Cardiac PET and Quantification of Absolute Myocardial Flow in Routine Cardiology Practices

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Disclosures

- Astellas – Speaker bureau, research grant
- Bracco – consultant
- Not an interventional cardiologist
  - Highly critical
Target Audience

- Physicians
- Technologists
- Basic principles and current data
- Will not be a scientific analysis:
  - Compartment models
  - Differences in software algorithms
### What is Flow and Why Measure It?

#### What
- Measurement of volume/time
- Cardiac purposes = volume blood/time/gram of myocardium
- Typically expressed as cc/min/gm

#### Why?
- Current revascularization practices only modestly effective
- Data
- Data
- Data
Current Revascularization Practice

- LHC (angiogram) – “Gold Standard”
- “See and Fix” approach based on % stenosis
- Current guidelines: 50% LM and 70% for revascularization
- FFR/Stress “intermediate lesions”
- FFR used in 6% of patients

1ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention JACC 2012
2Dattilo PB, et al. Contemporary patterns of fractional flow reserve. JACC. 2012;60(22):2337-2339.
A Brief Word on FFR

- FFR = Fractional flow reserve
- Pressure derived flow surrogate
- “stress test” of an artery in the cath lab

\[
FFR = \frac{\text{Distal Coronary Pressure (Pd)}}{\text{Proximal Coronary Pressure (Pa)}}
\]

(During Maximum Hyperemia)
resting state  maximum hyperemia (i.v. adenosine)
Revascularization guided by % stenosis will lead to better outcomes

DATA DATA DATA
COURAGE and STICH

- Revasc based on % stenosis
- Stress testing NOT mandatory
- Decisions to guide revascularization based on judgment of angiographer
- FFR not utilized


Revascularization guided by % stenosis will lead to better outcomes.
FAME I and II

- FFR guided revascularization
- I - FFR vs. Angio
- II - FFR vs. optimal medical therapy (OMT)

Ziadi MC, JACC. 2011;58:740-748.

Introduction to Coronary Blood Flow (CBF)

- Ischemia - Myocardial O2 supply vs. demand
- Adequate supply is maintained with ability to increase CBF
- 2 major resistances to flow
  - Epicardial arteries (>350 µm)
  - Arterioles and capillaries (microvasculature)
    - Resting microvascular (R₂) >>>> epicardial (R₁)
    - Normally regulation occurs at level of microvasculature
- CBF increases automatically to increase O2 demands
  - Exercise
  - Pharm stress
  - Neurohormonal
Pathologic Conditions

- $R_1 \gg R_2$
  - Coronary stenosis $\rightarrow$ Flow impaired at level of the epicardial artery

- $R_2 \gg R_1$
  - Diastolic dysfunction
  - HOCM
  - Non-ischemic myopathies/ infiltrative

- Clinical CAD is a combination of abnormal $R_1$ and $R_2$. 
Top: Normal flow response in left circumflex (LCX) artery without stenosis
Bottom: Flow response in LCX with 83% stenosis.

Baseline flow remains stable up to ~ 83% stenosis
Hyperemic flow declines steeply ~ 70% stenosis

R_{sys}

\[ R_{sys} \]

FFR

\[ FFR \]

CFR

\[ CFR \]

RFR \[= \frac{\text{MAX FLOW}_{s}}{\text{MAX FLOW}_{n}} \]

\[ RFR = \frac{\text{MAX FLOW}_{s}}{\text{MAX FLOW}_{n}} \]

In case of ISOLATED coronary artery stenosis

\[ RFR = FFR \]

(per unit of tissue mass)
67% 83%

CFR \geq 3.5 \quad CFR \leq 1.7
% Stenosis vs. FFR

Tonino, P. et al. J. Am Coll Cardiol. 2010:55;2816-2821
Flow vs. Stenosis Paradox

Why is there a huge disparity between flow and anatomy?
Flow Dynamics

- describes relation of pressure to flow in an artery
  - $f =$ constant of pressure loss due to friction
  - $S =$ constant of pressure loss due to expansion

- $F$ and $s$ are related to stenosis geometry:
  - $F = 8^2$, $S = 2$
  - $\mu =$ blood viscosity, $A =$ cross sectional area of stenosed artery, $A_n =$ cross section area of normal artery, $L =$ length stenosis, $\rho =$ blood density.
  - $Area = \pi / 4$

- Critical dimensions are 1) $L$ and 2) diameters of stenotic segment and normal segment to the fourth power.

