

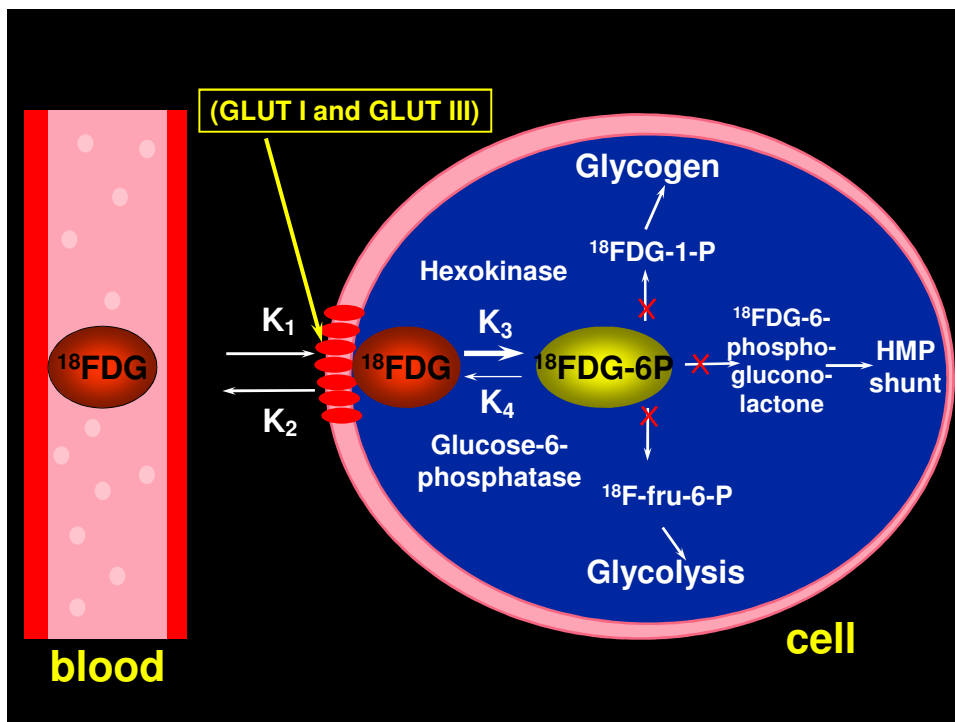
IAEA Regional Training Course (AFRA) on the Role of Nuclear Medicine in Endocrine Disease and Infection/Inflammation

The Role of [¹⁸F]FDG PET/CT in Vasculitis

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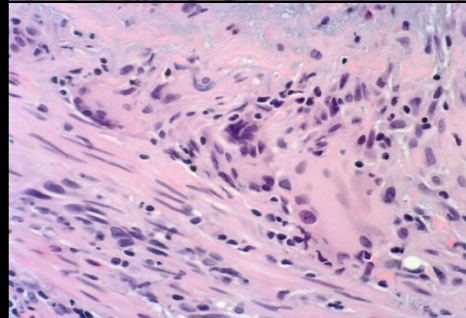
Pretoria, South Africa, Dec. 6-10, 2010



Why [¹⁸F]FDG PET in Inflammation?

- Intracellular accumulation of [¹⁸F]FDG is directly correlated to expression of the GLUT system on cell membranes.
- Expression of the GLUT system is closely dependent on energy demand of cells.
- Besides physiologic accumulation in neurons (where glucose is the sole source of energy), [¹⁸F]FDG accumulates intracellularly in tissues with enhanced glucose metabolism:
 - tumors
 - infection/inflammation

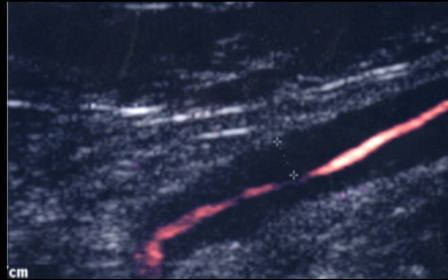
Diagnosis of Large Vessel Vasculitis



- Histopathology is the gold standard for active vascular inflammation, but it cannot be routinely employed for large-vessel vasculitis (aorta biopsy?)
- Clinical signs/symptoms and laboratory tests are not good surrogate markers.

