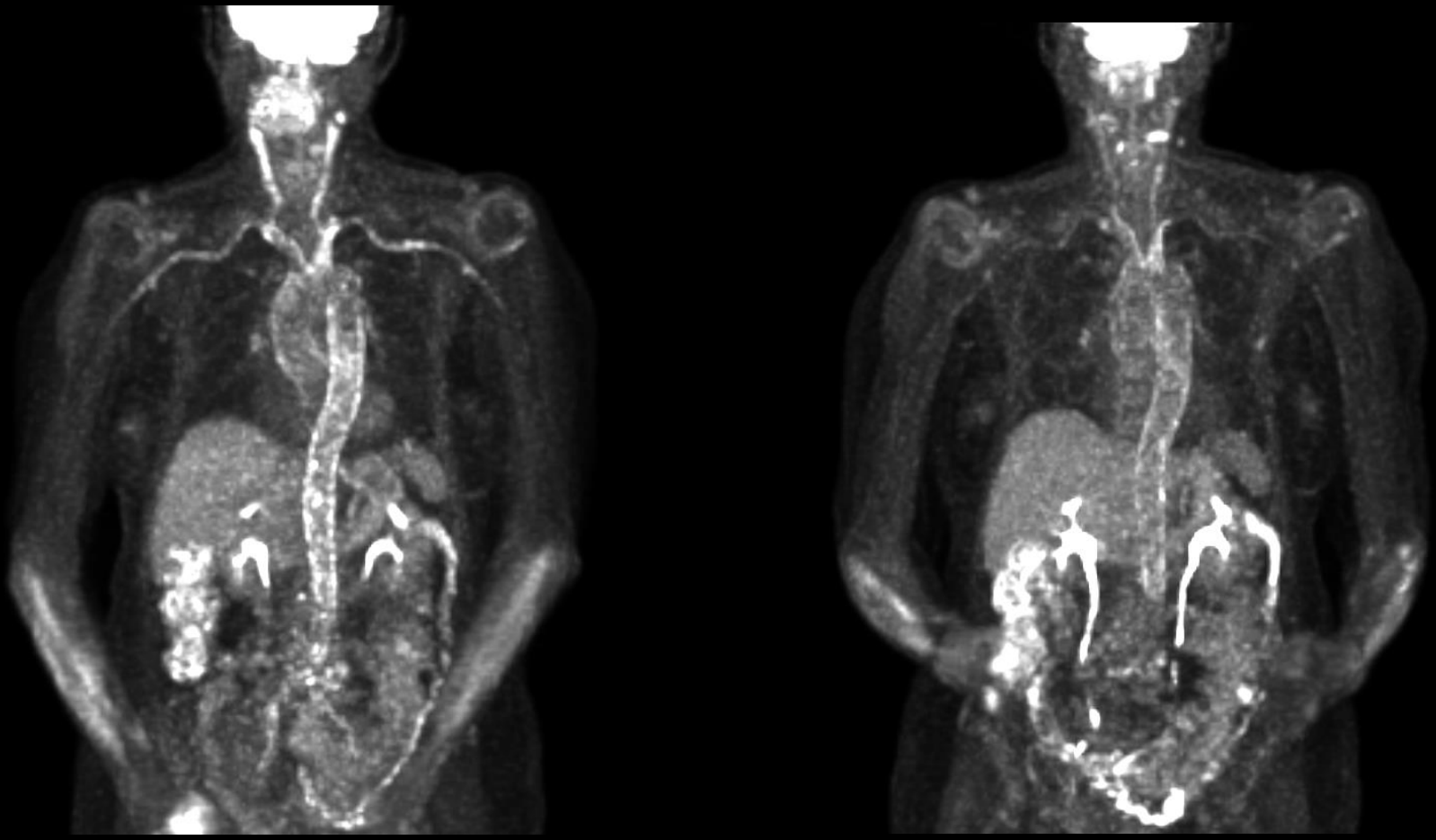
Multivariable regression: Change in GC dose and change in MTX dose independently associated with change in TBR of descending aorta

Effect of Prednisone



71 yo man with GCA
Treated with tapered
prednisone over 6 months

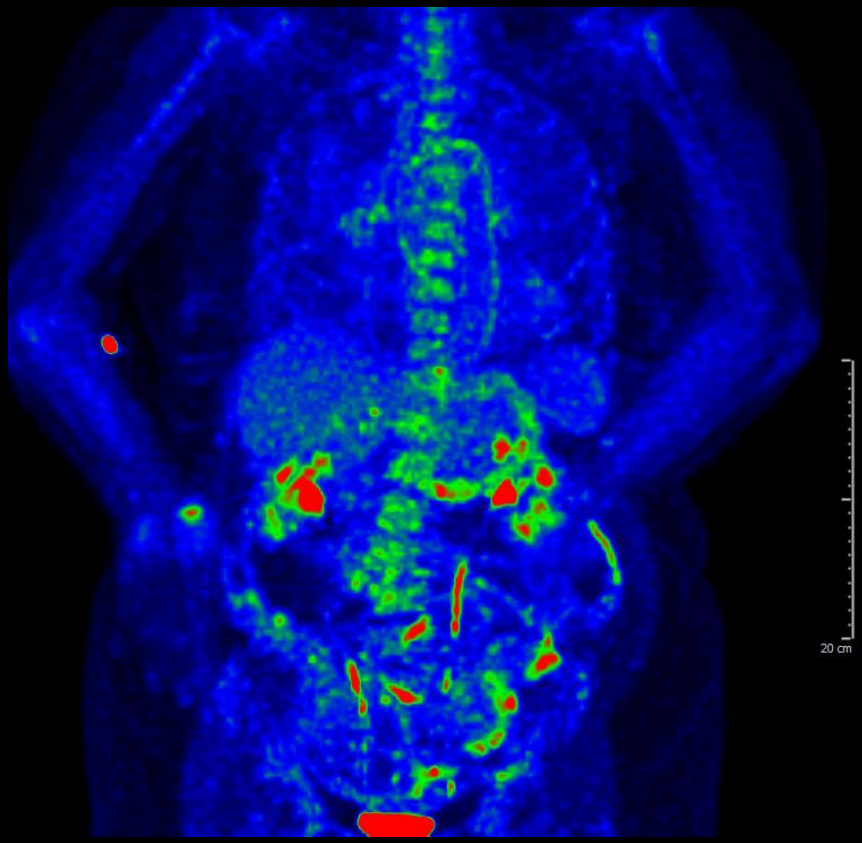
Effect of Methotrexate Alone



Before **After**

Combined Effect of Prednisone and Methotrexate

Before



After

Discussion

Evidence for Efficacy of Methotrexate in Large Vessel Vasculitis

- Conflicting evidence about efficacy in three RCTs
  - Trials only used clinical features as outcome measures
- Methotrexate reduced vascular FDG uptake
- Imaging based outcomes may provide unique and complimentary opportunities to assess drug efficacy

Limitations

- Small cohort
- Unable to assess correlation of DMARDS (other than methotrexate) and biologics on vascular FDG uptake

Conclusions

- Change in treatment is associated with change in vascular FDG uptake
- Dynamic change in PET activity is dependent on the region of the aorta
- Methotrexate and prednisone can reduce vascular FDG uptake
- FDG-PET might be useful to monitor vascular disease activity as an outcome measure in clinical trials of LVV

Acknowledgment