- Flow is proportional to diameter to the 4th power $\rightarrow$ a small decrease in diameter may cause a profound effect on flow.

A Little Physics (sorry!!)

- In 1738, Bernoulli published Hydrodynamic.
- \[ \Delta P = \frac{1}{A_s \cdot L \cdot V^2} \]
- \[ A_s = \pi r^2 \]
Gould, L. JACC Imag 2009; 2:1009
Flow vs. Stenosis Paradox

- Flow is determined by a combination of
  - Stenosis
  - Diffuse disease
  - Arterial remodeling
  - Microvascular function

- Impossible to visually determine the physiologic impact of aggregate disease
A - sMBF pre- and post-revascularization of quadrants with a baseline perfusion defect showing an improvement of $0.6\pm0.7$ cc/min/g ($1.1\pm0.4$ vs $1.7\pm0.8$, $p<0.001$). B - sMBF pre- and post-revascularization of quadrants without a baseline defect ($1.7\pm0.3$ vs $1.5\pm0.4$ cc/min/g, $p=0.16$). C - pre- and post-sMBF in quadrants without a baseline perfusion defect which were not revascularized ($2.0\pm0.6$ vs $1.9\pm0.7$, $p=0.7$). sMBF - stress myocardial blood flow.
Cardiac PET and Flow

- High spatial resolution combined with quantitative measures
  - Relative Images – Attenuation corrected
  - Absolute flow (cc/min/gm)
- Gold standard for assessment of myocardial blood flow.
Conceptual Thresholds of Flow Causing Ischemia

% patients

CFR or stress flow in cc/ min/ gm
Ischemic Thresholds for Absolute Stress Flow

# Ischemic Thresholds for Absolute Stress Flow

<table>
<thead>
<tr>
<th>First Author</th>
<th>Citation</th>
<th>n</th>
<th>Ischemia</th>
<th>Reference Standard</th>
<th>CFR [No units]</th>
<th>Stress Flow [UIA/MIA/gm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Santucci</td>
<td>Am J Cardiol 1993;12:990</td>
<td>33</td>
<td>N-12</td>
<td>Glycerol ST depression</td>
<td>1.75</td>
<td>0.99</td>
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<tr>
<td>Matti</td>
<td>J Am Coll Cardiol 1998;31:534</td>
<td>91</td>
<td>N-13</td>
<td>Clinically normal group and cash area</td>
<td>2.74</td>
<td>0.91</td>
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<tr>
<td>Newman</td>
<td>Eur J Nucl Med Mol Imaging 2009;36:1394</td>
<td>48</td>
<td>0-18</td>
<td>Cash %NST &gt;50 (plus FFIR in half of patients)</td>
<td>1.15</td>
<td>0.6</td>
</tr>
<tr>
<td>Hagin</td>
<td>J Am Coll Cardiol Img 2005;2:781</td>
<td>27</td>
<td>N-13</td>
<td>Cash %NST &gt;70</td>
<td>2.0</td>
<td>0.80</td>
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<tr>
<td>Aladjer</td>
<td>Circulation 2013;127:608</td>
<td>107</td>
<td>0-18</td>
<td>Cash %NST &gt;50 or FFIR&gt;0.8</td>
<td>2.0</td>
<td>0.96</td>
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<tr>
<td>Jobst</td>
<td>J Am Coll Cardiol Img 2011;4:390</td>
<td>1.674</td>
<td>Rs-62</td>
<td>PET defect, glycerol angina/ST</td>
<td>1.74</td>
<td>0.53</td>
</tr>
<tr>
<td>Rosing</td>
<td>J Am Coll Cardiol 2012;60:1549</td>
<td>41</td>
<td>N-13</td>
<td>Cash %NST &gt;70</td>
<td>2.44</td>
<td>0.83</td>
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<tr>
<td>Fischler</td>
<td>J Nucl Med 2012;53:1230</td>
<td>73</td>
<td>N-13</td>
<td>Cash %NST &gt;50</td>
<td>2.0</td>
<td>0.92</td>
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<tr>
<td>Sardan</td>
<td>J Nucl Med 2013:45:65</td>
<td>120</td>
<td>0-18</td>
<td>Cash %NST &gt;50 (plus FFIR in third of patients)</td>
<td>2.30</td>
<td>0.81</td>
</tr>
</tbody>
</table>