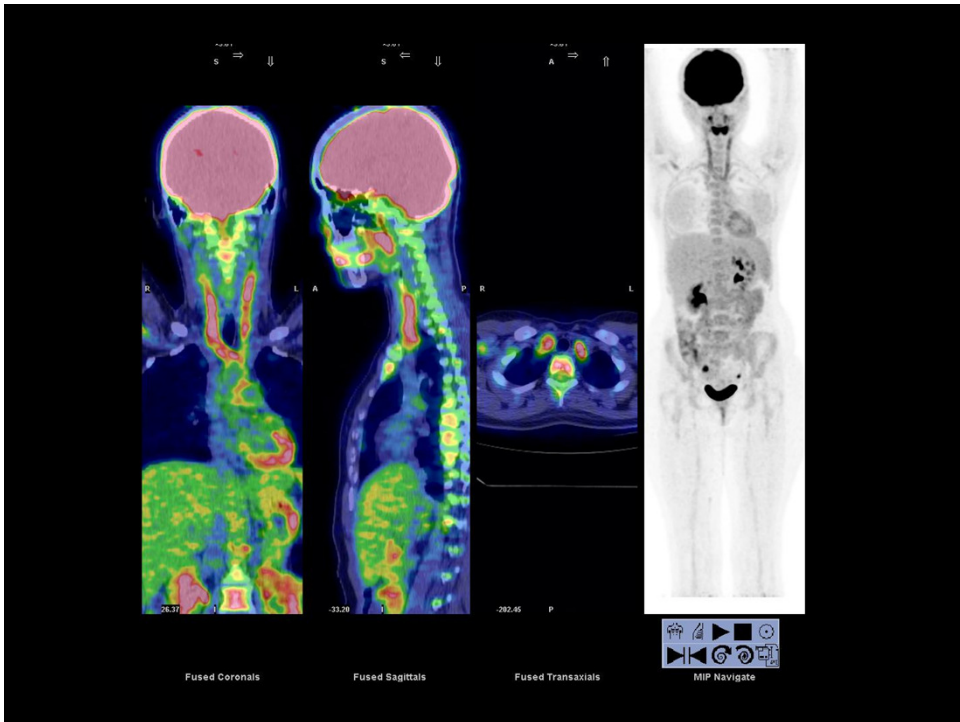
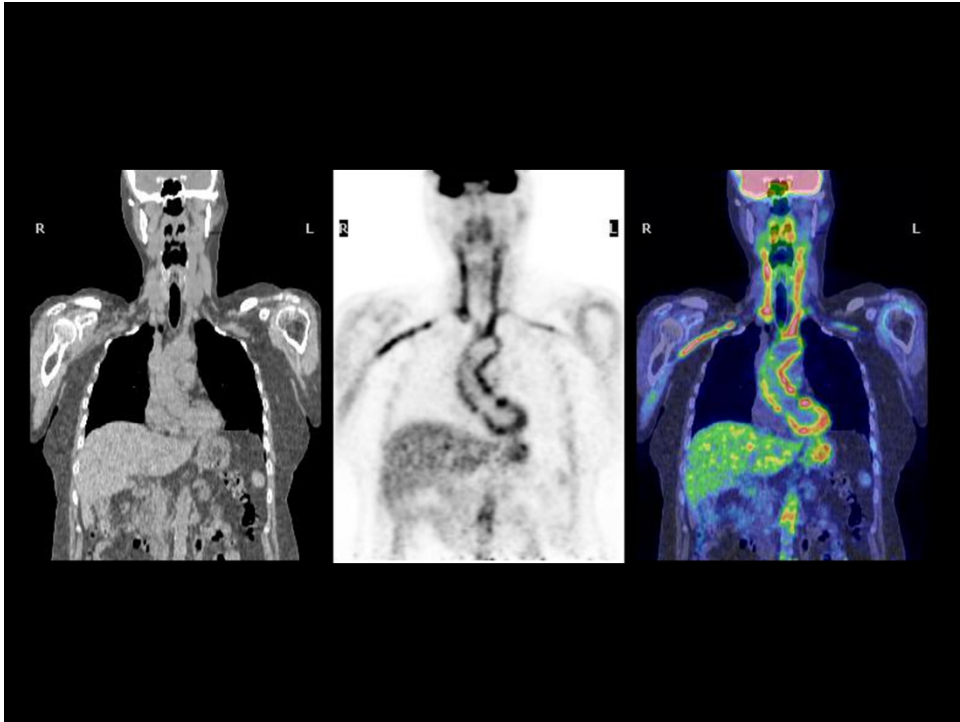
Imaging of Large Vessel Vasculitis

