Molecular Imaging of Coronary Plaques

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Understanding CAD is Changing

Fibroatheroma: Stable Plaque
TCFA with Cap Rupture

Narula & Willerson, JACC (ed)
Narula & Virmani, 1999
Anatomical to Molecular Imaging

Tissue level

Anatomical level

Cellular and molecular Level

Imaging Probes

Sensitivity

PET

MRI

CT

Radioactive
Small Molecules

Paramagnetic
Superparamagnetic

Radiodense

Payload required
Orders of Magnitude in Drug (Contrast Agent) Dosing:
Exploiting the Exploratory IND (eIND) Mechanism

<table>
<thead>
<tr>
<th>Modality</th>
<th>“Typical” Intravenous Human Dose (g)</th>
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<tbody>
<tr>
<td>CT</td>
<td>75 cc of 930 mM solution = 56 g</td>
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<tr>
<td>MRI</td>
<td>15 cc of 500 mM solution = 7 g</td>
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<tr>
<td>Optical (NIR)</td>
<td>5 cc of a 1 mM solution = 5 mg</td>
</tr>
<tr>
<td>SPECT</td>
<td>20 mCi (10,000 Ci/mmol) = 2 µg</td>
</tr>
<tr>
<td>PET</td>
<td>20 mCi (10,000 Ci/mmol) = 2 µg</td>
</tr>
</tbody>
</table>

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**eIND-Eligible**
FDG Uptake in Carotid Artery Disease

Weissberg P et al., Circulation 2004

Simvastatin Attenuates Plaque Inflammation

Tahara et al JACC 2006
Measuring atherosclerosis FDG-PET/CT

- Identifies cells with increased metabolic activity
- Measures plaque glycolysis (inflammation)
- Used to assess changes in plaque inflammation
- Statins, anti-inflammatory drugs, TZDs
- Predictor of future risk of atherothrombosis

FDG Visualization of Inflamed Coronary Plaque

Culprit Lesions in ACS

<table>
<thead>
<tr>
<th>ACS: New Stent</th>
<th>Stable Syndrome; Old Stent</th>
<th>Stable Syndrome; New Stent</th>
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</thead>
<tbody>
<tr>
<td><img src="chart1.png" alt="" /></td>
<td><img src="chart2.png" alt="" /></td>
<td><img src="chart3.png" alt="" /></td>
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I. Rogers et al JACC CV Imaging 2010
Coronary Arterial $^{18}$F-FDG Uptake by Fusion of PET and Coronary CT Angiography at Sites of Percutaneous Stenting for Acute Myocardial Infarction and Stable Coronary Artery Disease

Victor Y. Cheng1,2, Piotr J. Slomka1,2, Ludovic Le Meunier3, Balaji K. Tamarapu3, Ryo Nakazato3, Daminii Day1,2, and Daniel S. Berman1,2

1Heart Institute and Department of Imaging, Cedars-Sinai Medical Center, Los Angeles, California; 2David Geffen School of Medicine, UCLA, Los Angeles, California; 3Department of Medicine, Cleveland Clinic Foundation, Cleveland, Ohio; and 4Department of Biomedical Sciences and Biomedical Imaging Research Institute, Cedars-Sinai Medical Center, Los Angeles, California

• 27 PCI patients studied with FDG PET/CT
• 1-6 days p PDI: 20 STEMI; 7 stable CAD
• Increased uptake in: 12/20 STEMI; 1/7 Stable


FDG Uptake at Stent Site in Acute STEMI

Absence of FDG Uptake at Stent Site in Stable CAD


In vivo PET imaging

18F-Galacto-RGD

PET/CT Imaging
Angiogenesis

Patient 2 Wks Post Anterior MI

CMR DE 131I-Ammonia 18F-RGD

4 Chamber View
2 Chamber View

Sinusas lecture: ASNC 2009
Direct Imaging of Myocardial Ischemia (FDG)

He et al, Narula, Jain. Circulation 2003

18Fluoro-Deoxy Glucose
‘The ring of fire’

Aortic Ring Inflammation

Sodium $^{18}$Fluoride

Aortic Stenosis

Dweck et al. Circulation 2012;125:76-86

$^{18}$Fluoro-Deoxy Glucose

‘The ring of fire’

Dweck et al. Circulation 2012;125:76-86
Calcification more important than Inflammation

Dweck et al. Circulation 2012;125:76-86

Dweck et al JACC 2012
F-18 NaF Uptake in Coronary Plaque

Dweck M...Newby D ACC 2012

10 year FRS for Controls and Patients with CAC who did and did not have 18F-NaF uptake

Dweck et al JACC 2012
**Tc-99m Annexin V: Probe for Vulnerable Plaque**

Annexin V binding followed by 2D-crystallization.

**Annexin-V Imaging For Apoptosis**

**Old TIA**

**Recent TIA**

Transverse

Coronal

Annexin IHC in Endarterectomy

Keitselaar, Hofstra, Narula; NEJM 2004
RGD tracer uptake is increased in atherosclerotic plaque

Oil Red O  $^{18}$F RGD uptake  $\alpha\nu\beta^3$  Autoflour

Tamarappoo, et al 2010

Direct Imaging of Myocardial Ischemia (FDG)

He et al, Narula, Jain. *Circulation* 2003
Molecular Imaging to Detect Vulnerable Plaque Clinical Applications Emerging in 2020

Molecular Imaging Across CAD Spectrum

Conventional Imaging
Coronary Calcium/Plaque
Stenosis/Perfusion
Coronary Atherosclerosis
Disease Activity Plaque Vulnerability

Molecular Imaging
Plaque Activity
Remodeling
Guiding Specific therapy

Function Geometry
Myocardial Ischemia/Infarction
Heart Failure