Relative vs. Absolute Perfusion

A

Absolute Flow Reserve

2.7

(1.8)

(3.0)

Relative Perfusion

60%

100%

B

(1.2)

1.8

(2.0)

60%

100%

C

(1.1)

1.3

(1.4)

79%

100%
Kinetic Models

- **Time sequenced** measurement of radiotracer concentration in blood &/or tissues
- Mathematically illustrates “real life”
- Various models – all correct
- Each isotope has its own model(s)
- Simplified Rb-82 model example
Flow = \( \frac{M}{T_m} \left[ 1 - e^{-\left(0.45 + 0.16 \text{Flow}\right)/\text{Flow}} \right] A [C_a] [C_m] \)

- \( M \): myocardial activity (measured)
- \( A \): input function (measured)
- \( T_m \): Time duration of image
- \( C_{am} \): partial volume corrections
Simplified model for Rb-82

Yoshida, Mullani, Gould JNM 1996;37:1701

- Aortic activity
- Single image arterial input
- "Instantaneous" myocardial uptake
- Myocardial activity
Acquisition of Cardiac Images for Rb-82 Rest/Stress in List Mode

1. Attenuation Scan
2. Injection of Rb-82 bolus and start of scan
3. Acquisition of arterial input (0-120 secs)
4. Acquisition of myocardial uptake (90-420 sec)
5. Generator recovery and start of dipyridamole infusion
6. Gating
7. Acquisition of arterial input (0-120 secs)
8. Acquisition of myocardial uptake (90-420 sec)
9. Injection of Rb-82 bolus and start of stress scan
10. Gating
Can My Practice Measure Flow?

- Various software packages available
- No standardized reporting guidelines
- Training for physician interpretation
- Training for technologists
- Physician leadership within the practices needs to "own" it
Should My Practice Measure Flow?

- **Cannot be done casually**
- Requires specific interest, commitment, training, and experience
- Physician must be able to:
  - Provide accurate and reliable myocardial perfusion and absolute flow
  - Integrate physiologic data
  - Management decision for each individual patient.
Software Packages

- Corridor4DM™ - Invia
- ImagenQ™ - CVIT
- FlowQuant™ - Ottawa Heart
- FlowTool™ - Emory
- QPET™ - Cedars
Other Software Packages

- CFRQuant™ - Sold through Positron
- SyngoMBF™ - Siemen's
Anatomic Versus Physiologic Assessment of Coronary Artery Disease

Role of Coronary Flow Reserve, Fractional Flow Reserve, and Positron Emission Tomography Imaging in Revascularization Decision-Making

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Houston, Texas; Kansas City and St. Louis, Missouri; Ottawa, Ontario, Canada; Hannover and Munich, Germany; New Orleans, Louisiana; Milan, Italy; Cleveland, Ohio; Boston, Massachusetts; Zurich and Geneva, Switzerland; Amsterdam, the Netherlands; Turku, Finland; Niagara Falls and New York, New York; Los Angeles, California; Frederick and Baltimore, Maryland; Detroit, Michigan; and Birmingham, Alabama
CASE #1

- 49 y/o woman admitted for CP
- DM, HTN and tob use
- Presenting BP 173/109
- Trp negative
- ECG sinus with NSSTabn
CASE #1