- Angiography
- CT
- MR
- Ultrasonography



Shepherd et al. N Engl J Med 1999

Accumulation of [^{18}F]FDG in the metabolically active inflammatory cells within the affected vessel walls in patients with large-vessel vasculitis



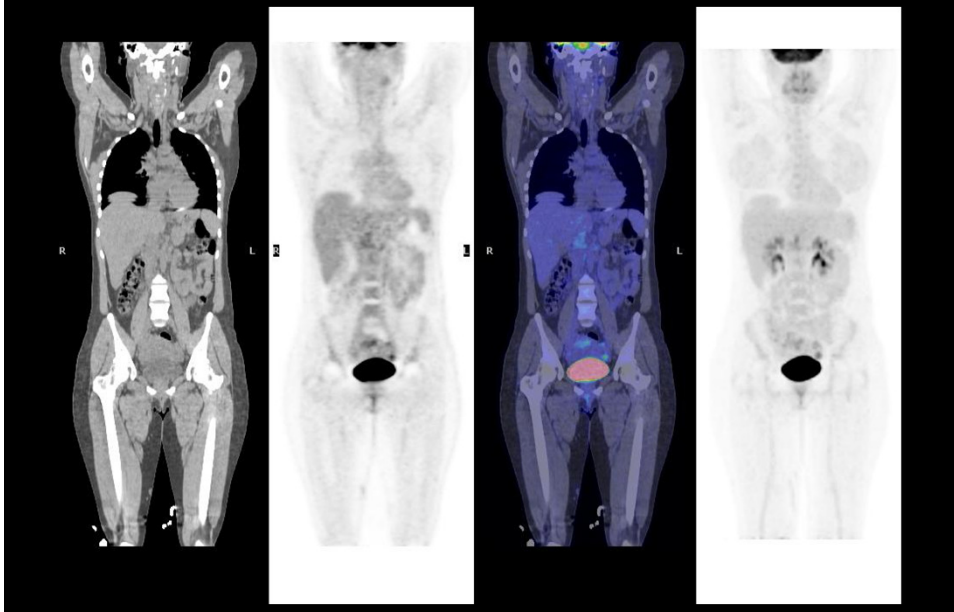
[¹⁸F]FDG PET in Large-Vessel Vasculitis

Four-point scale proposed for [¹⁸F]FDG uptake:

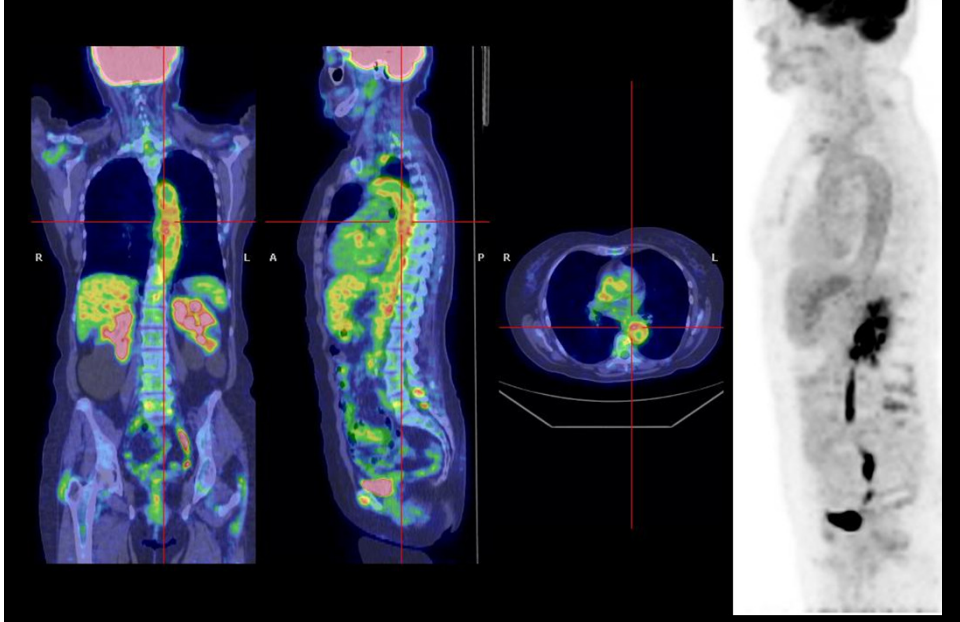
- Grade 0 = no uptake
- Grade 1 = minimal uptake (< liver)
- Grade 2 = moderate uptake (≈ liver)
- Grade 3 = marked uptake (> liver)

