



# Garbage in, garbage out...Protocols and processing for PET MBF.

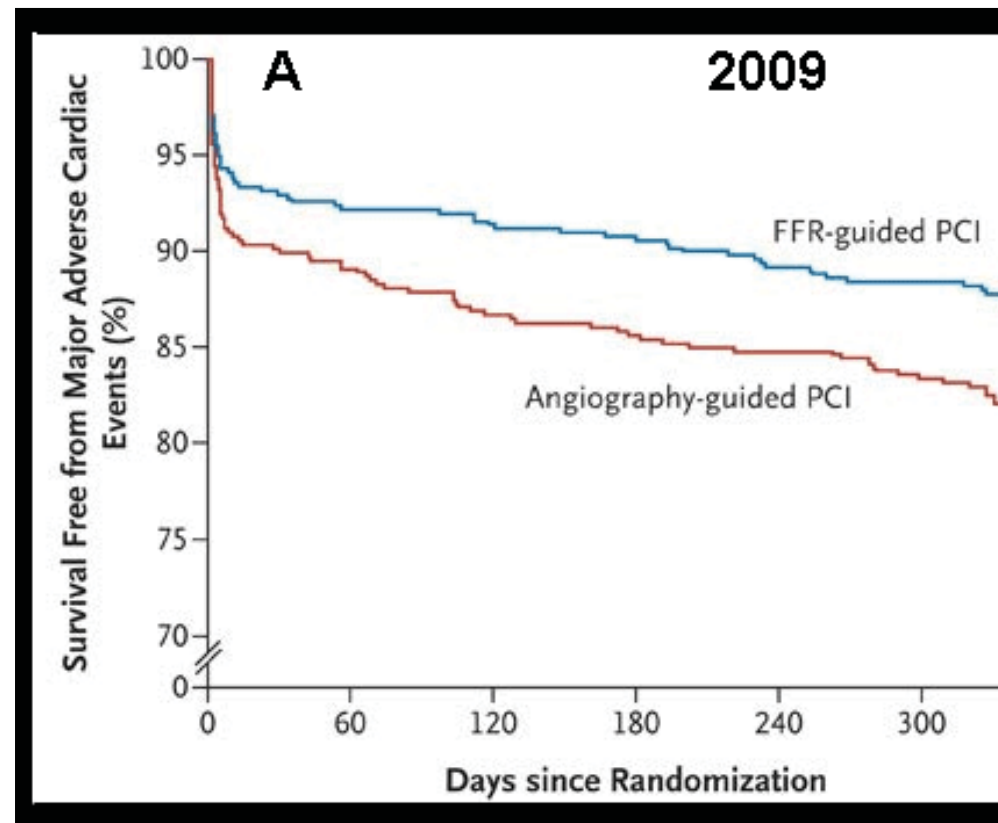
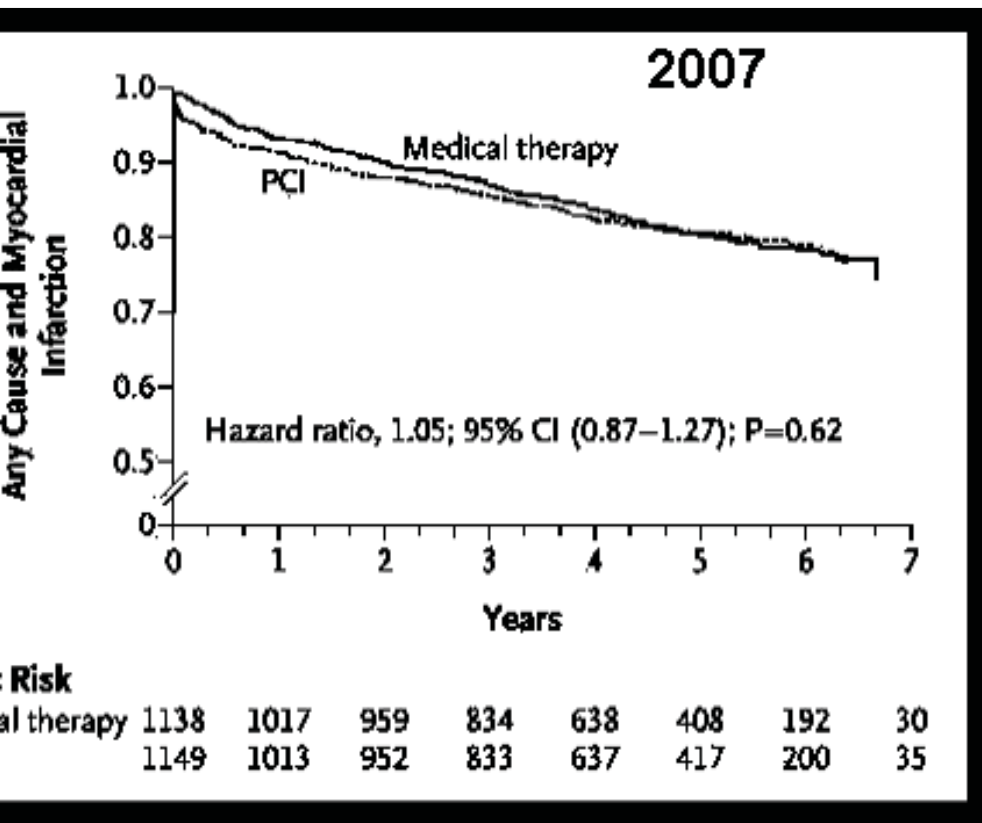
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Amanda Roby MBA, PET, RT(N)  
Weatherhead PET Imaging Center  
Houston, TX

The background of the slide is a dark gray ECG (heart rate) tracing on a grid. The grid consists of vertical and horizontal lines, with a dotted pattern. The ECG line is black and shows several cardiac cycles. The text is overlaid on the middle of the grid.

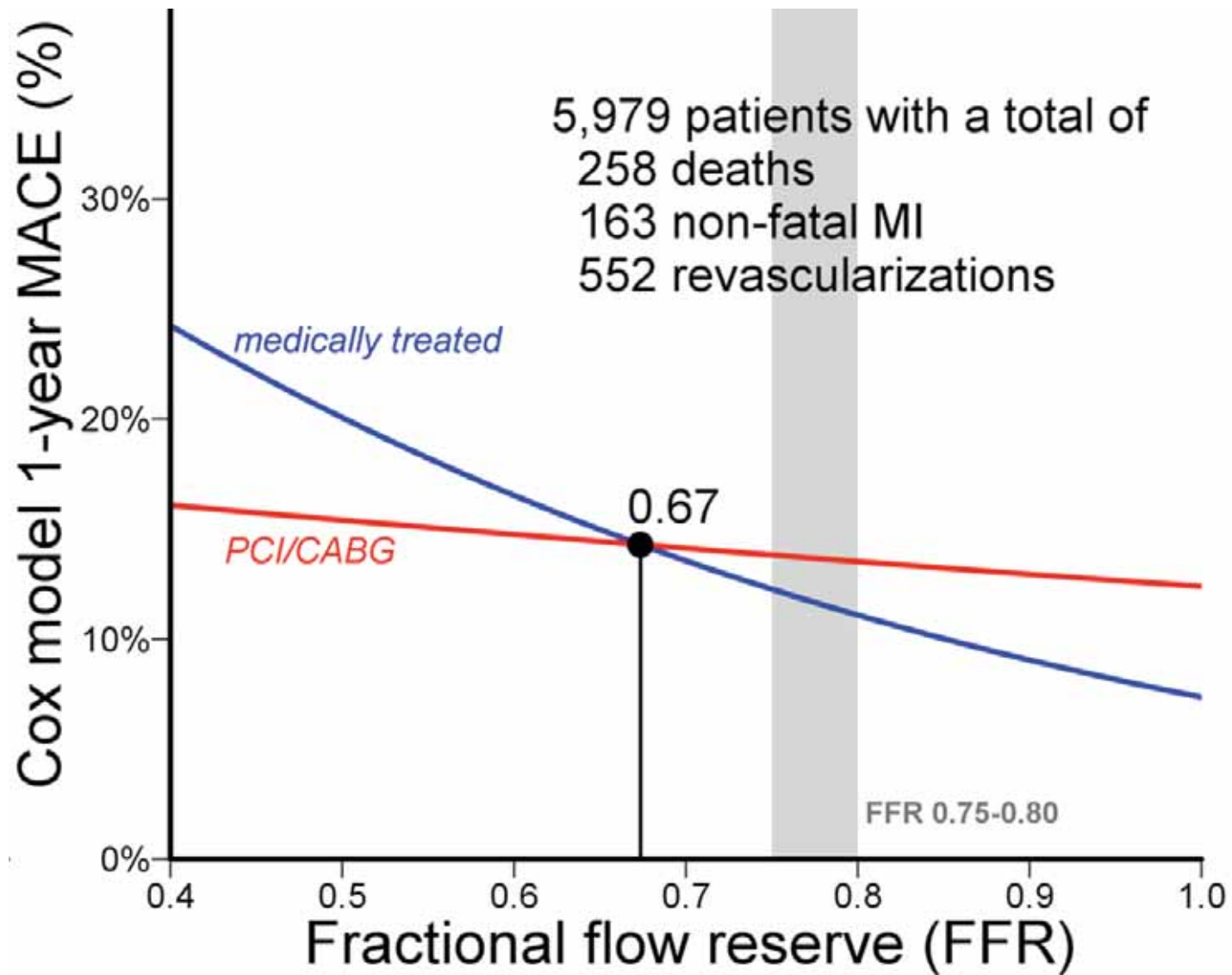
# WHAT IS MYOCARDIAL BLOOD FLOW?

Courage Trial: PCI vs Medical Rx In Non-Acute CAD **No benefit of stents over medical treatment alone based on angiogram**  
 FAME I showed physiology plays a major role.



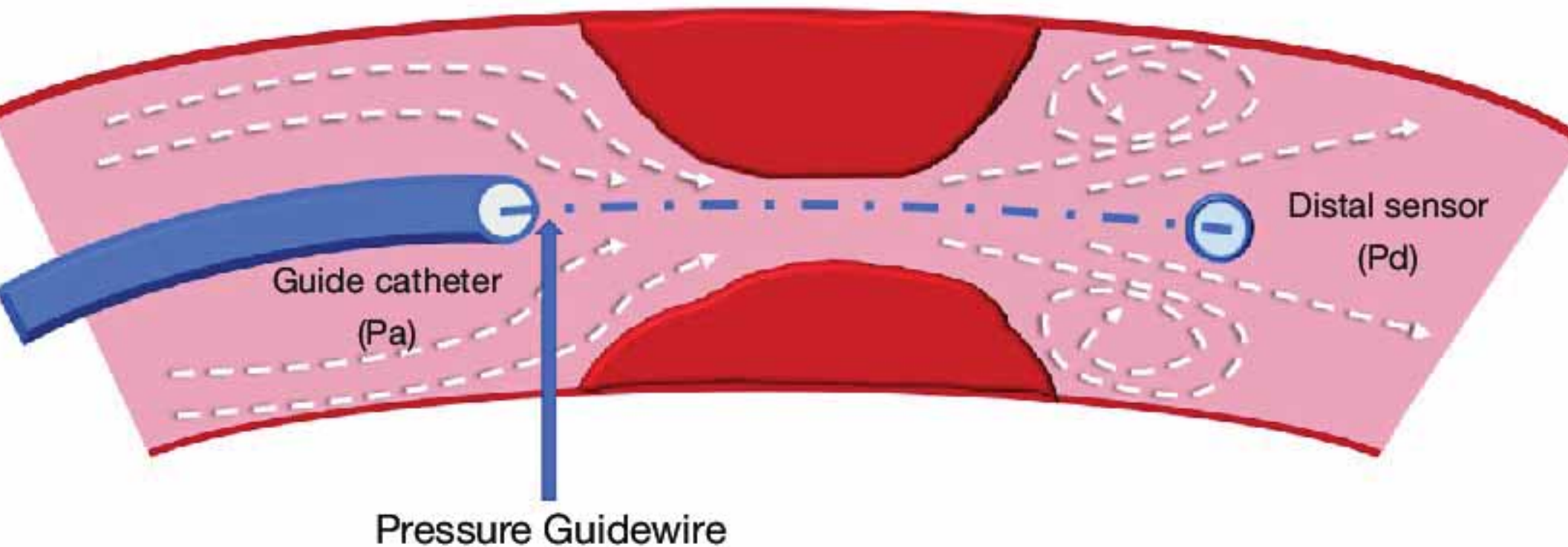
et al. N Engl J Med 2007;356:1503

Tonino et al. N Engl J Med 2009;360:213 and Defer trial 5 yr f/u JACC 2010



et al. JACC 2014;64:1641 original, adapted for Gould et al. Circ CV Imag 2015;8:e003099.

# CA-FFR (fractional flow reserve)



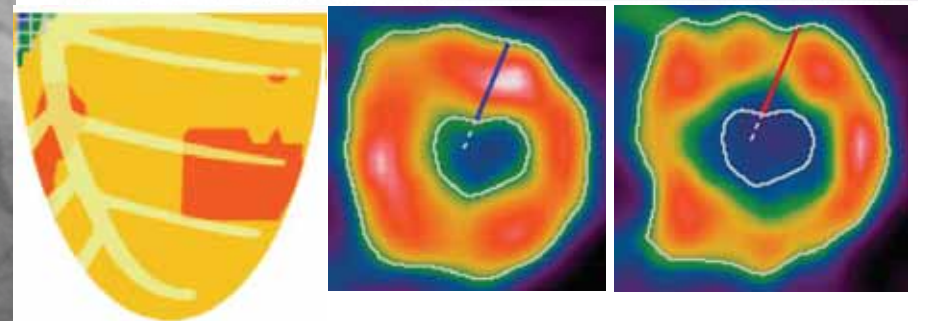
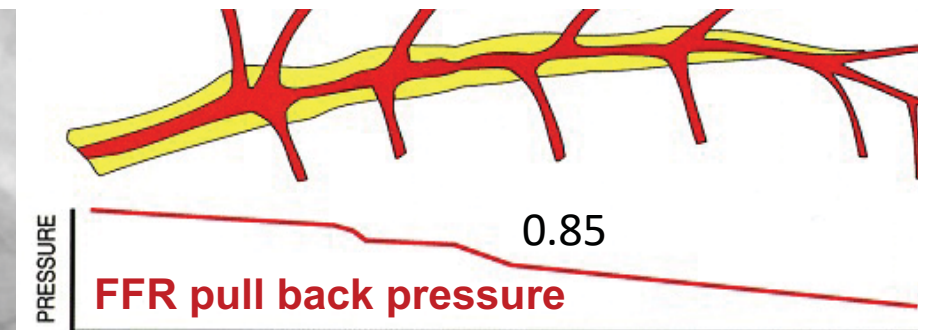
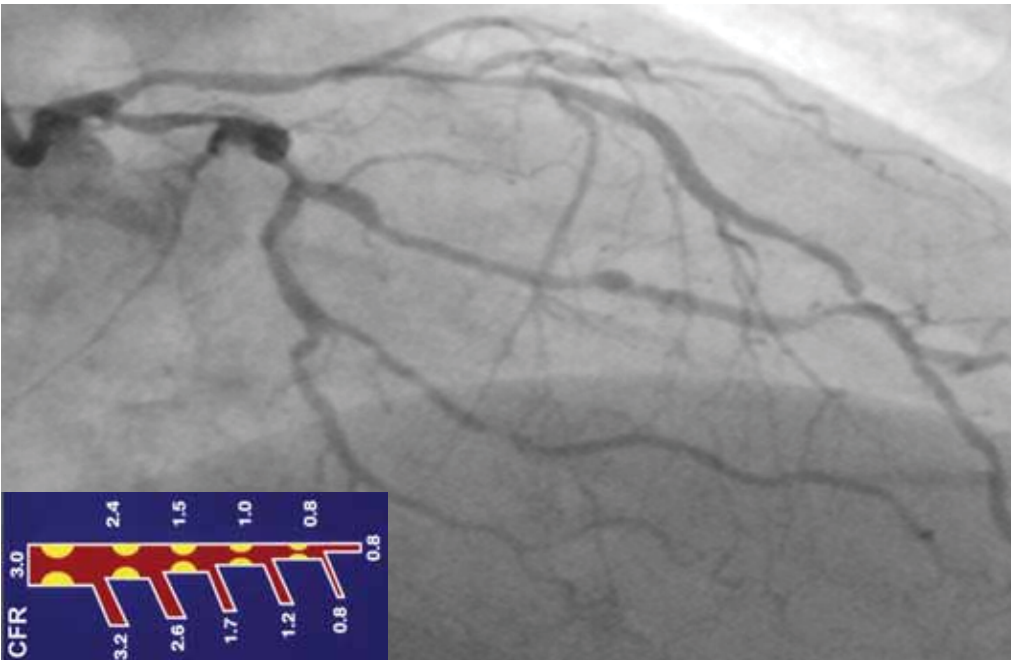
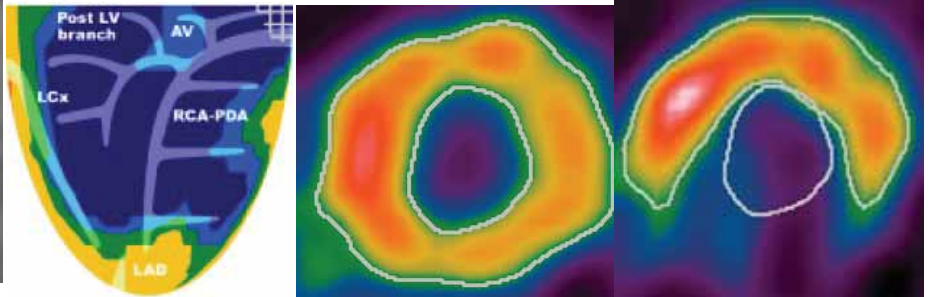
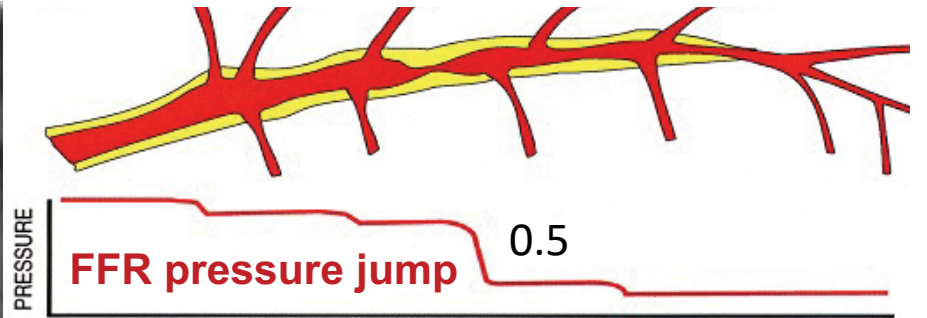
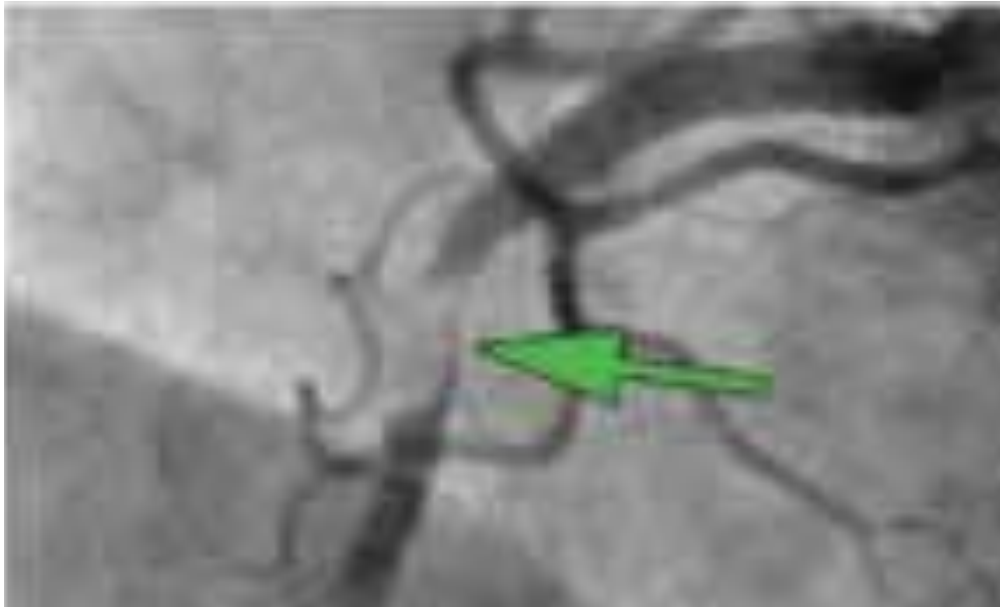
# Invasive Coronary Angiography - FFR