49 y/o woman admitted for CPDM, HTN and tob use

Presenting BP 173/109

Trp negative

ECG sinus with NSSTabn

CASE #1
Case #1

Rest flow (cc/min/gm)
- LAT average = 1.09
- INF average = 1.04
- SEP average = 0.93
- ANT average = 1.13

Stress flow (cc/min/gm)
- LAT average = 3.24
- INF average = 3.36
- SEP average = 3.13
- ANT average = 3.36

Coronary flow reserve
- LAT average = 2.99
- INF average = 3.28
- SEP average = 3.38
- ANT average = 2.99
Coronary Flow Map

88% Normal flow capacity comparable to healthy young volunteers.
8% No ischemia. Minimally reduced flow capacity.
4% No ischemia. Mildly reduced flow capacity.
0% Moderately reduced flow capacity.
0% Severely reduced flow capacity.
CASE #2

- 65 y/o man CP and DOE
- HTN, DM, HPL, BMI 42 (6’0 315lbs)
- Tchol 206, TG 1326, HDL 20
- ECG - nsr with inc RBBB
CASE #2
Case #2

Coronary Flow Map

0% Normal flow capacity comparable to healthy young volunteers.
2% No ischemia: Minimally reduced flow capacity.
62% No ischemia: Mildly reduced flow capacity.
24% Moderately reduced flow capacity.
13% Severely reduced flow capacity (largest single contiguous region: 9%).
(5% Myocardial steal.)
Case #3

- 44 y/o woman transferred for TMR for lifestyle limiting angina
- h/o >5 PCI's, 5VCABG, 4/5 grafts occluded
- Known RCA and LCX occlusion
- Patent SVG jump to OM1-OM2
- Pt. arrived and PCI of LAD performed
- Angina walking to bathroom later that PM
Case #3
Case 3

Rest flow (cc/min/gm) (max=0.95 min=0.24 whole=0.52 arterial=10.42)
LAT average=0.70
INF average=0.48
SEP average=0.43
ANT average=0.46

Stress flow (cc/min/gm) (max=1.46 min=0.37 whole=0.75 arterial=9.03)
LAT average=0.70
INF average=0.78
SEP average=0.89
ANT average=0.63

Coronary flow reserve (max=2.59 min=0.60 whole=1.52)
LAT average=1.02
INF average=1.59
SEP average=2.04
ANT average=1.45
Case #3

Coronary Flow Map

0% Normal flow capacity comparable to healthy young volunteers.
0% No ischemia. Minimally reduced flow capacity.
23% No ischemia. Mildly reduced flow capacity.
21% Moderately reduced flow capacity.
56% Severely reduced flow capacity (largest single contiguous region: 55%).
(10% Myocardial steal.)

14% Non-transmural myocardial infarction (single contiguous region).
Case #4

- 65 y/o woman with CP in ED
- BP 170/110
- Tob use, HTN, unknown lipids, denies DM
- ECG- LVH strain
- Trp borderline
Case #4
Case #4
Case #4

Coronary Flow Map

0% Normal flow capacity comparable to healthy young volunteers.
12% No ischemia. Minimally reduced flow capacity.
43% No ischemia. Mildly reduced flow capacity.
15% Moderately reduced flow capacity.
30% Severely reduced flow capacity (largest single contiguous region: 23%).
(16% Myocardial steal.)
Case #5

- 87 y/o man with CP and SOB
- Found to be in afib with RVR
- HTN, HPL, DM
- Trp 3.5
- Beta-blockers → converted to sinus
- LHC occluded RCA and "3VD" referred for CABG
- PET requested for 2nd opinion by patient
Case #5
Case #5

Coronary Flow Map

0% Normal flow capacity comparable to healthy young volunteers.
16% No ischemia. Minimally reduced flow capacity.
63% No ischemia. Mildly reduced flow capacity.
9% Moderately reduced flow capacity.
32% Severely reduced flow capacity (single contiguous region).
(6% Myocardial steal.)