Meller J et al. Eur J Nucl Med Mol Imaging 2003

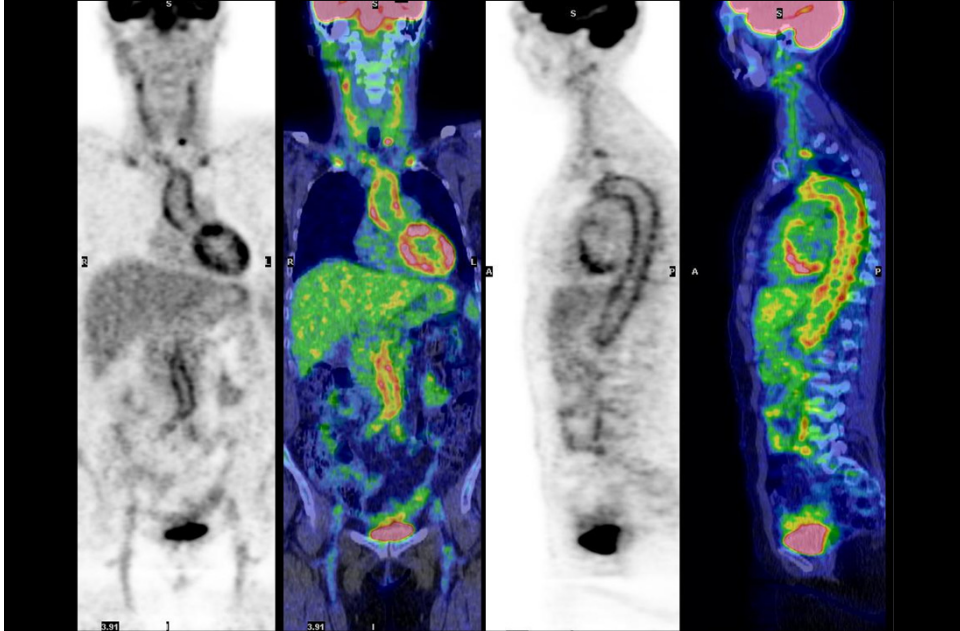
[¹⁸F]FDG-PET/CT: Grade 0 Uptake



[¹⁸F]FDG-PET/CT: Grade 2 Uptake



[¹⁸F]FDG-PET/CT: Grade 3 Uptake



Clinical Interpretation of [¹⁸F]FDG Uptake in Large-Vessel Vasculitis

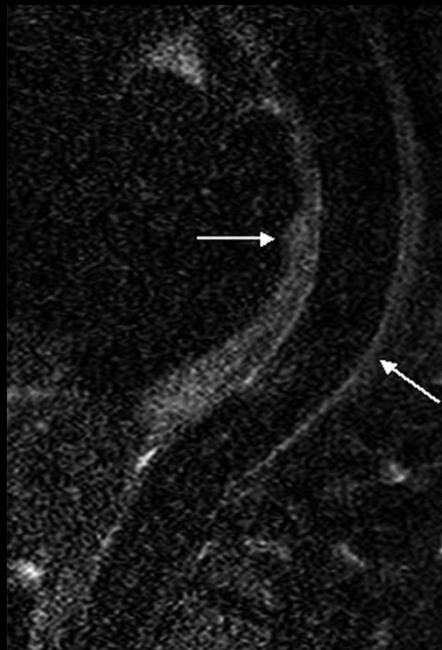
Untreated patients

- Grades 2 and 3 are usually considered relatively specific for vasculitis.
- Grade 1 (rarely grade 2) uptake can be observed in atherosclerotic lesions.