## Pros

New gold standard for evaluating stenosis severity.  
Eval and deploy therapy at the same time.

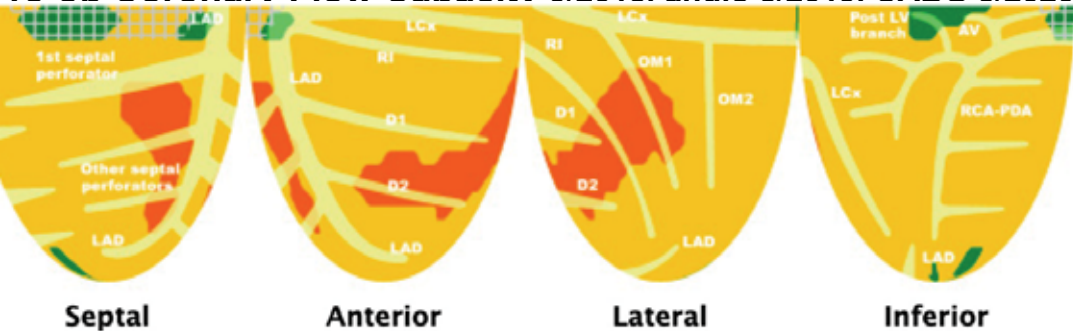
## Cons

- Invasive
- Requires highly skilled invasive cardiologist
- Additional time
- Additional equipment
- Difficult to evaluate regional impact or diffuse disease



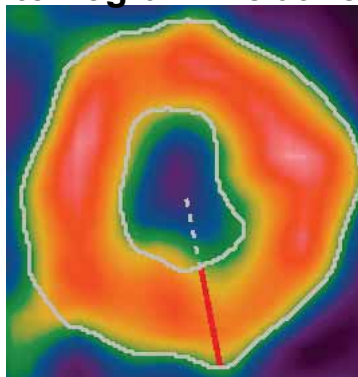
on renal dialysis with dyspnea on exertion, no angina, has HTN, DM, stress EF 65%, anemia, hypothyroidism, coronary calcium, no angina or ST changes during stress.  
 surgeon: "No renal transplant until CABG is done". Angiogram called 60% to 90% DS.

Pre-op Coronary Flow Capacity 9/2018. andio 8/2019. CABG 5/2020

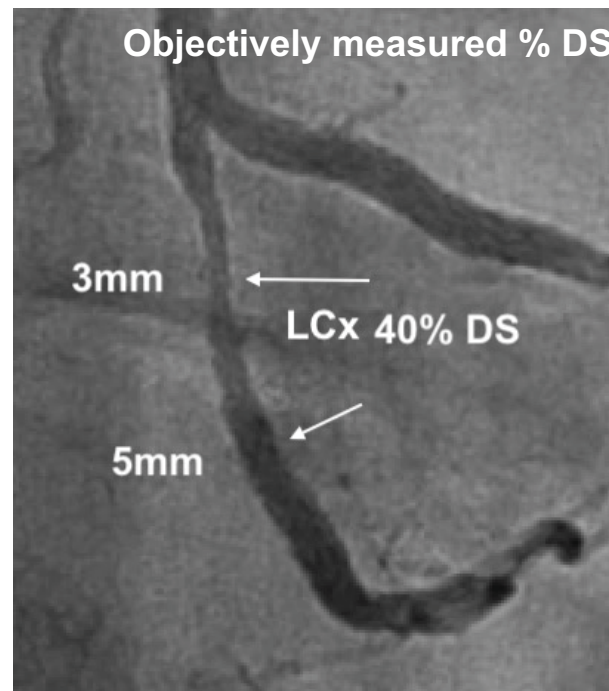


0% Normal, from healthy young volunteers  
 11% Minimally reduced, risk factors only  
 87% Mildly reduced  
 2% Moderately reduced  
 0% Severely reduced, definite ischemia

tomogram - relative

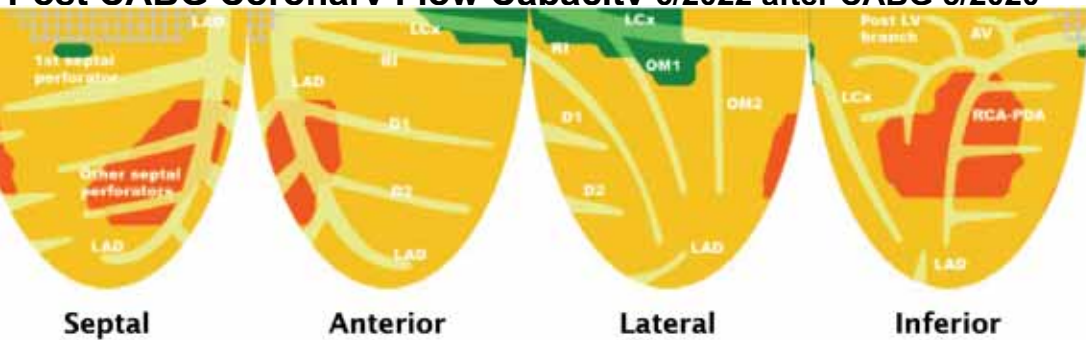


normal subendocardial stress perfusion



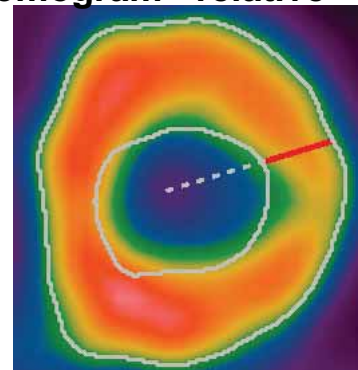
Post CABG CFC shows microvascular dysfunction & non-obstructive coronary calcification.

Post CABG Coronary Flow Capacity 6/2022 after CABG 5/2020

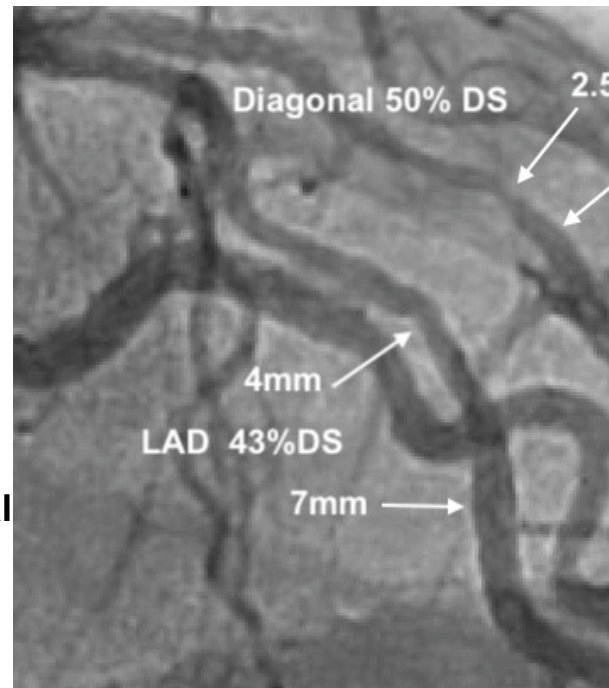


0% Normal, from healthy young volunteers  
 14% Minimally reduced, risk factors only  
 81% Mildly reduced  
 5% Moderately reduced  
 0% Severely reduced, definite ischemia

tomogram - relative

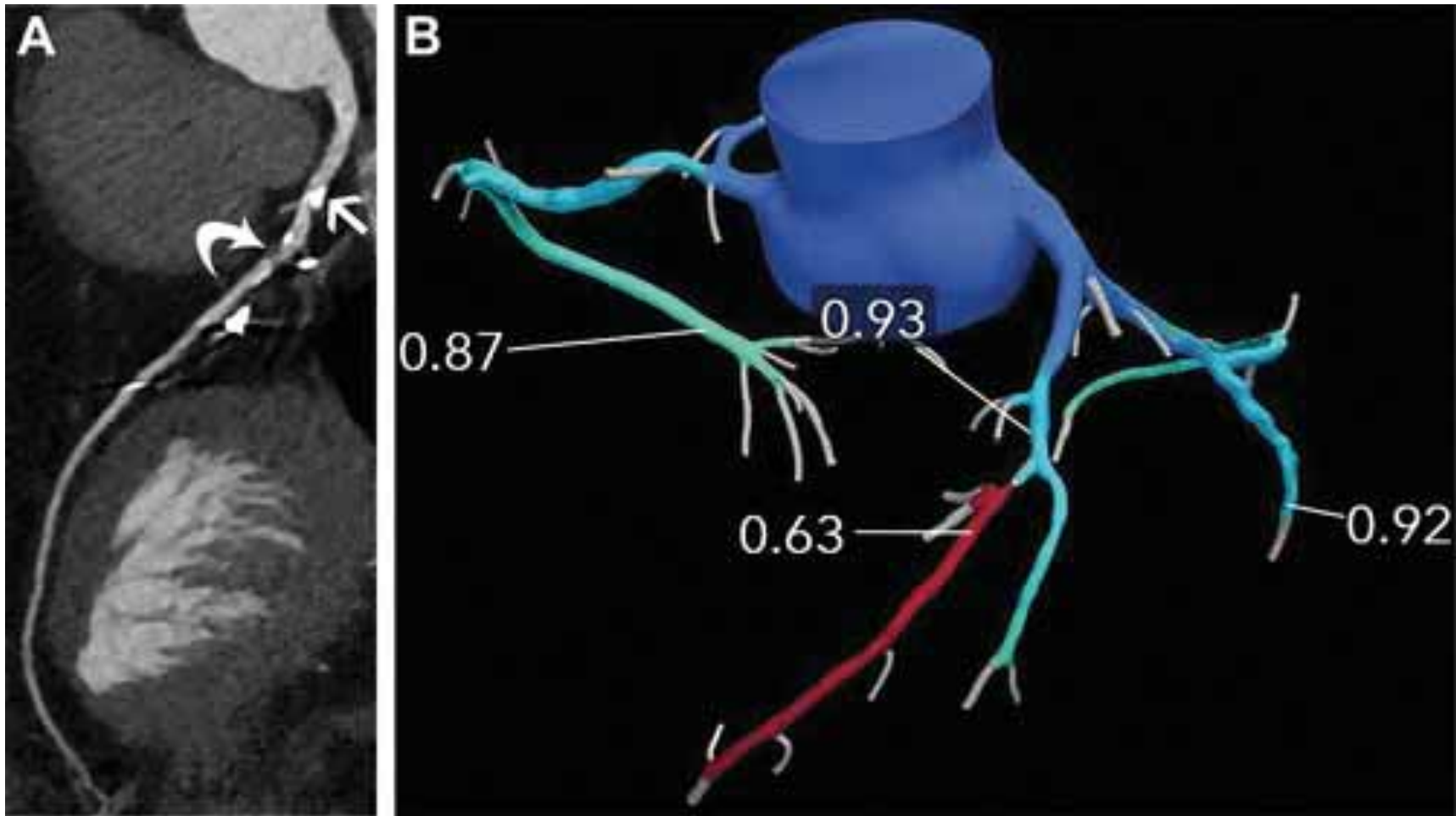


normal subendocardial stress perfusion





# CTA with $FFR_{CT}$



# FFR<sub>CT</sub> (HeartFlow)

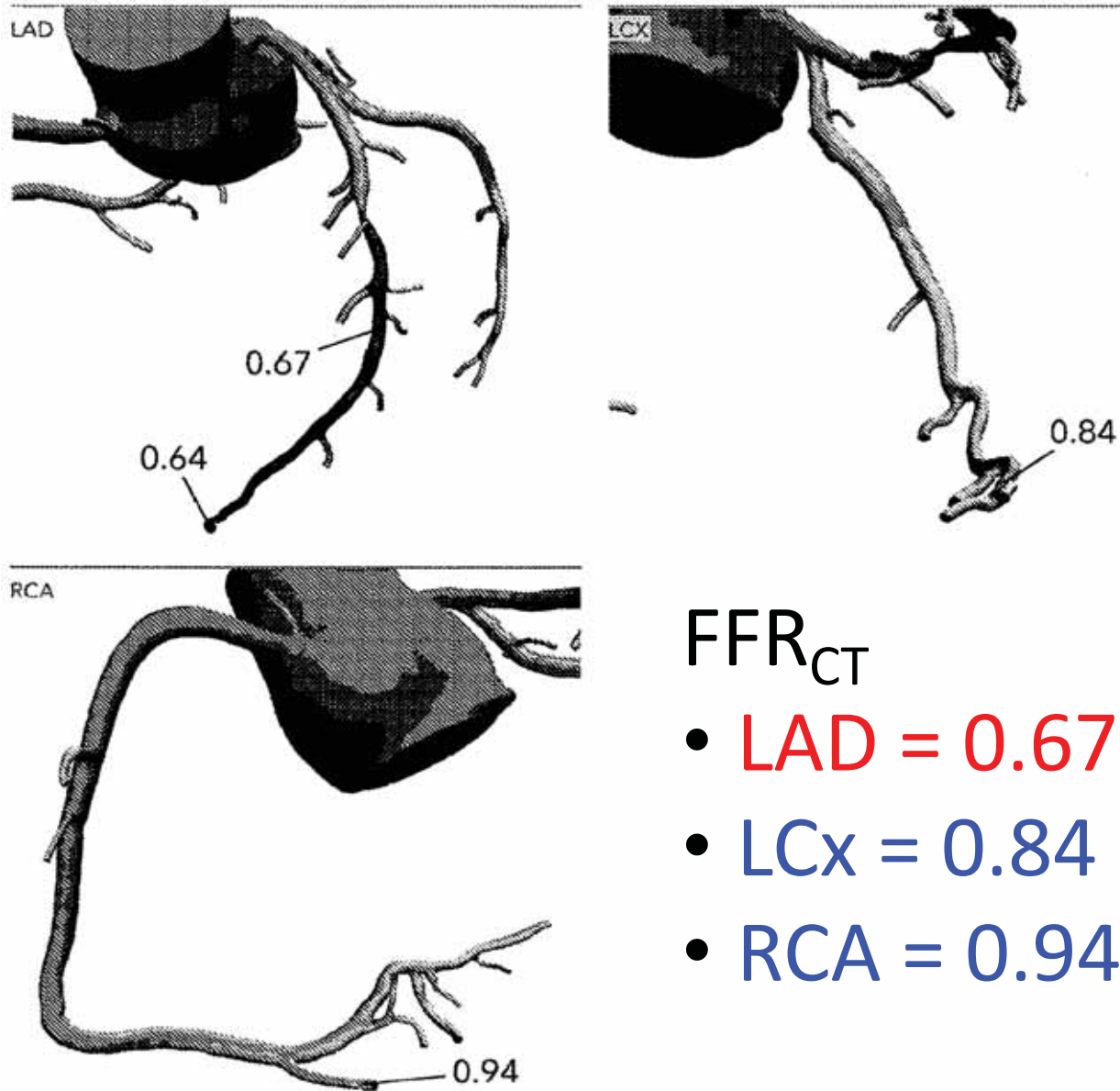
## Pros

- Easily reimbursed
- FFR<sub>CT</sub> performs better than CTA alone

## Cons

- More expensive than SPECT, Echo, and CMR
- DeFACTO low specificity (54%) and positive predictive value (67%).
- NXT trial confirmed the positive predictive value of only 65%.
- Lower accuracy in intermediate lesions and high false+ in terminal vessels.
- Contraindication for contrast or prep
- Difficult in diffuse disease and serial stenosis

