The Role of [$^{18}$F]FDG PET/CT in Vasculitis

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Why $[{^{18}}{F}]$FDG PET in Inflammation?

- Intracellular accumulation of $[{^{18}}{F}]$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), $[{^{18}}{F}]$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


Accumulation of $^{18}$FDG in the metabolically active inflammatory cells within the affected vessel walls in patients with large-vessel vasculitis
[\textsuperscript{18}F]FDG PET in Large-Vessel Vasculitis

Four-point scale proposed for [\textsuperscript{18}F]FDG uptake:

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


[\textsuperscript{18}F]FDG-PET/CT: Grade 0 Uptake
[\textsuperscript{18}F]FDG-PET/CT: Grade 2 Uptake

[\textsuperscript{18}F]FDG-PET/CT: Grade 3 Uptake
Clinical Interpretation of $[^{18}\text{F}]$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.

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

Thus,

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

*Meller J et al. Eur Radiol 2003*

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

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

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

*(in untreated patients with elevated inflammatory markers)*


### Fever of Unknown Origin (FUO)

- Infectious disease
- Non-infectious inflammatory disease
- Tumors
[⁴¹⁸F]FDG PET for Management of Large-Vessel Vasculitis

Very helpful for assessing and monitoring disease activity.


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


Takayasu Arteritis

Pre-therapy

Post-therapy
Giant Cell Arteritis

Very helpful for assessing and monitoring disease activity.


[\[^{18}\text{F}]\text{FDG PET for Management of Large-Vessel Vasculitis}\]

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

[^{18}F]FDG-PET

Extent of vascular involvement in the whole body

[^{18}F]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 [^{18}F]FDG-PET/CT studies.

• [^{18}F]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 $[^{18}F]$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 ESR values were higher ($p = 0.026$) in pts with vascular $[^{18}F]$FDG uptake.

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 $[^{18}F]$FDG uptake.
Large-Vessel Vasculitis: PET Score, Acute-Phase Reactants, and Clinical Activity

<table>
<thead>
<tr>
<th></th>
<th>R</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESR</td>
<td>0.41</td>
<td>0.013</td>
</tr>
<tr>
<td>IL-6</td>
<td>0.48</td>
<td>0.037</td>
</tr>
<tr>
<td>CRP</td>
<td>0.20</td>
<td>ns</td>
</tr>
</tbody>
</table>

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.

Hara M et al. J Comput Assist Tomogr 1999
Limitations of $^{18}$F-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.
- $^{18}$F-FDG PET is not specific for vasculitis, as vascular uptake increases with older age.

Brommann M et al. Rheumatology (Oxford) 2004

Uptake of $^{18}$F-FDG in Acute Aortic Dissection: A Determinant of Unfavorable Outcome

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

<table>
<thead>
<tr>
<th>Site</th>
<th>Controls (n = 36)</th>
<th>Favorable AAD (n = 20)</th>
<th>Unfavorable AAD (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P vs. controls</td>
<td>Data</td>
<td>P vs. controls</td>
</tr>
<tr>
<td>Prefemoral</td>
<td>DLw,mean 2.31 ± 0.29</td>
<td>3.91 ± 1.90 0.0001*</td>
<td>4.33 ± 1.63 0.0001*</td>
</tr>
<tr>
<td></td>
<td>SAlw,mean 2.4 ± 0.24</td>
<td>3.09 ± 0.83 0.0001*</td>
<td>3.18 ± 1.07 0.0001*</td>
</tr>
<tr>
<td>Maximum</td>
<td>DLw,mean 2.34 ± 0.32</td>
<td>3.19 ± 1.18 0.1310</td>
<td>4.02 ± 1.44 &lt;0.0001*</td>
</tr>
<tr>
<td></td>
<td>SAlw,mean 1.85 ± 0.18</td>
<td>2.38 ± 0.53 0.1880</td>
<td>3.44 ± 0.87 &lt;0.0001*</td>
</tr>
<tr>
<td>Distal</td>
<td>DLw,mean 2.59 ± 0.34</td>
<td>3.64 ± 0.96 0.0001*</td>
<td>3.94 ± 0.96 0.0001*</td>
</tr>
<tr>
<td></td>
<td>SAlw,mean 2.00 ± 0.21</td>
<td>2.71 ± 0.67 0.0001*</td>
<td>2.86 ± 0.66 0.0001*</td>
</tr>
</tbody>
</table>

*P < 0.05.
Data are presented as mean ± SD.

**J Nucl Med 2010**
Large-Vessel Vasculitis *versus* Atherosclerosis on $[^{18}\text{F}]$FDG PET

- Vasculitis $\Rightarrow$ more intense $[^{18}\text{F}]$FDG uptake
  
  *Kissin EY et al. Curr Opin Rheumatol 2004*

- Vasculitis $\Rightarrow$ involvement of vessels usually spared by atherosclerosis

- Different patterns of $[^{18}\text{F}]$FDG uptake:
  - atherosclerotic plaques $\Rightarrow$ hot spots
  - vasculitic lesions $\Rightarrow$ smooth and linear
  
  *Blockmans D. Clin Exp Rheumatol 2003*

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*Normal*  
*Atherosclerosis*  
*Vasculitis*

*Pipitone N et al. Rheumatology, 2008*
[\textsuperscript{18}F]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 [\textsuperscript{18}F]FDG-PET as a new gold standard of disease activity in patients with vasculitis.