Patients under steroid treatment

- Grade 1 is suspicious for vasculitis.

Belhocine T et al. Eur J Nucl Med Mol Imaging 2003



MRI

MRI and [¹⁸F]FDG PET

Inflammatory cell infiltration (revealed by PET) is likely to precede the development of edema of the vessel wall (depicted by MRI).

Thus,

[¹⁸F]FDG PET may be more sensitive than MRI in early-stage large-vessel vasculitis.

Meller J et al. Eur Radiol 2003

MRI and [¹⁸F]FDG PET

whole-body ¹⁸F-FDG PET can be used as the investigation of choice if vasculitis of the large arteries is suspected, because the chance of a positive finding may be higher with PET than with MRI.

Meller J et al. J Nucl Med 2007

[¹⁸F]FDG PET for the Diagnosis of Large-Vessel Vasculitis

- Sensitivity 77% - 92%
- Specificity 89% - 100%

(in untreated patients with elevated inflammatory markers)

Meller J et al. J Nucl Med 2007



Fever of Unknown Origin (FUO)

- Infectious disease
- Non-infectious inflammatory disease
- Tumors

[¹⁸F]FDG PET for Management of Large-Vessel Vasculitis

Very helpful for assessing and monitoring disease activity.

Webb M et al. Eur J Nucl Med Mol Imaging 2004

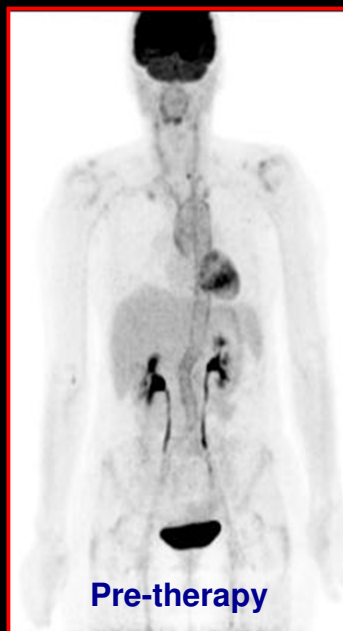
Walter MA et al. Eur J Nucl Med Mol Imaging 2005

Very helpful for evaluating the extent of vascular involvement in the whole body.

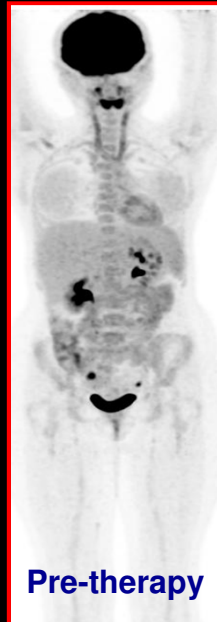
Blockmans D et al. Arthritis Rheum 2006

Bongartz T et al. Curr Opin Rheumatol 2006

Takayasu Arteritis



Giant Cell Arteritis



[¹⁸F]FDG PET for Management of Large-Vessel Vasculitis

Very helpful for assessing and monitoring disease activity.

Webb M et al. Eur J Nucl Med Mol Imaging 2004
Walter MA et al. Eur J Nucl Med Mol Imaging 2005

Very helpful for evaluating the extent of vascular involvement in the whole body.