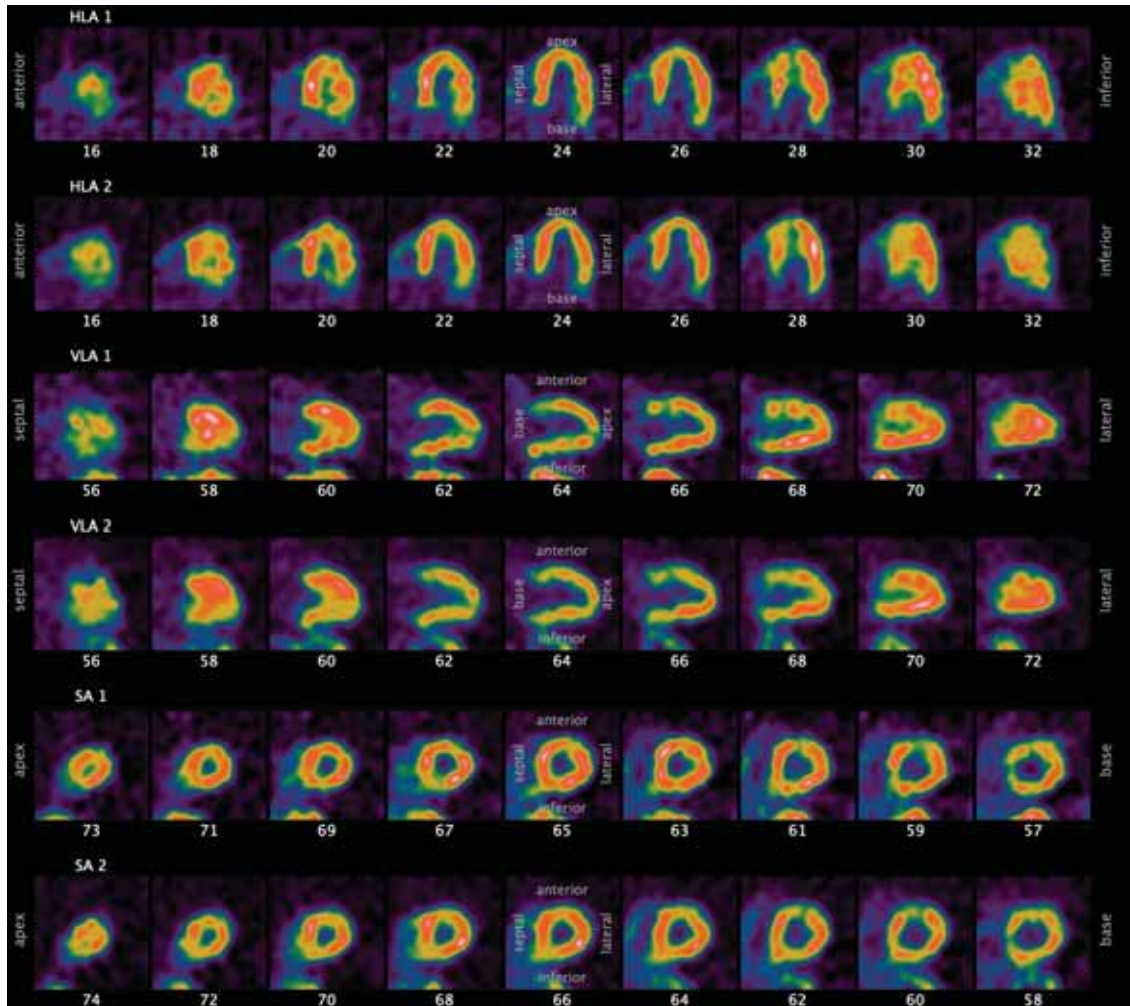
# FFR<sub>CT</sub> report



FFR<sub>CT</sub>

- **LAD = 0.67**
- **LCx = 0.84**
- **RCA = 0.94**

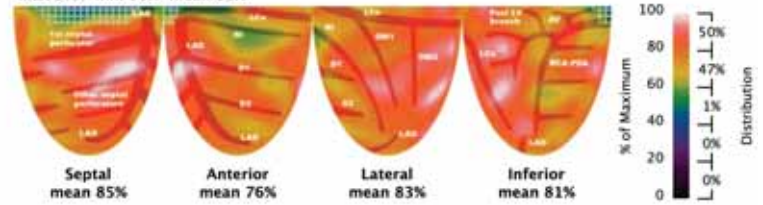
# PET images



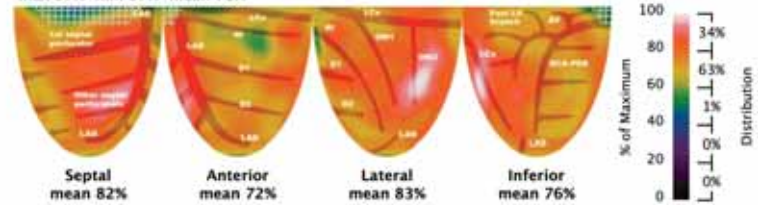
## Clinical Report

Name: Age: 59 Sex: Male ID: GE15507 Date: Aug 12 2019 Isotope: Rb  
 Rest Arterial=9.56 Stress Arterial=8.28

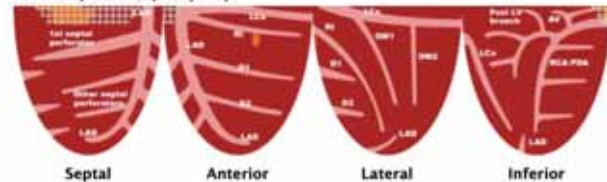
**Rest Uptake**  
 max 97% min 60% mean 81%



**Stress Uptake**  
 max 97% min 57% mean 78%

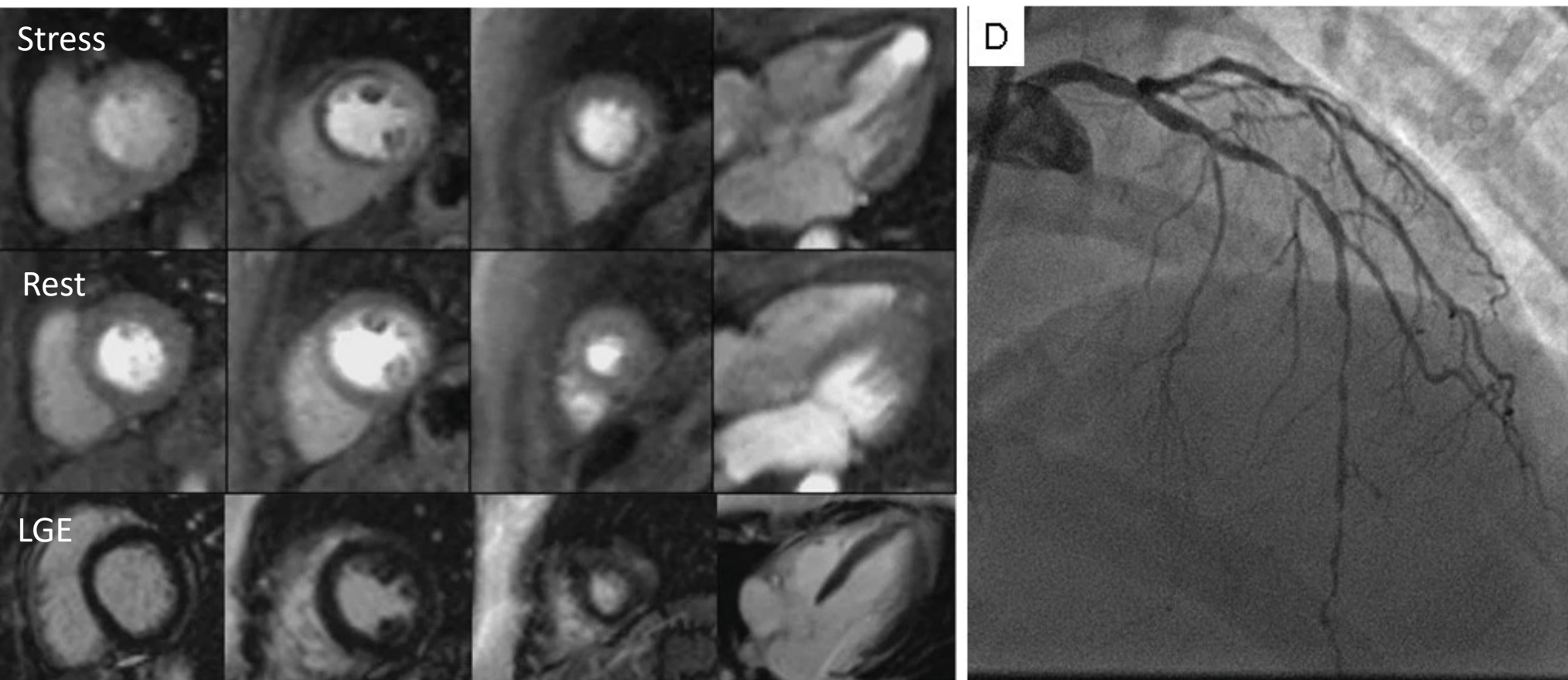


## Coronary Flow Capacity Map



- 100% Normal, from healthy young volunteers
- <1% Minimally reduced, risk factors only
- 0% Mildly reduced
- 0% Moderately reduced
- 0% Severely reduced, definite ischemia

# CMR-CFR (coronary flow reserve)



# CMR Perfusion and CFR

## **Pros**

Gold standard for anatomy, wall motion, and viability.

No ionizing radiation

Similar accuracy to ICA-FFR

## **Cons**

- Least available in US
- Poorly reimbursed
- Device contraindications
- Technically difficult
- Contrast contraindications
- Small number of slices
- Poor artery specific perfusion

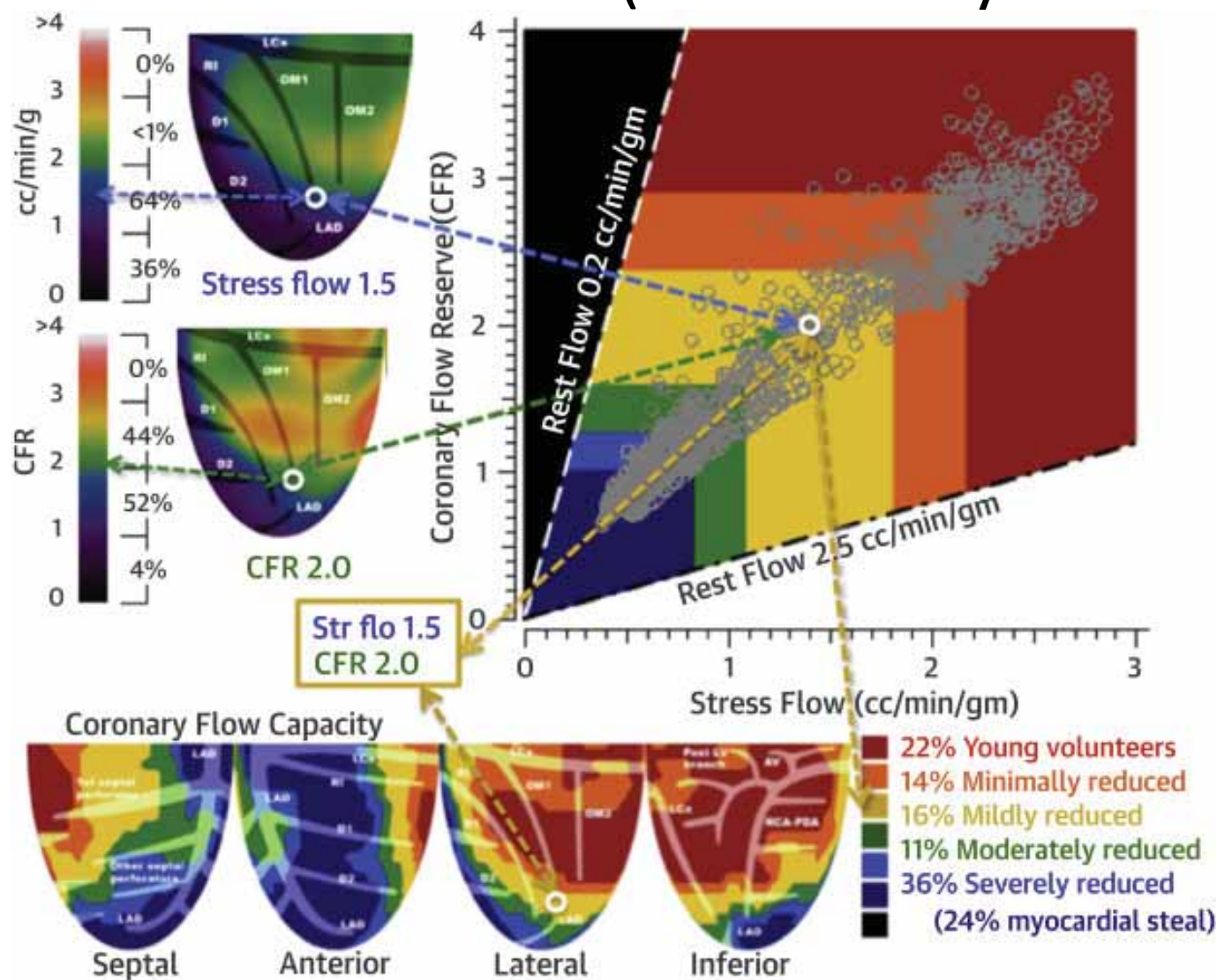
# Stress CMR = PET

## Functionally significant CAD

| Test        | Sensitivity (%),<br>(95% CI) | Specificity (%),<br>(95% CI) |
|-------------|------------------------------|------------------------------|
| ICA         | 68 (60–75)                   | 73 (55–86)                   |
| Stress ECG  | no data                      |                              |
| Stress echo |                              |                              |
| CCTA        | 93 (89–96)                   | 53 (37–68)                   |
| SPECT       | 73 (62–82)                   | 83 (71–90)                   |
| PET         | 89 (82–93)                   | 85 (81–88)                   |
| Stress CMR  | 89 (85–92)                   | 87 (83–91)                   |

- FFR as reference
- stable CAD
- 23 studies
- 4131 subjects

# ET MPI with CFR & CFC (coronary flow capacity)





# PET Myocardial Perfusion Imaging (MPI) Myocardial Blood Flow (MBF)

## Pros

- Artery specific perfusion
- Fast patient turnaround
- PET flow precision is the same as ICA FFR 10%
- Improves mortality when used to direct patient management.
- Accurate in high BMI

## Cons

- Expensive capital investment
- Technical expertise required
- Reimbursement challenges