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Bongartz T et al. Curr Opin Rheumatol 2006



[¹⁸F]FDG-PET

Extent of vascular involvement in the whole body

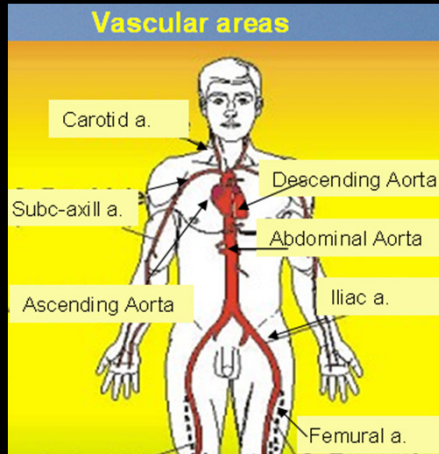
[¹⁸F]FDG PET in Large-Vessel Vasculitis: the Reggio Emilia Experience

- 28 consecutive pts under steroid therapy:
 - 23 with Takayasu Arteritis;
 - 5 with Giant Cell Arteritis.
- Total of 38 [¹⁸F]FDG-PET/CT studies.
- [¹⁸F]FDG PET (new score) correlated with:
 - Erythrocyte Sedimentation Rate (ESR)
 - C-Reactive Protein (CRP)
 - Interleukin-6 (IL-6)
 - Disease activity (Kerr's criteria, NIH)

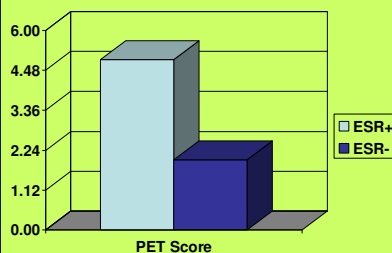
New Combined [¹⁸F]FDG Score for Large-Vessel Vasculitis: Intensity and Extension

- 0: no uptake
- 1: uptake < liver
- 2: uptake ≈ liver
- 3: uptake > liver

Graded in 7 vascular areas to calculate a combined score from 0 (negative) to 21 (max).

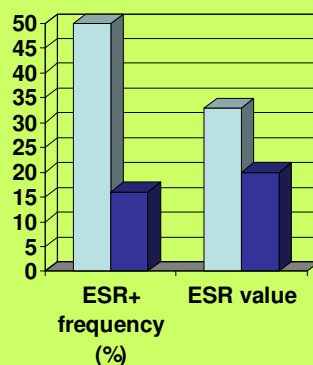


Large-Vessel Vasculitis: PET Score and ESR



The PET score was higher ($p = 0.02$) in pts with high ESR

The frequency of elevated ESR values was higher ($p = 0.049$) in pts with vascular [¹⁸F]FDG uptake



The ESR values were higher ($p = 0.026$) in pts with vascular [¹⁸F]FDG uptake

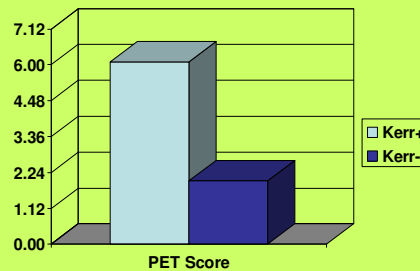
Legend:
 □ FDG uptake+
 ■ FDG uptake-

Large-Vessel Vasculitis: PET Score, Acute-Phase Reactants, and Clinical Activity

	R	p
ESR	0.41	0.013
IL-6	0.48	0.037
CRP	0.20	ns

Significant correlation with ESR
and IL-6 but not with CRP

The PET score was higher ($p = 0.01$)
in pts with active disease



[¹⁸F]FDG PET and Large-Vessel Vasculitis

- [¹⁸F]FDG PET is both sensitive and specific in evaluating disease activity.
- The use of [¹⁸F]FDG PET for assessing response to treatment is well supported by published evidence.

Meller J et al. Eur J Nucl Med Mol Imaging 2003

Hara M et al. J Comput Assist Tomogr 1999

Andrews J et al. Ann Rheum Dis 2004

Limitations of [¹⁸F]FDG PET for Large-Vessel Vasculitis

- Some arteries, such as the temporal and renal arteries, cannot reliably be visualized because of their small size.
- PET evaluation possible for vessels with diameter > 4 mm.
- [¹⁸F]FDG PET is not specific for vasculitis, as vascular uptake increases with older age.