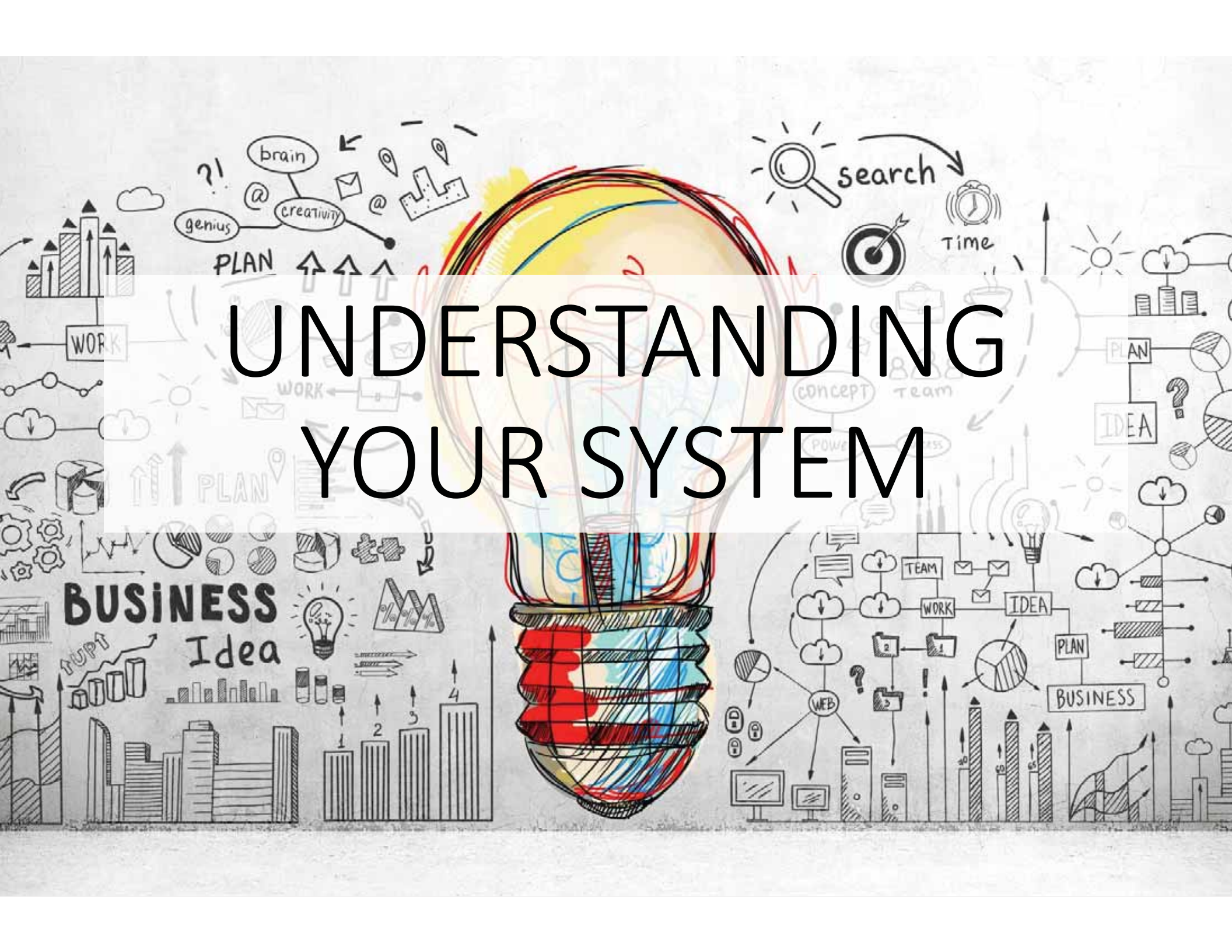
# WHICH TOOL WOULD YOU WANT?

|                   | <u>Accuracy</u><br><u>vs FFR*</u> | <u>Accuracy</u><br><u>vs PCI/CABG</u> | <u>Imaging</u><br><u>failure</u> |
|-------------------|-----------------------------------|---------------------------------------|----------------------------------|
| PET               | 86%                               |                                       | 2%                               |
| SPECT             | 68-76%                            | 73%                                   | 2%                               |
| FFR <sub>CT</sub> | 70%                               | 63%                                   | 13%                              |

patient on intention-to-diagnose basis in PACIFIC, successful scans vs FFR in ReASSESS

Diessen RS, *JACC*. 2019 Jan 22;73(2):161-173. (Table 4 and results text)

S = Sand NPR, *JACC Cardiovasc Imaging*. 2018 Nov;11(11):1640-1650. (Figure 4 and Table 7)



# UNDERSTANDING YOUR SYSTEM

**BUSINESS**  
Idea

BUSINESS

# PET Hardware

**2D**

Some have list-mode

Capable of imaging a bolus 45-50mCi of Rb-82 or 20mCi of N-13 ammonia.

Improved image quality over SPECT, but still has difficulty imaging patients with BMI > 30

**3D**

- Most have list-mode
- Capable of imaging a bolus of 30mCi or more of Rb-82.
- Improved image quality over 2D PET
- Diagnostic images up to table limit
  - 500-550 lbs

# Example beaker test with Rb-82/N-13

Rb-82 Decay in 500cc Beaker

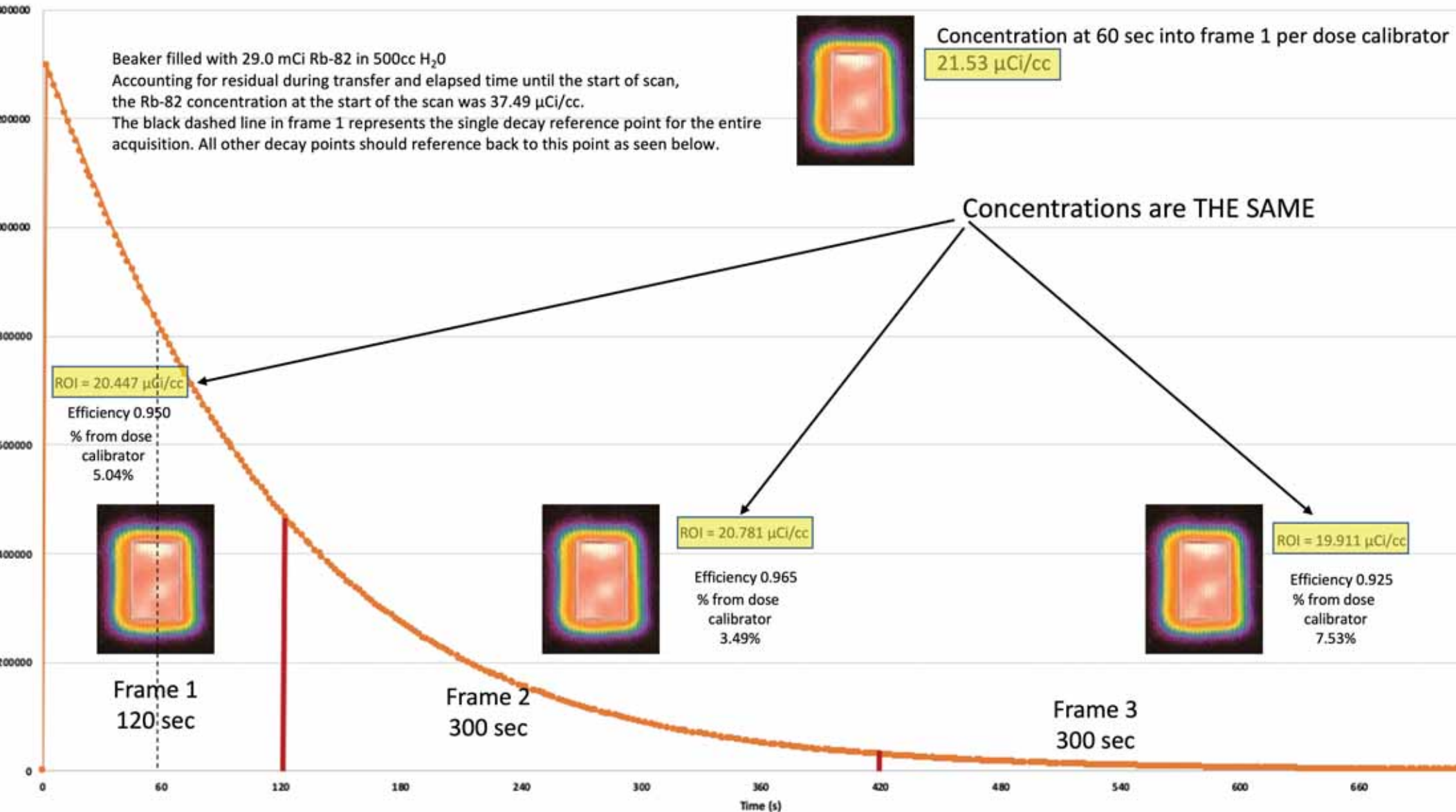


Image courtesy of Dr. Robert Bober (Ochsner, New Orleans)

# PV Phantom tests

- Partial Volume test (ACR or Bracco)
  - Fill with Rb-82/N-13 tracer solution
  - Measure the uCi/cc of a small ROI divided by the large ROI
  - Measures how well the system can resolve the thickness of the myocardium.



16mm

25mm

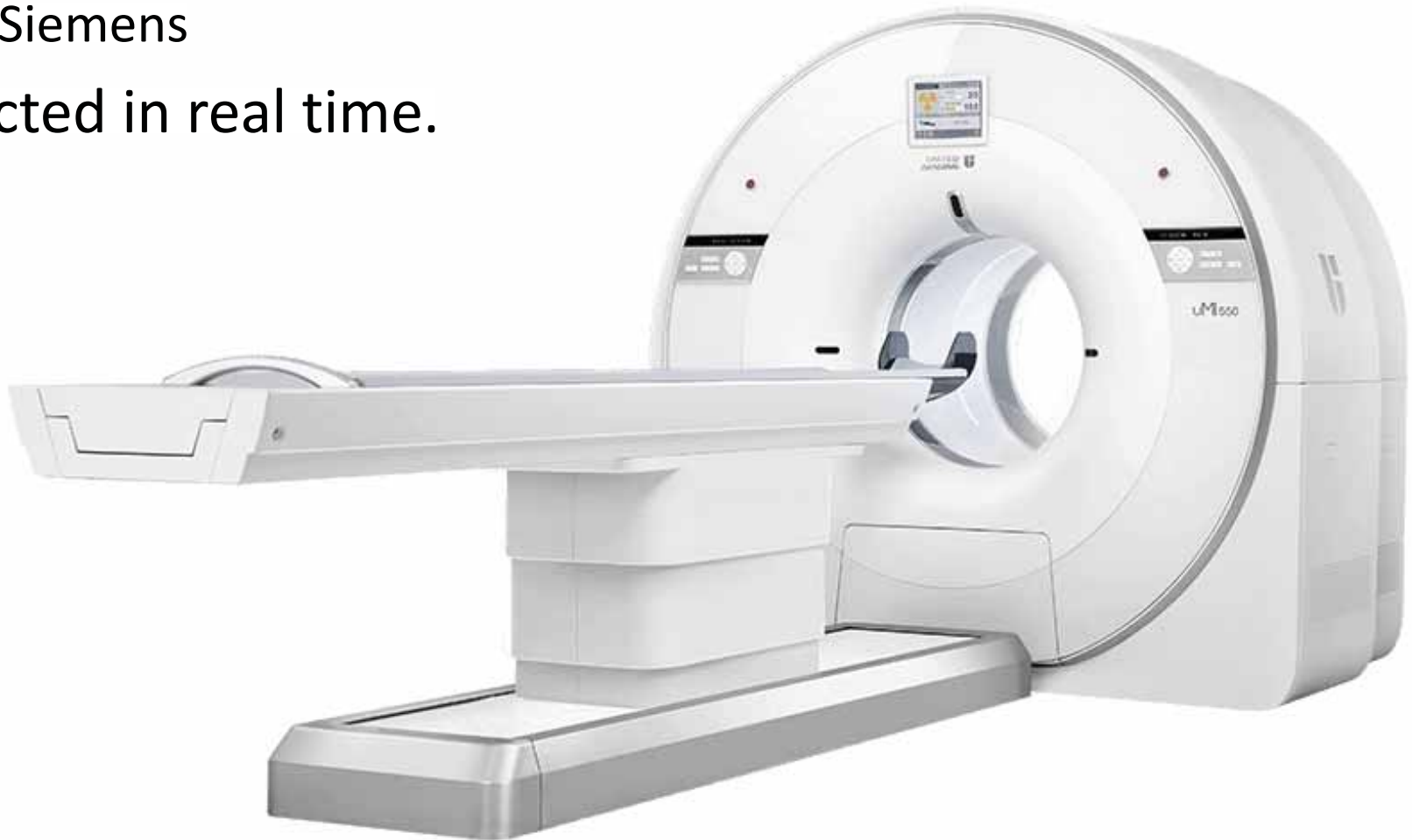
# List mode structure

PET corrections attached to the acquisition and recon protocol.

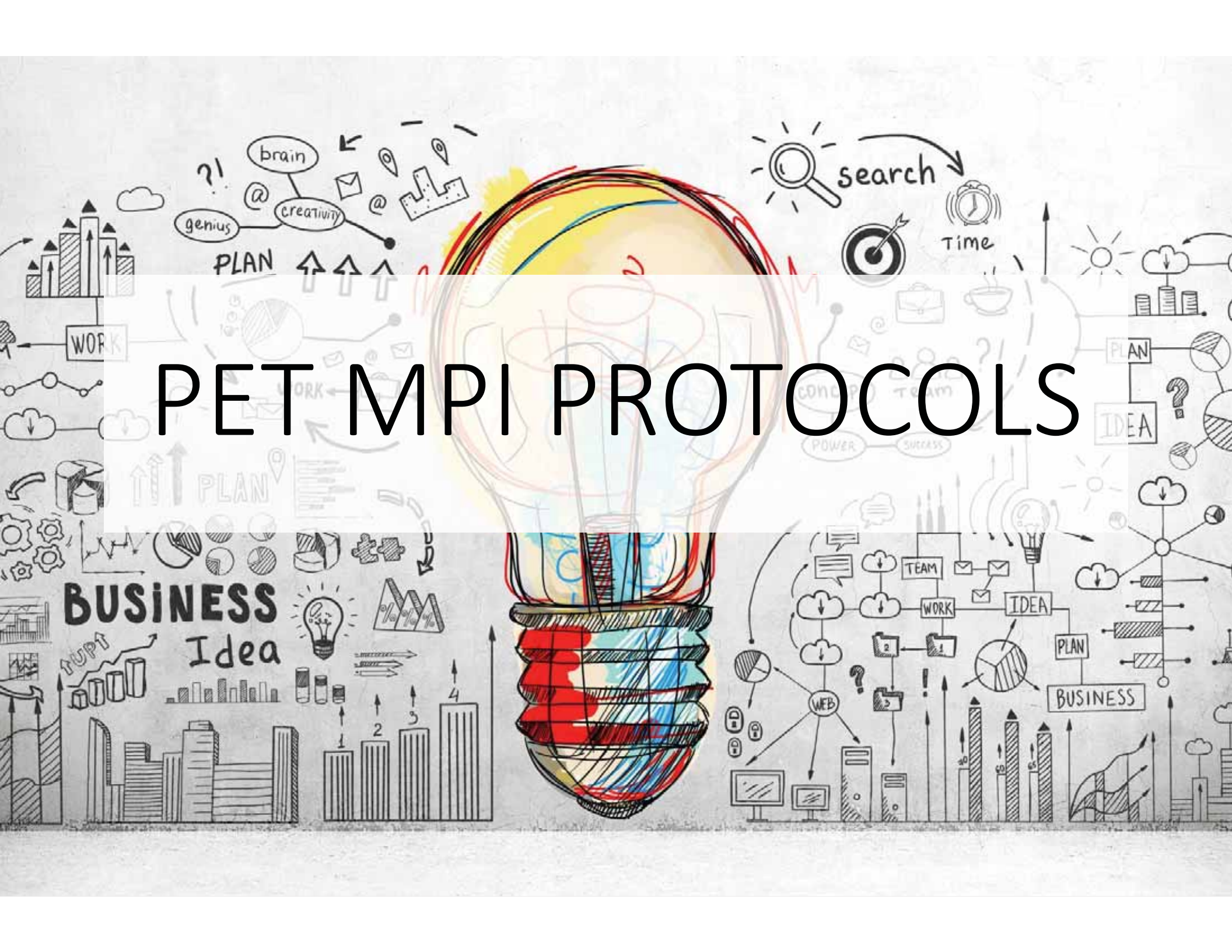
- GE and Siemens

PET corrected in real time.

- United



# PET MPI PROTOCOLS





# Tracers are not interchangeable

## Rb-82 (Bracco or RUBY-FILL)

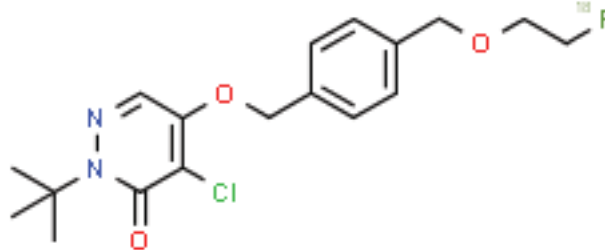
- Fastest
- Most difficult to correct
- 2 min flow, 5 min uptake

## N-13 Ammonia (cyclotron/IONETIX)

- Myocardial washout
- Extra-cardiac uptake
- 80 sec flow, 10 min uptake

## F-18 flurpiridaz (GE)

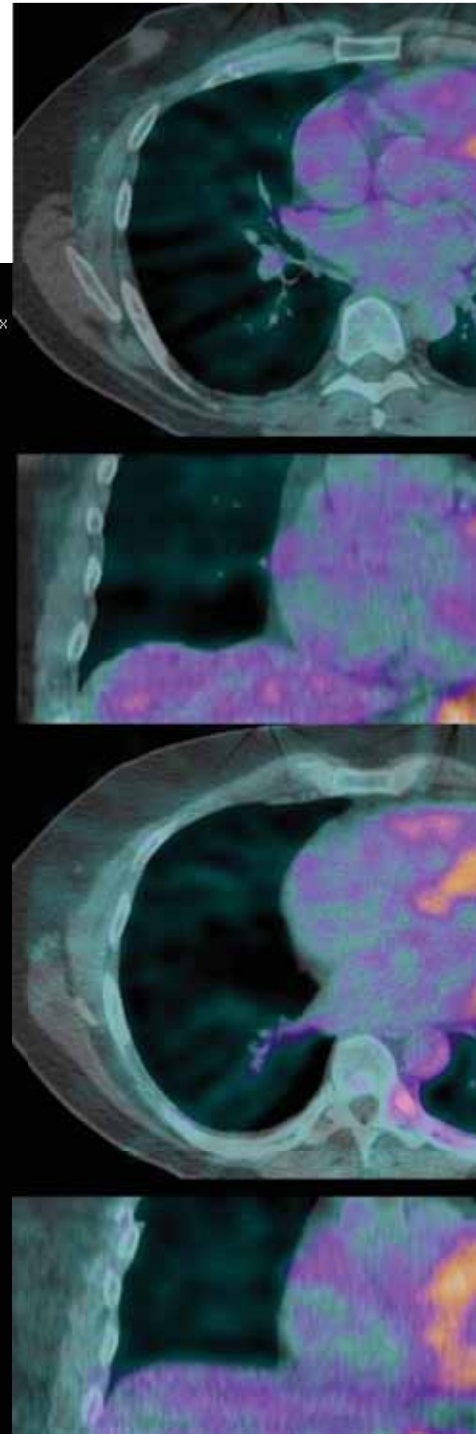
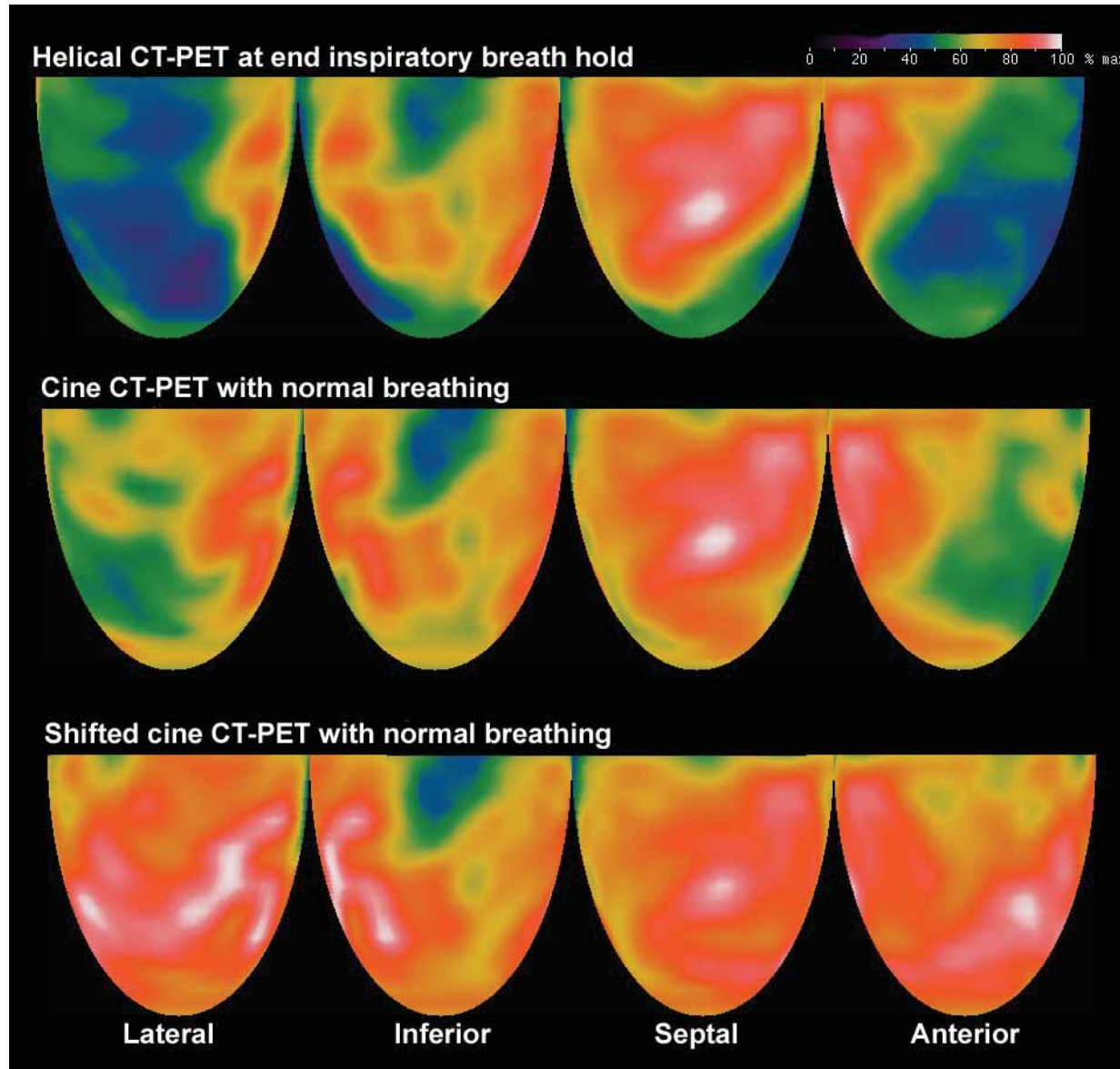
- Not yet approved by FDA
- MUST have subtraction
- Not validated for flow

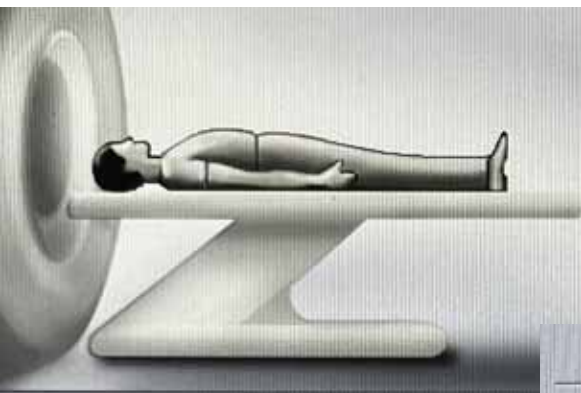


# Attenuation Correction

Gould et al. J Nuclear Medicine 2007

Helical CT  
Acquire 1st  
Best map  
United  
GE  
Helical  
Acquire  
2nd  
Best for  
anatomy





XY

AutoFilm Setup

Camera  
HPColorJet\_1

Patient Orientation  
Head First

Patient Position  
Supine

Copy Pt.Orient.

Auto Store

Auto Transfer gear

Dose Report Auto Transfer

Dose SR Report Auto Transfer

00:07:00

System Countrate (kcps)

0

Trues Rate: 0 kcps  
Randoms Rate: 0 kcps  
Total Prompts: 0 c

Scan Description Rest\_RAW  
Series Description c\_resL

Add Scan

Insert Scan

Delete Selected Scan

Enter the Desired Scan Phase Information

# of Phases 1 Total Scan Time 00:05:00

Prior Next

| Phase | Pre-Frame Delay | # of Frames | Time Per Frame | Time Per Phase |
|-------|-----------------|-------------|----------------|----------------|
| 1     | 00:00:00        | 5           | 00:01:00       | 00:05:00       |

OK Cancel

| Pages | Scan Type             | Start Location | End Location | Dir  |
|-------|-----------------------|----------------|--------------|------|
| 1-355 | Dynamic Rest Record   | \$0.000        | I195.300     | To F |
| 1-355 | Dynamic Stress Record | \$0.000        | I195.300     | To F |



| Dose     | Nuclide/Tracer                     |
|----------|------------------------------------|
| 0.00 mCi | <sup>82</sup> Rb Rubidium chloride |
| 0.00 mCi | <sup>82</sup> Rb Rubidium chloride |

Cancel

Prior Series

Next Series

Create New Series

Repeat Series

Delete Series

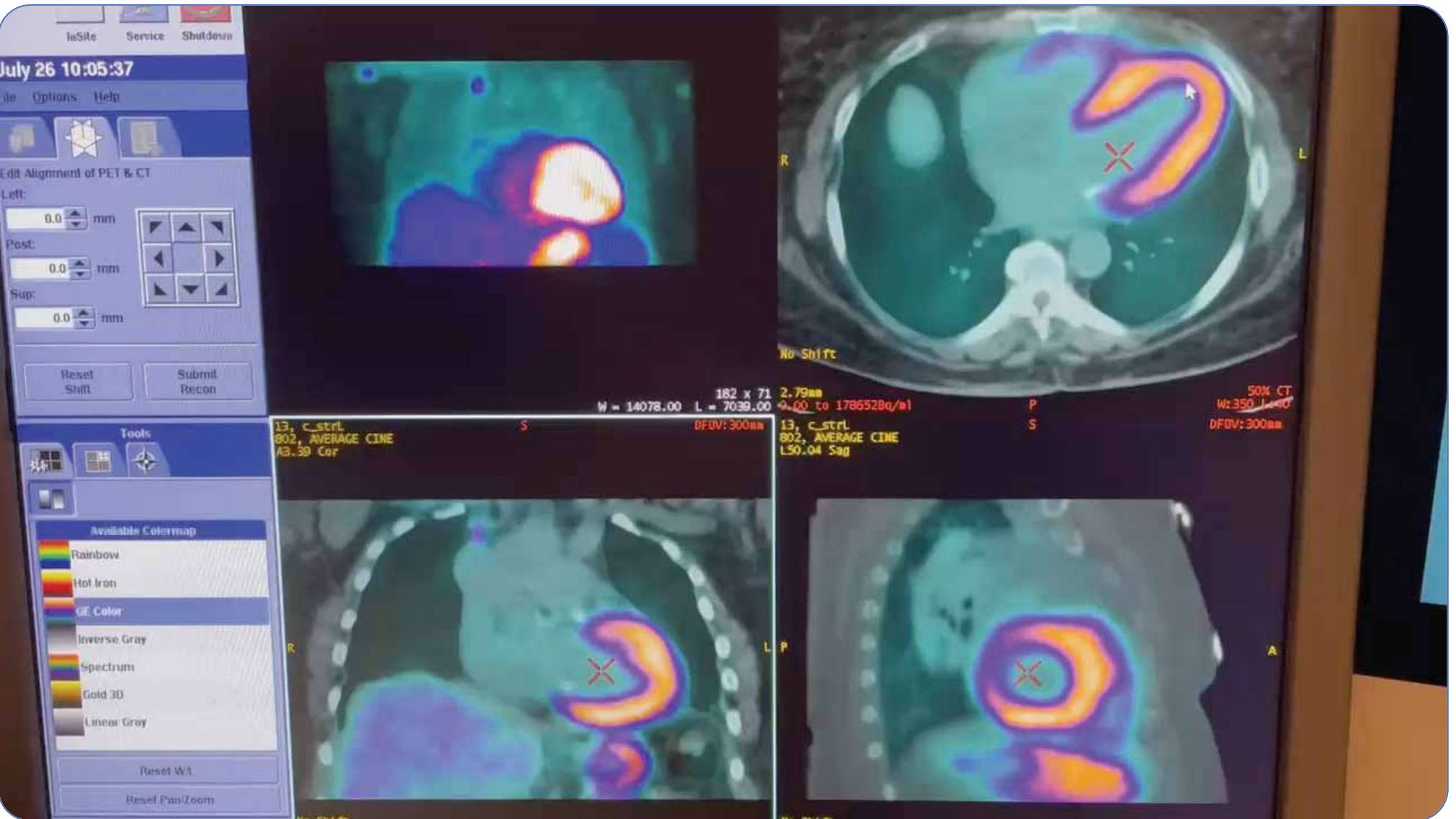
CT

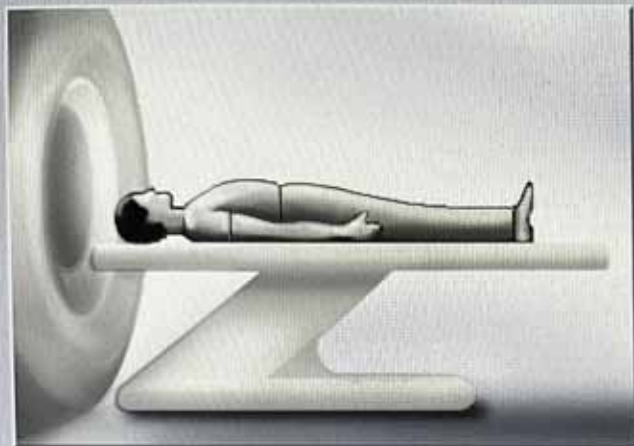
PET

Auto Scan

Accept

# GE Discovery MI





Anatomical Reference **ViP - Replay** Filming

SN

AutoFilm Setup

Camera  
**HPColorJet 2**

Patient Orientation  
Head First

Enter the Desired Scan Phase Information

|             |                 |   |      |
|-------------|-----------------|---|------|
| # of Phases | Total Scan Time | <input type="button" value="▲"/> <input type="button" value="▼"/> |      |
| 1           | 00:05:00        | Prior   | Next |

| Phase | Pre-Frame Delay | # of Frames | Time Per Frame | Time Per Phase |
|-------|-----------------|-------------|----------------|----------------|
| 1     | 00:00:00        | 10          | 00:00:30       | 00:05:00       |

OK Cancel

Scan Description: Rest Static Emission  
Series Description: c\_resL

Add Scan Insert Scan Delete Selected Scan

| Images | Scan Type           | Start Location | End Location | Scan Direction |
|--------|---------------------|----------------|--------------|----------------|
| 1-71   | Dynamic Rest Record | I124.555       | I319.855     | Toward Feet    |
| 1-710  | Dynamic Rest Replay | I124.555       | I319.855     | Toward Feet    |
| 1-1704 | Dynamic Rest Replay | I124.555       | I319.855     | Toward Feet    |
| 1-568  | Gated-C Rest Replay | I124.555       | I319.855     | Toward Feet    |

PET Scan Status  
Scan Time Remaining  
**00:07:00**

System Countrate (kcps)

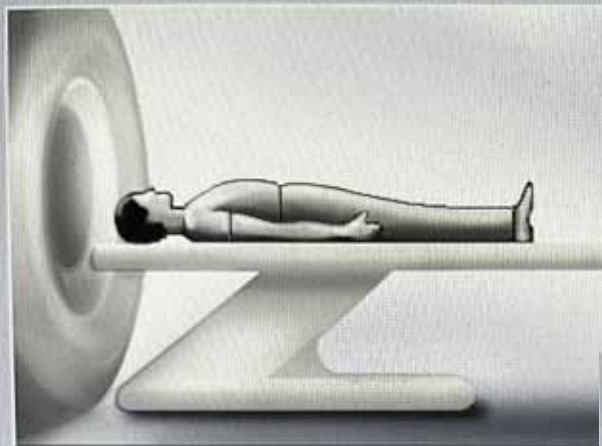
**0**

Trues Rate: 0 kcps  
Randoms Rate: 0 kcps  
Total Prompts: 0 c



| AutoCnt Audible Scan | Dose     | Nuclide/Tracer         |
|----------------------|----------|------------------------|
| N / Y                | 0.00 mCi | 82Rb Rubidium chloride |
| Y / N                | 0.00 mCi | 82Rb Rubidium chloride |
| Y / N                | 0.00 mCi | 82Rb Rubidium chloride |
| Y / N                | 0.00 mCi | 82Rb Rubidium chloride |

Cancel Prior Series Next Series Create New Series Repeat Series Delete Series CT PET Auto Scan Accept



Anatomical Reference **ViP - Replay** Filming

SN

AutoFilm Setup

Camera  
HPColorJet 2

Patient Orientation  
Head First

Patient Position  
Supine

Copy

Auto

Auto Transfer

Dose Report Auto

Dose SR Report Auto Transfer

Scan Description Rest Static Emission

Series Description c\_resL

PET Scan Status

Scan Time Remaining

00:07:00

System Countrate (kcps)

0

Trues Rate: 0 kcps

Randoms Rate: 0 kcps

Total Prompts: 0 c

Enter the Desired Scan Phase Information

# of Phases: 1 Total Scan Time: 00:02:00

Phase 1 Pre-Frame Delay: 00:00:00 # of Frames: 24 Time Per Frame: 00:00:05 Time Per Phase: 00:02:00

OK Cancel

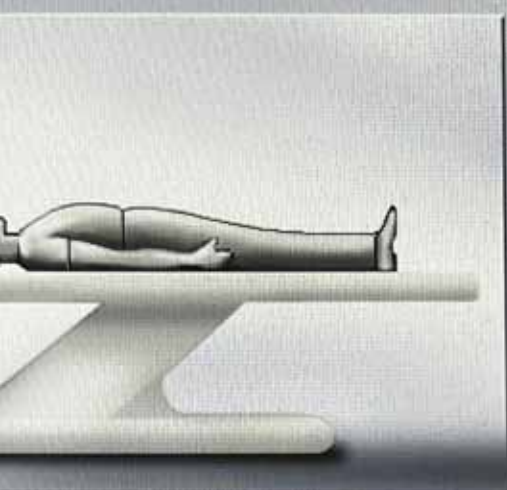
Add Scan Insert Scan Delete Selected Scan

| Images | Scan Type           | Start Location | End Location | Scan Direction |
|--------|---------------------|----------------|--------------|----------------|
| 1-71   | Dynamic Rest Record | I124.555       | I319.855     | Toward Feet    |
| 1-710  | Dynamic Rest Replay | I124.555       | I319.855     | Toward Feet    |
| 1-1704 | Dynamic Rest Replay | I124.555       | I319.855     | Toward Feet    |
| 1-568  | Gated-C Rest Replay | I124.555       | I319.855     | Toward Feet    |

Icons for: Head, Radiation, Heart/Kidneys, and a camera icon.

| AutoCnt / Audible Scan | Dose     | Nuclide/Tracer         |
|------------------------|----------|------------------------|
| N / Y                  | 0.00 mCi | 82Rb Rubidium chloride |
| Y / N                  | 0.00 mCi | 82Rb Rubidium chloride |
| Y / N                  | 0.00 mCi | 82Rb Rubidium chloride |
| Y / N                  | 0.00 mCi | 82Rb Rubidium chloride |