Brodmann M et al. Rheumatology (Oxford) 2004
Zhang Z et al. BMC Nucl Med 2006

Uptake of ¹⁸F-FDG in Acute Aortic Dissection: A Determinant of Unfavorable Outcome

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TABLE 3. Accumulation of ¹⁸F-FDG in Aortic Wall in Controls, Favorable AAD Patients, and Unfavorable AAD Patients on 50-Minute Images

Site	Controls (n = 14)	Favorable AAD (n = 20)		Unfavorable AAD (n = 8)			P (ANOVA)	
		Data	P vs. controls	Data	P vs. controls	P vs. favorable AAD		
Proximal	SUV _{max}	2.31 ± 0.29	3.91 ± 1.00	0.0001*	4.33 ± 1.63	0.0001*	0.932	<0.0001*
	SUV _{mean}	1.84 ± 0.23	3.03 ± 0.83	0.0001*	3.18 ± 1.07	0.0007*	1.0000	<0.0001*
Maximum	SUV _{max}	2.34 ± 0.32	3.10 ± 1.18	0.1310	4.52 ± 1.44	<0.0001*	0.0069*	0.0001*
	SUV _{mean}	1.85 ± 0.18	2.36 ± 0.93	0.1680	3.44 ± 0.87	<0.0001*	0.0043*	0.0001*
Distal	SUV _{max}	2.59 ± 0.34	3.64 ± 0.96	0.0018*	3.84 ± 0.96	0.0036*	1.0000	0.0007*
	SUV _{mean}	2.00 ± 0.21	2.71 ± 0.67	0.0024*	2.86 ± 0.66	0.0039*	1.0000	0.0008*

*P < 0.05.

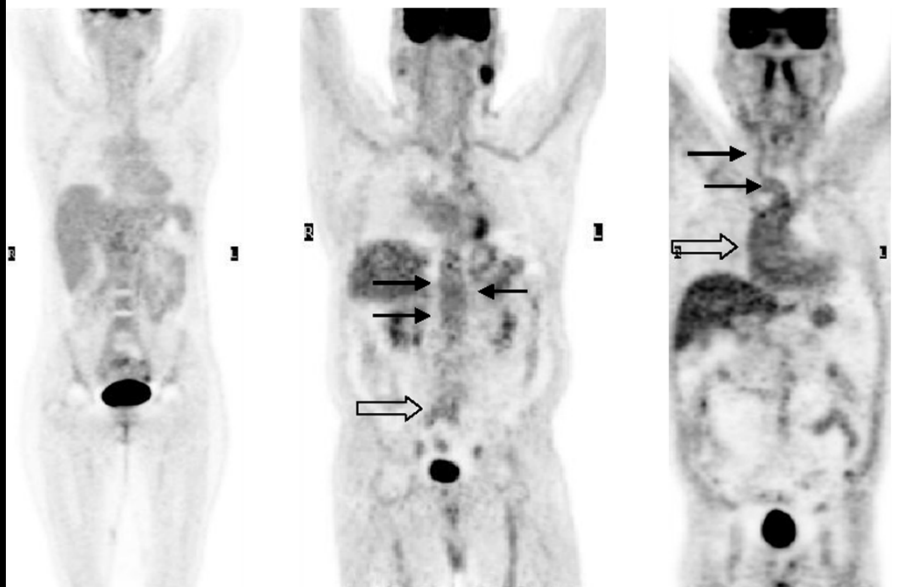
Data are presented as mean ± SD.

J Nucl Med 2010

Large-Vessel Vasculitis versus Atherosclerosis on [¹⁸F]FDG PET

- Vasculitis → more intense [¹⁸F]FDG uptake
 - Kissin EY et al. Curr Opin Rheumatol 2004*
- Vasculitis → involvement of vessels usually spared by atherosclerosis
- Different patterns of [¹⁸F]FDG uptake:
 - atherosclerotic plaques → hot spots
 - vasculitic lesions → smooth and linear

Blockmans D. Clin Exp Rheumatol 2003



Normal

Atherosclerosis

Vasculitis

Pipitone N et al. Rheumatology, 2008

[¹⁸F]FDG-PET in Large-Vessel Vasculitis: Conclusions

- Important and growing role in:
 - **diagnosis and follow-up**
 - **assessing disease activity and extent**
- Large-scale comparative follow-up studies will clarify the role of [¹⁸F]FDG-PET as a new gold standard of disease activity in patients with vasculitis.