Cancel Prior Series Next Series Create New Series Repeat Series Delete Series CT PET Auto Scan Accept



Anatomical Reference

SN

Patient Orientation  
Head First

Patient Position

VIP - Replay  
Filming

AutoFilm  
Setup

Camera  
HPColorJet\_2

PET Scan Status  
Scan Time Remaining

00:07:00

System Countrate (kcps)

0

Trues Rate: 0 kcps  
Randoms Rate: 0 kcps  
Total Prompts: 0 c

Enter the Desired Scan Phase Information

# of Phases: 3      Total Scan Time: 00:07:00

Prior      Next

| Phase | Pre-Frame Delay | # of Frames | Time Per Frame | Time Per Phase |
|-------|-----------------|-------------|----------------|----------------|
| 1     | 00:00:00        | 24          | 00:00:05       | 00:02:00       |
| 2     | 00:00:00        | 28          | 00:00:05       | 00:02:20       |
| 3     | 00:00:00        | 16          | 00:00:10       | 00:02:40       |

OK      Cancel

Description: Rest Static Emission

Description: c\_resL

Insert Scan      Delete Selected Scan

Scan type      Start Location      End Location      Scan Direction

| Scan type            | Start Location | End Location | Scan Direction |
|----------------------|----------------|--------------|----------------|
| Dynamic Rest record  | I124.555       | I319.855     | Toward Feet    |
| Dynamic Rest replay  | I124.555       | I319.855     | Toward Feet    |
| Static-C Rest replay | I124.555       | I319.855     | Toward Feet    |

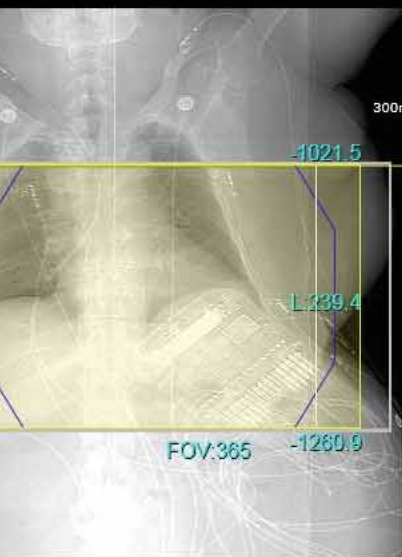
AutoCnt Audible Scan

| Dose     | Nuclide/Tracer         |
|----------|------------------------|
| 0.00 mCi | 82Rb Rubidium chloride |
| 0.00 mCi | 82Rb Rubidium chloride |
| 0.00 mCi | 82Rb Rubidium chloride |

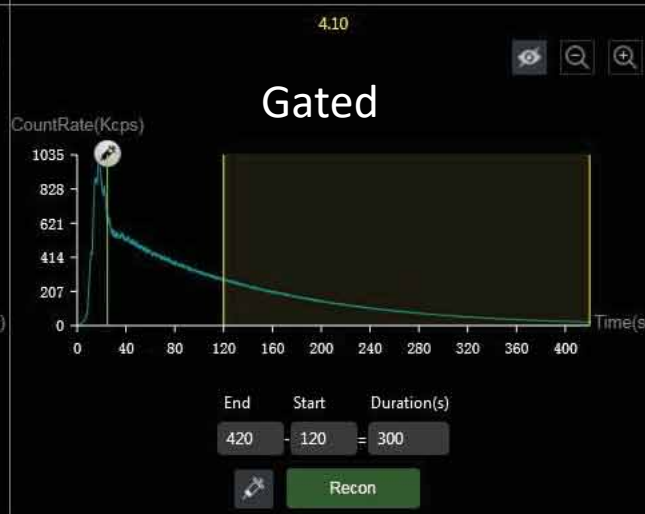
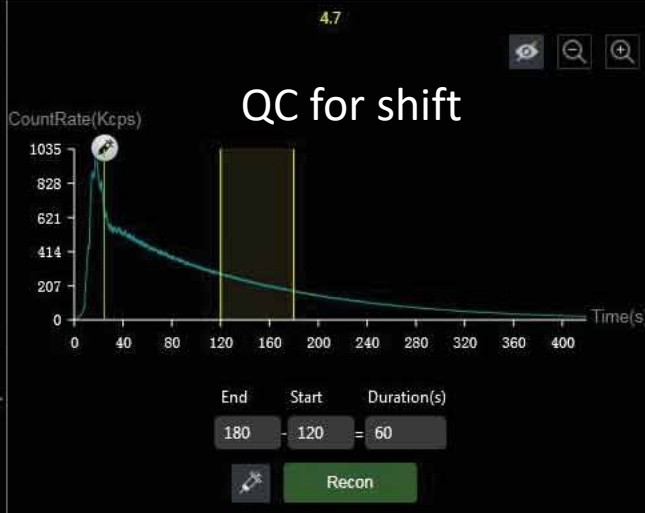
Prior Series      Next Series      Create New Series      Repeat Series      Delete Series      CT      PET      Auto Scan      Accept

H

Weatherhead PET Imaging  
CT  
UIH uMI 550  
OP: United



Zoom: 0.91  
727\*768  
WW: 200 WVL: -900



- 4.2 cs\_strL
- 4.3 cs\_strE
- 4.4 cgs\_strL
- 4.5 cs\_strL
- 4.6 cs\_strE
- 4.7 QC\_PET STRES
- 4.8 cs\_strL
- 4.9 cs\_strE
- 4.10 cgs\_strL
- 5 CARDIAC HELICAL

Recon Parameters

Algorithm: OSEM

FOV: 365mm

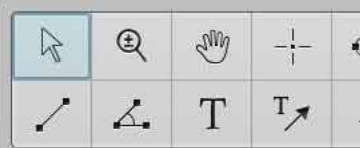
X-Center: 40.00mm

Y-Center: 0.00mm

TOF

PSF

CT Contra



| Count Rate (cps) | ENV          |
|------------------|--------------|
| Prompts 1.1 k    | TEMP 24.4 °C |
| Randoms 1.1 k    |              |
| Singles 790.5 k  |              |

Bed Position

Horizontal: [input] [dropdown]

Vertical: [input] [Save]

Base:  CT  PET

|            | A  | B  |
|------------|----|----|
| Horizontal | -- | -- |
| Vertical   | -- | -- |
| Base       | -- | -- |

Offline Recon

Register

Offline Recon

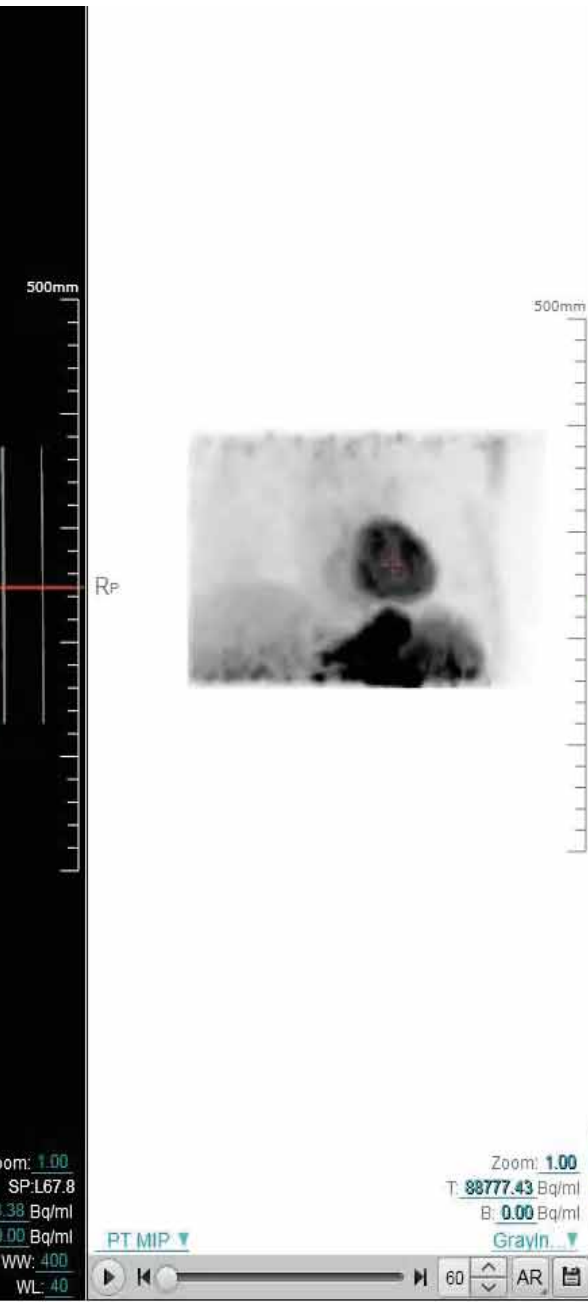
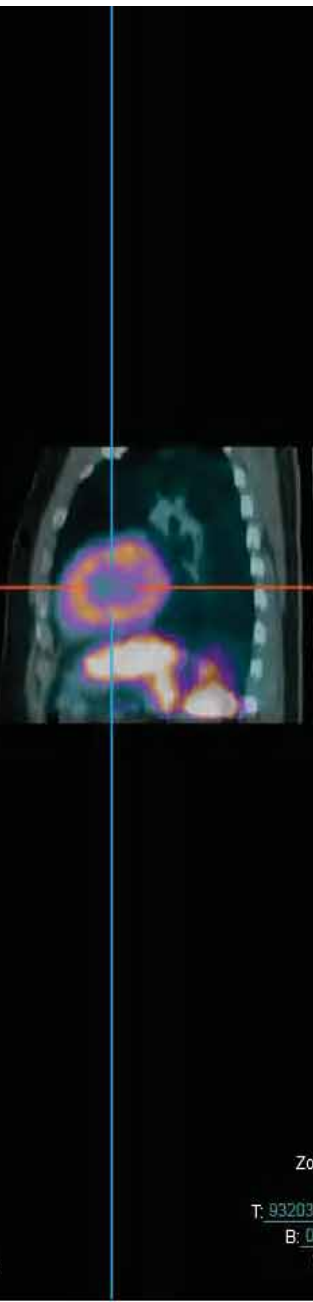
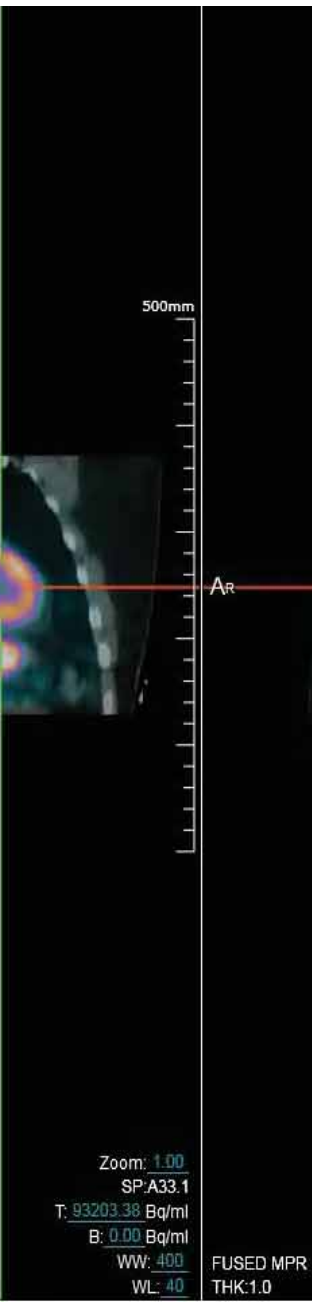
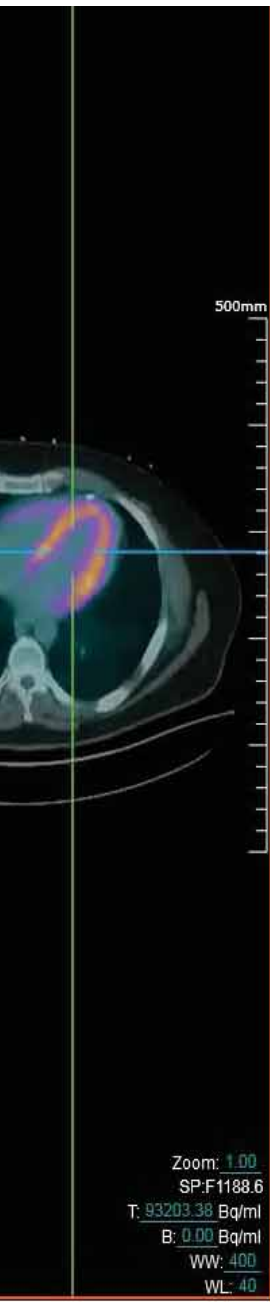
Review

Filming

Report







QC\_PET REST  
 301

- cs\_resL  
302
- cs\_resE  
303
- cgs\_resL  
304
- un\_resL

Analysis

2D 3D

Display

Visibility

Regist

PT MIP

60 AR

# Recon Parameters

Description:

ACCT:

Algorithm:

Iterations:

Subsets:

TOF  PSF

Recon Range (bed)

Begin/End:

Recon Range

Base on:

From/To:  /

## Correction

Attenuation Correction

Scatter Correction

Alignment Matrix

Decay Correction

Randoms Correction

Normalization

CT Contrast Artifact

HU:

Image Size:

Thickness:

Smoothing:

FWHM:

HYPER DLR

Head Model:

Match CT SL Loc.:

FOV:

X-Center:

Y-Center:

## Distribution

Auto-Archive

Dynamic Recon

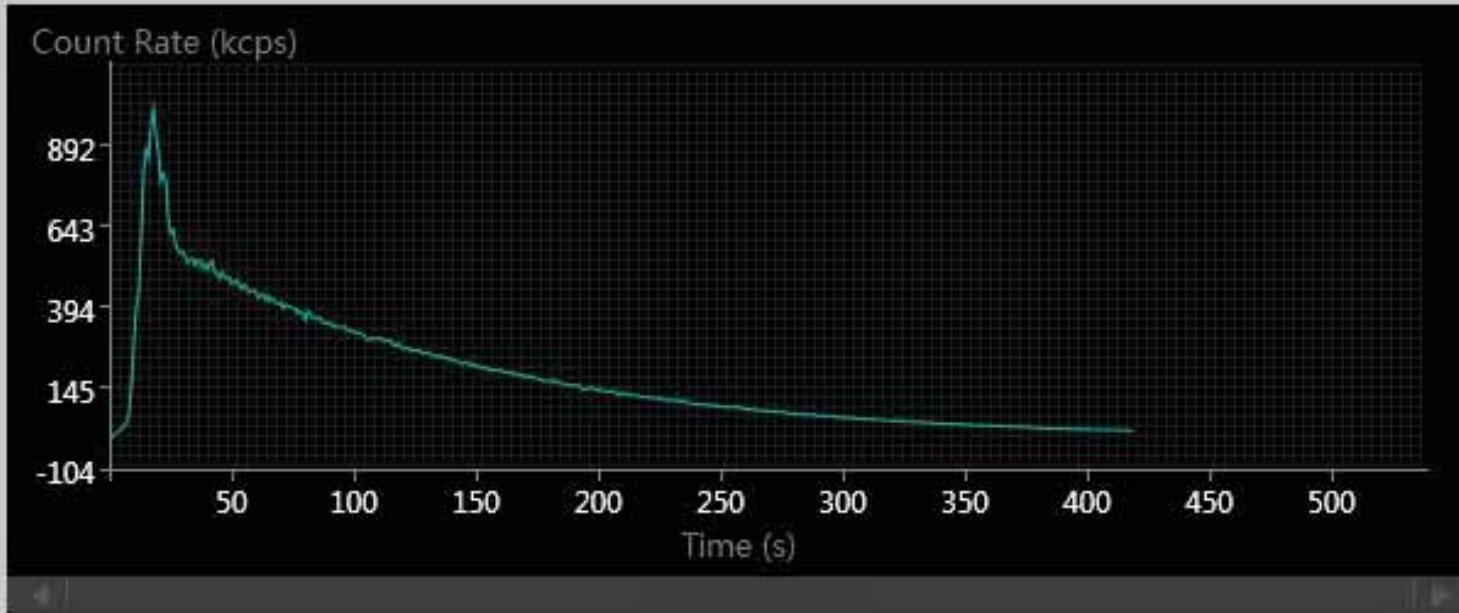
Gating

Gating Report

Self Gating

HYPER Focus

# Dynamic Recon



| No. | Frame Duration | Include in recon                    |
|-----|----------------|-------------------------------------|
| 1   | 5              | <input checked="" type="checkbox"/> |
| 1   | 5              | <input checked="" type="checkbox"/> |
| 1   | 5              | <input checked="" type="checkbox"/> |
| 1   | 5              | <input checked="" type="checkbox"/> |
| 1   | 5              | <input checked="" type="checkbox"/> |
| 1   | 5              | <input checked="" type="checkbox"/> |

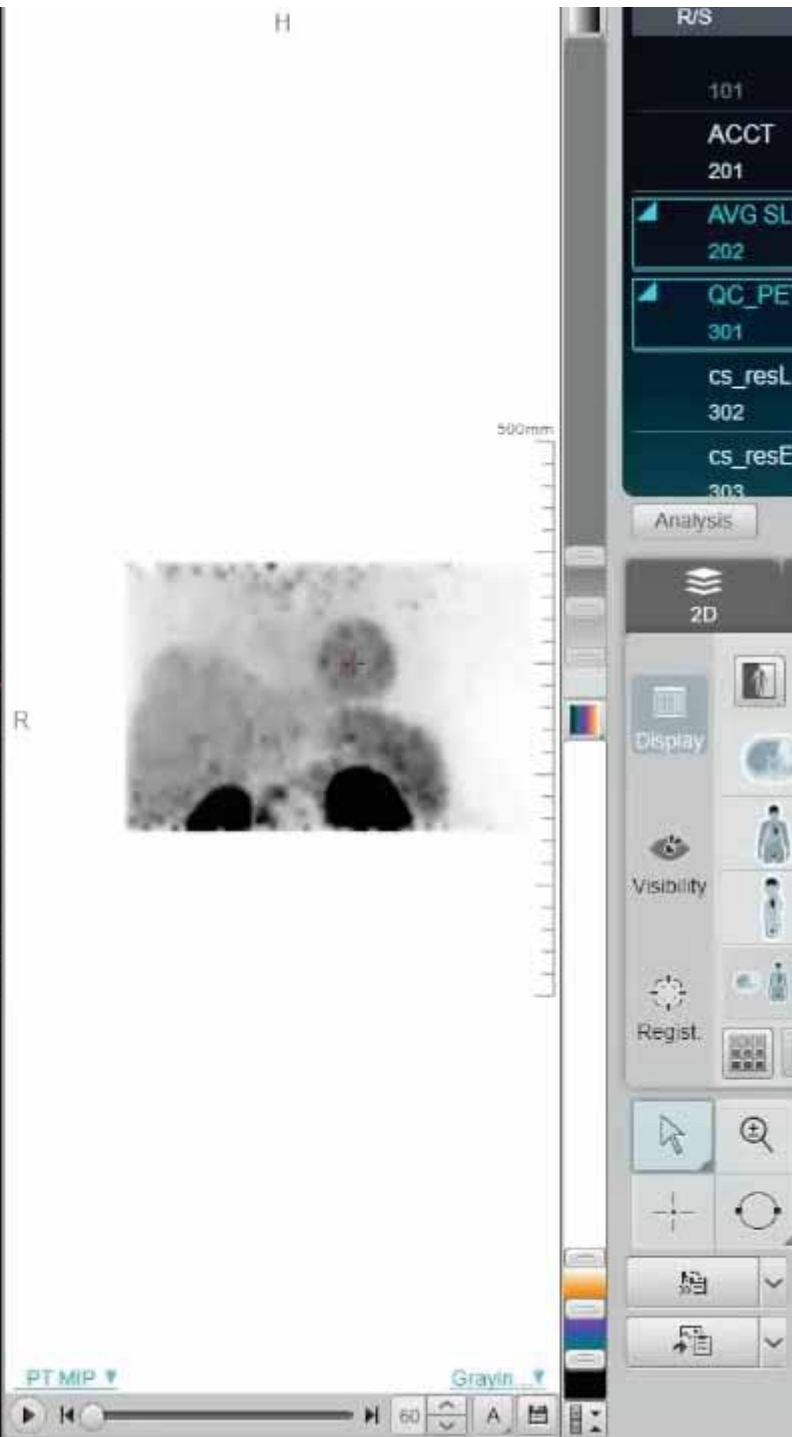
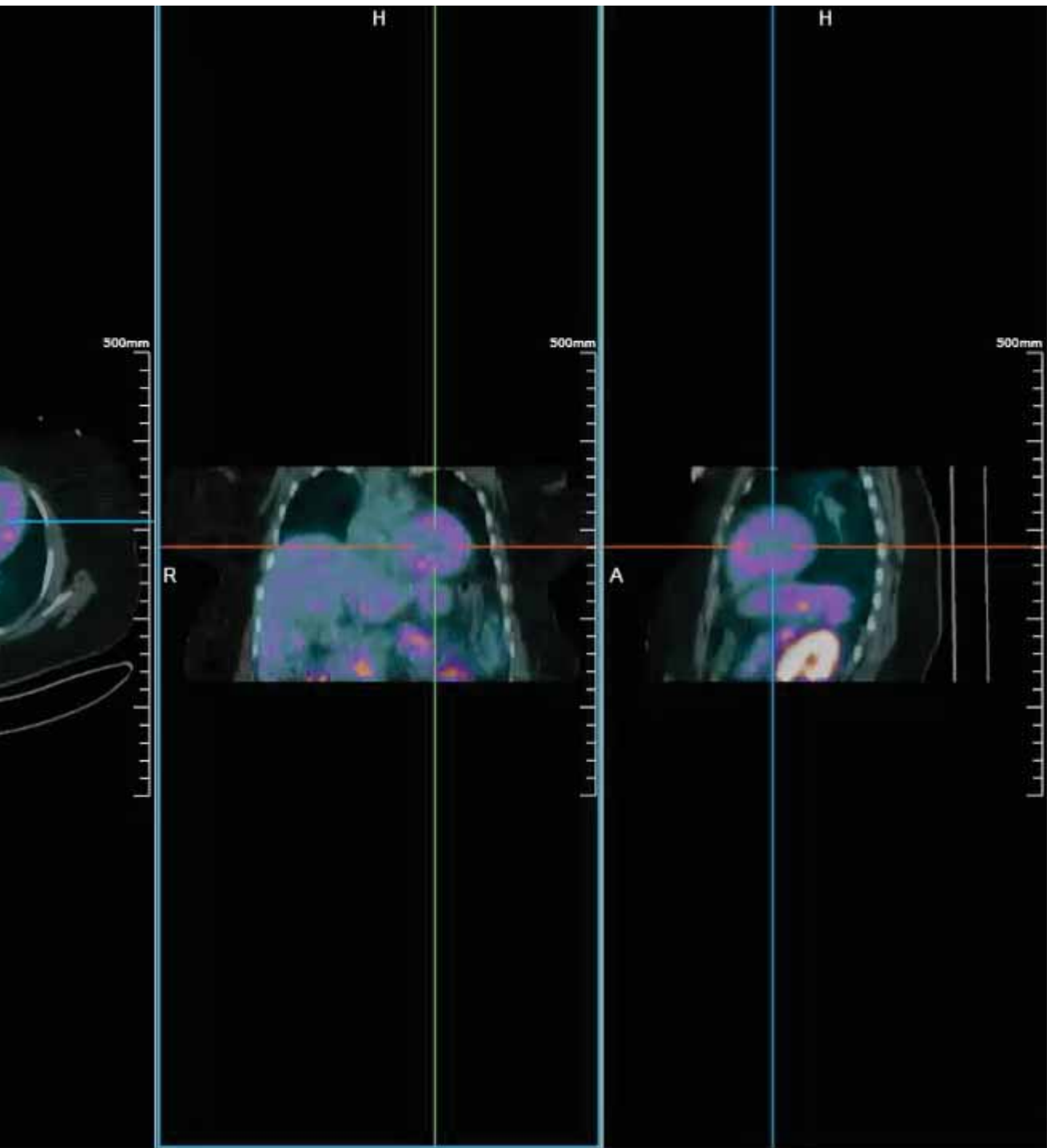
Total ACQ

420

Sec ▼



OK



R/S

101

ACCT

201

AVG SLIC

202

QC\_PET

301

cs\_resL

302

cs\_resE

303

Analysis

2D

Display

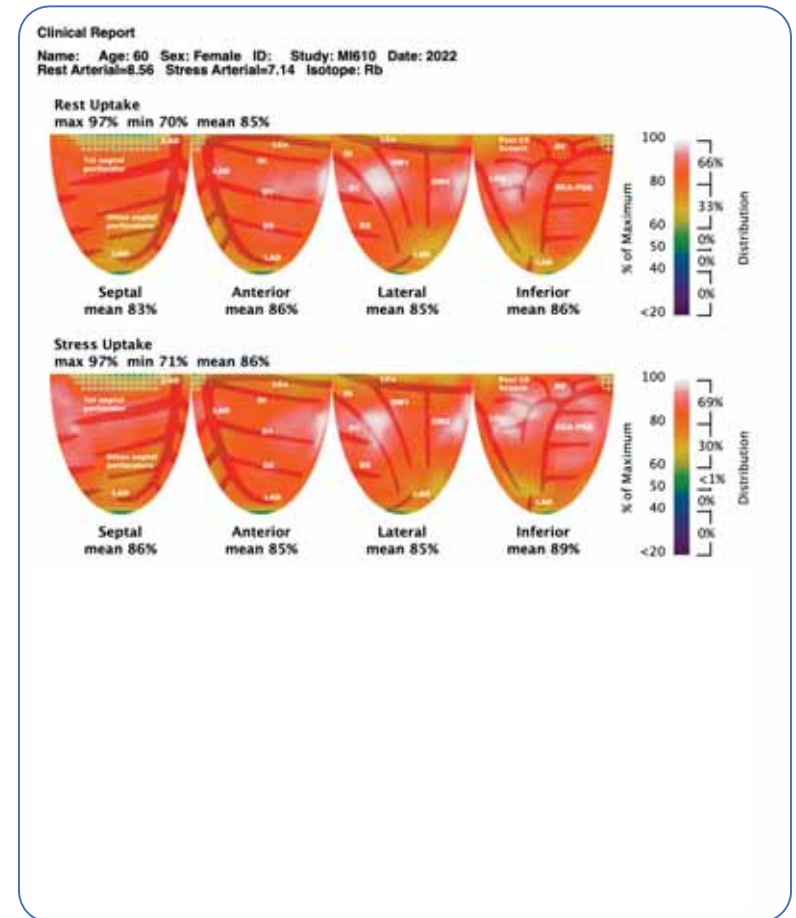
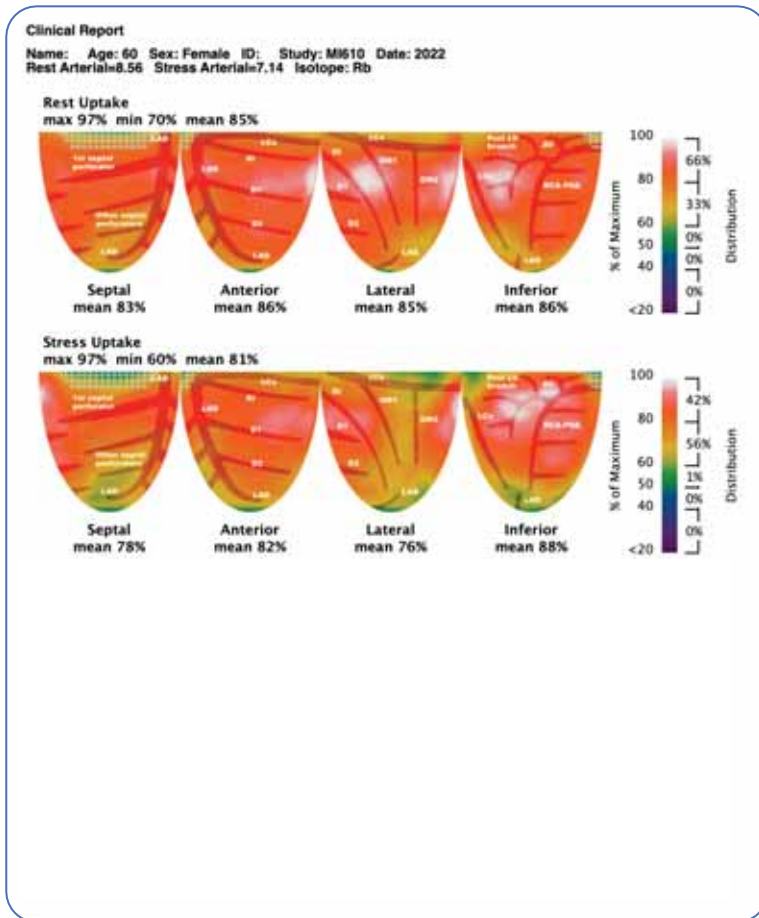
Visibility

Regist.

PTMP

Grayin

# Unshifted stress image dramatically effects the flow.

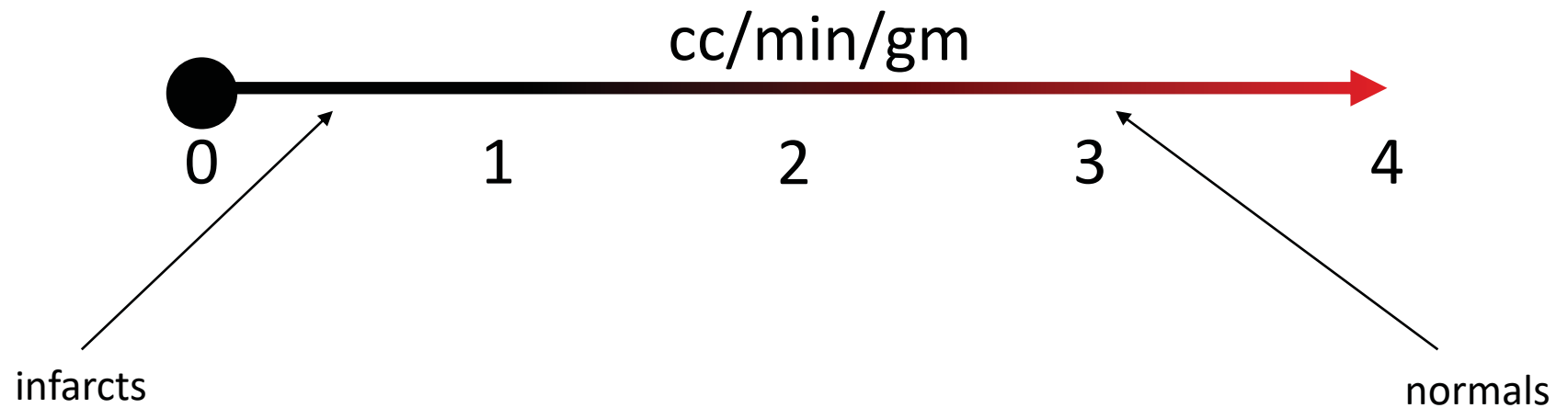


# Philosophy = flow package

| Feature            | Description  | Citation                        | N    |
|--------------------|--|---------------------------------|------|
| Animal validation  | Comparison of PET against flow meter or microspheres                   | Yoshida (1996) <sup>6</sup>     | 24   |
| Flow spectrum      |  |                                 |      |
| Normal volunteers  | Rest and stress flow in young, healthy people (not patients)           | Sdringola (2011) <sup>7</sup>   | 125  |
| Ischemia           | Stress-induced perfusion defect with severe angina or ECG changes      | Johnson (2011) <sup>8</sup>     | 1674 |
| Stress agents      | Interplay of vasodilator pharmacodynamics and radiotracer timing       |                                 |      |
| Dipyridamole       |  | Kitkungvan (2017) <sup>9</sup>  | 120  |
| Adenosine          |  | Kitkungvan (2017) <sup>10</sup> | 127  |
| Regadenoson        |  | Johnson (2015) <sup>11</sup>    | 176  |
| Test/retest        | Separate biologic variation from stochastic effects of imaging         | Kitkungvan (2017) <sup>9</sup>  | 708  |
| Arterial input     | Scan-specific customization of arterial input to avoid underestimation | Vasquez (2013) <sup>12</sup>    | 288  |
| Clinical outcomes  | Size/severity association with outcomes as modified by treatment       | Gould (2021) <sup>14</sup>      | 5274 |
| Cost effectiveness | Cost simulation ideally based on data from a randomized trial          | Delgado (2014) <sup>15</sup>    | N/A  |
| Randomized trial   | Impact of PET-guided management on clinical outcomes                   | Kitkungvan (2021) <sup>16</sup> | 1028 |

Johnson NP and Gould KL. "How shall we judge a PET flow model?" *J Nucl Cardiol.* 2021 Sep 24. doi: 10.1007/s12350-021-02805-5. (Table 1)

# Spectrum of perfusion

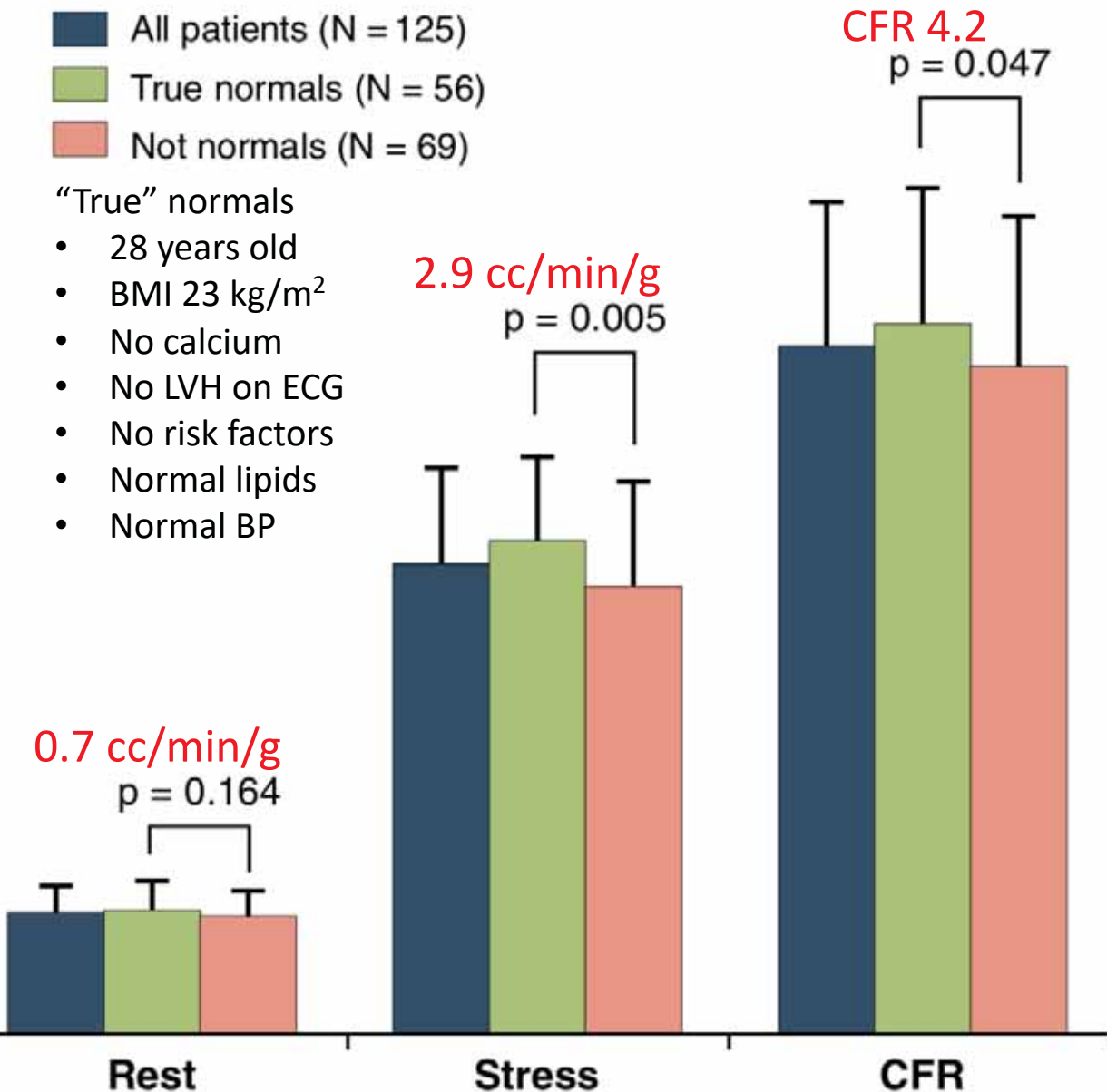


# Are you normal?

- All patients (N = 125)
- True normals (N = 56)
- Not normals (N = 69)

“True” normals

- 28 years old
- BMI 23 kg/m<sup>2</sup>
- No calcium
- No LVH on ECG
- No risk factors
- Normal lipids
- Normal BP

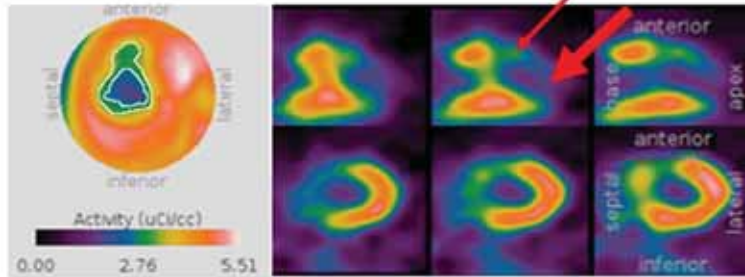
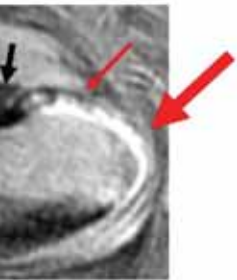


| Isotope | Sample size | Author              | Citation                   | Rest flow<br>(cc/min/g) | Stress flow<br>(cc/min/g) |
|---------|-------------|---------------------|----------------------------|-------------------------|---------------------------|
| F-18    | 7           | Packard             | JNM 2014;55:1438           | 0.73 ± 0.13             | 2.9                       |
| N-13    | 20          | Chan                | JACC 1992;20:979           | 1.10 ± 0.20             | 4.2                       |
| N-13    | 18          | Czernin             | Circulation 1993;88:62     | 0.76 ± 0.17             | 3.5                       |
| N-13    | 11          | Dayankli            | Circulation 1994;90:808    | 0.66 ± 0.09             | 2.9                       |
| N-13    | 5           | Beanlands           | JACC 1995;26:1465          | 0.62 ± 0.09             | 2.9                       |
| N-13    | 6           | Sawada              | JNC 1995;2:413             | 0.68 ± 0.12             | 2.9                       |
| N-13    | 11          | Czernin             | JNM 1995;36:575            |                         | 2.9                       |
| N-13    | 19          | de Jong             | JNM 1995;36:581            | 0.96 ± 0.02             |                           |
| N-13    | 8           | DeGrado             | JNC 1996;3:494             | 0.70 ± 0.14             | 2.9                       |
| N-13    | 10          | Muzik               | JACC 1996;28:757           | 0.74 ± 0.15             | 3.5                       |
| N-13    | 14          | Yokoyama            | JNM 1996;37:1937           | 0.70 ± 0.17             | 2.9                       |
| N-13    | 15          | Nitzsche            | Circulation 1996;93:2000   | 0.64 ± 0.09             | 2.9                       |
| N-13    | 30          | Nagamachi           | JNM 1996;37:1626           | 0.64 ± 0.15             | 2.9                       |
| N-13    | 10          | Böttcher            | JNM 1997;38:442            | 0.61 ± 0.09             | 1.1                       |
| N-13    | 10          | Campisi             | AJC 1997;80:27             | 0.68 ± 0.16             | 2.9                       |
| N-13    | 20          | Muzik               | JACC 1998;31:534           | 0.67 ± 0.11             | 2.9                       |
| N-13    | 14          | Lortie              | EJNMMI 2007;34:1765        | 0.69 ± 0.09             | 2.9                       |
| N-13    | 10          | Mather              | Obesity 2009;18:63         | 0.61 ± 0.14             |                           |
| N-13    | 10          | Vincenti            | Nuklearmedizin 2010;49:173 |                         | 2.9                       |
| N-13    | 14          | Teragawa            | EJNMMI 2010;37:368         | 0.86 ± 0.21             | 2.9                       |
| N-13    | 26          | Valenta             | JNC 2010;17:1023           | 0.71 ± 0.13             | 2.9                       |
| N-13    | 13          | Scholtens           | JNC 2011;18:238            | 0.70 ± 0.16             | 1.1                       |
| N-13    | 15          | Slomka              | JNM 2012;53:171            | 0.87 ± 0.24             | 3.5                       |
| N-13    | 14          | Renaud              | JNC 2013;20:578            | 0.71 ± 0.15             | 2.9                       |
| O-15    | 4           | Iida                | Circulation 1988;78:104    | 0.97 ± 0.07             |                           |
| O-15    | 11          | Senneff             | JNM 1991;32:2037           | 1.16 ± 0.32             | 4.2                       |
| O-15    | 11          | Araujo              | Circulation 1991;83:875    | 0.84 ± 0.09             | 3.5                       |
| O-15    | 8           | Yamamoto            | Circulation 1992;86:167    | 0.95 ± 0.13             |                           |
| O-15    | 21          | Uren                | NEJM 1994;330:1782         | 1.13 ± 0.26             | 3.5                       |
| O-15    | 15          | Nitzsche            | Circulation 1996;93:2000   | 0.66 ± 0.12             | 2.9                       |
| O-15    | 19          | Laine               | JACC 1998;32:147           | 0.81 ± 0.21             | 3.5                       |
| O-15    | 61          | Kaufmann            | JACC 2000;36:103           | 0.87 ± 0.14             | 3.5                       |
| O-15    | 11          | Lin                 | JNM 2001;42:201            | 0.92 ± 0.19             | 1.1                       |
| O-15    | 12          | Furuyama            | Circulation 2002;105:2878  | 0.79 ± 0.18             | 3.5                       |
| O-15    | 11          | Yoshinaga           | JNC 2003;10:275            | 0.96 ± 0.19             | 3.5                       |
| O-15    | 11          | Wyss                | JNM 2003;44:146            | 1.24 ± 0.19             | 5.0                       |
| O-15    | 27          | Vermeltfoort        | JNC 2011;18:650            | 1.20 ± 0.31             | 3.5                       |
| O-15    | 11          | Prior               | EJNMMI 2012;39:1037        | 1.00 ± 0.24             | 3.5                       |
| O-15    | 128         | Danad               | EJNMMI 2012;39:102         | 1.02 ± 0.32             | 3.5                       |
| O-15    | 20          | Tomiyama            | JMRI 2015;42:754           | 0.71 ± 0.11             | 3.5                       |
| O-15    | 10          | Ochi                | J Card 2016;68:316         | 0.66 ± 0.10             | 4.2                       |
| Rb-82   | 11          | Lin                 | JNM 2001;42:201            | 0.82 ± 0.26             | 1.1                       |
| Rb-82   | 14          | Lortie              | EJNMMI 2007;34:1765        | 0.69 ± 0.14             | 2.9                       |
| Rb-82   | 15          | Manabe              | JNM 2009;50:68             | 0.80 ± 0.25             | 3.5                       |
| Rb-82   | 125         | Sdringola           | JACC CV Img 2011;4:402     | 0.70 ± 0.15             | 2.9                       |
| Rb-82   | 11          | Prior               | EJNMMI 2012;39:1037        | 1.03 ± 0.42             | 3.5                       |
| Rb-82   | 14          | Renaud              | JNC 2013;20:578            | 0.68 ± 0.12             | 2.9                       |
| Rb-82   | 10          | Pelletier-Galarneau | JNM 2018;59:100            | 0.45 ± 0.08             | 2.9                       |
| All     | 881         |                     |                            | 0.8                     |                           |

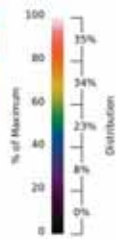
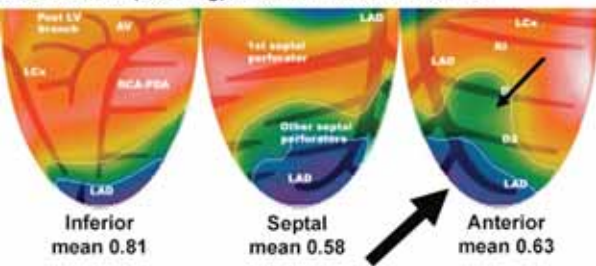


# How low can you go?

B



Heart rest flow (cc/min/g) max 1.24 min 0.21 mean .73

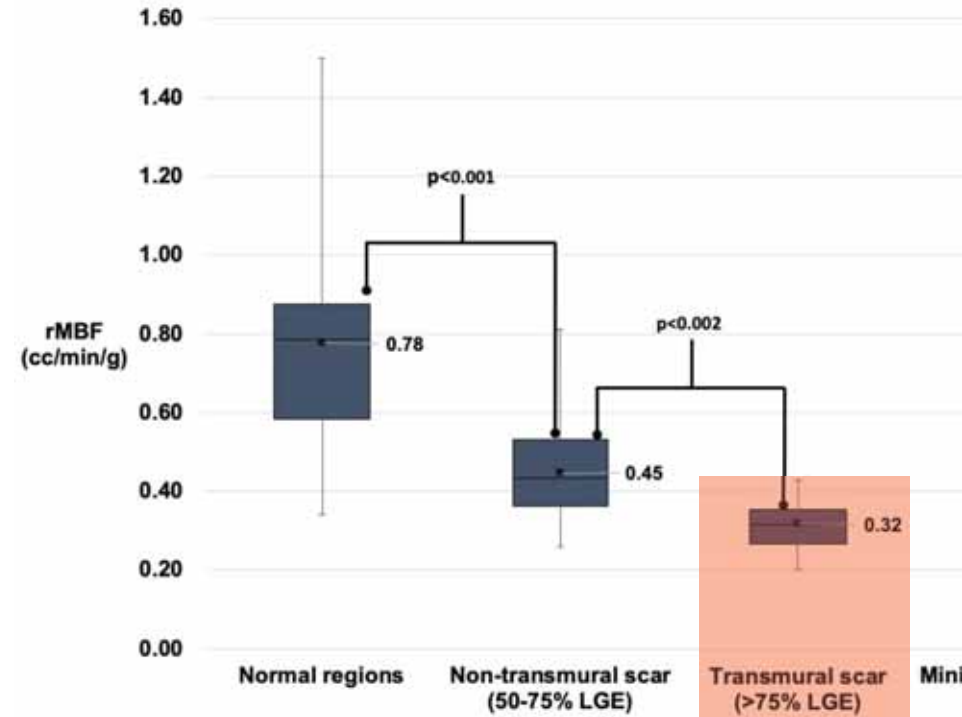


**Total scar (blue and green regions)**  
Corresponds to >50% DHE  
Total area: 26%  
Relative uptake mean: 50% maximum  
Rest flow mean: 0.45 cc/min/g

**Non-transmural scar (green region, thin arrows)**  
Corresponds to 50-75% DHE  
Total area: 12%  
Relative uptake mean: 59% maximum  
Rest flow mean: 0.58 cc/min/g

**Transmural scar (blue region, thick arrow)**  
Corresponds to >75% DHE  
Total area: 14%  
Relative uptake mean: 42% maximum  
Rest flow mean: 0.34 cc/min/g

Resting Myocardial Blood Flow in Normal Regions  
Regions of Transmural and Nontransmural Scar

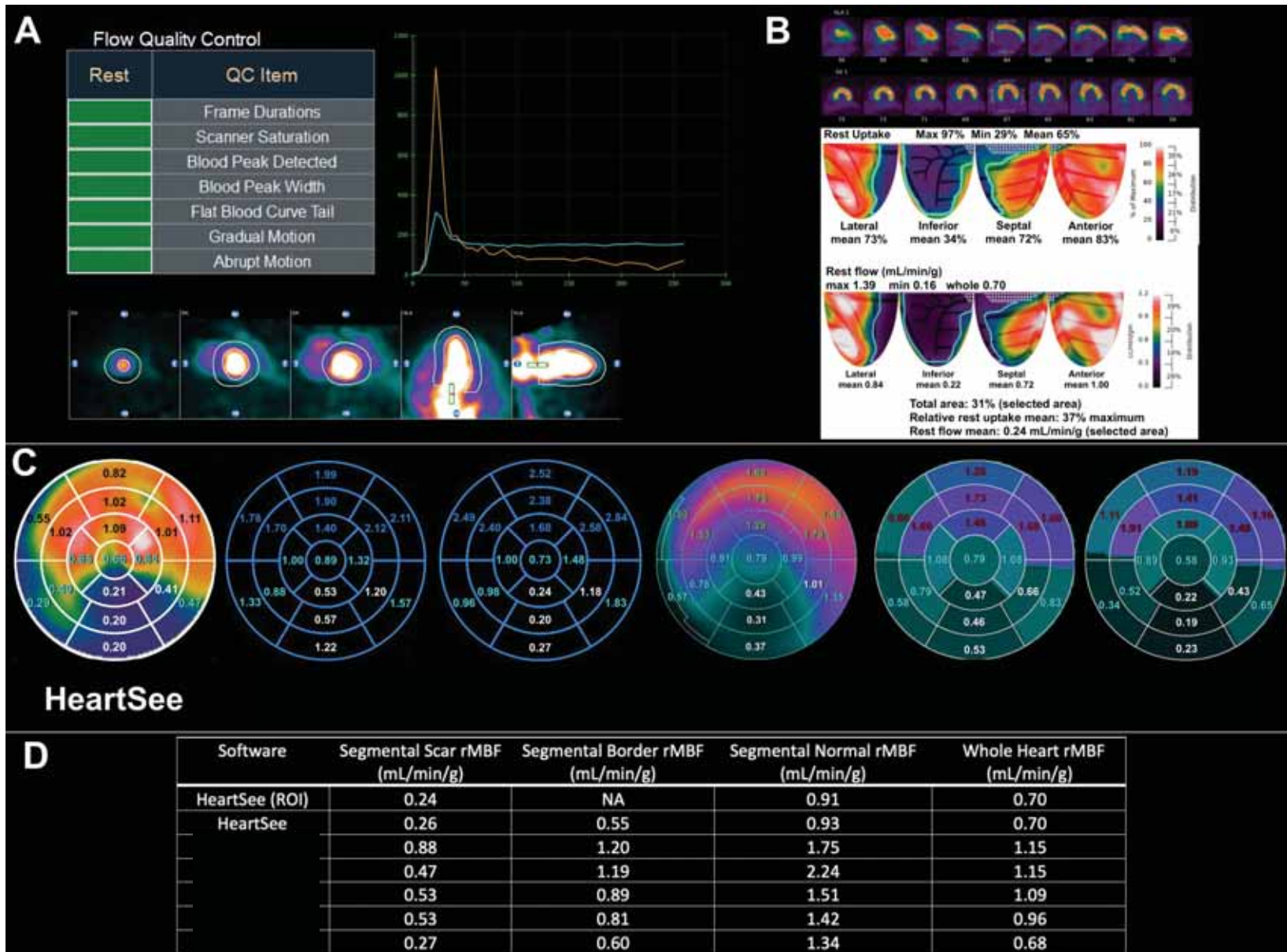


| Study author    | Study patients (n) | Isotope          | rMBF in myocardial scar | rMBF in normal tissue | Minimal rest flow |
|-----------------|--------------------|------------------|-------------------------|-----------------------|-------------------|
| Leberich et al. | 22                 | N <sup>13</sup>  | 0.32                    | 0.83                  | NR                |
| Leberich et al. | 19                 | N <sup>13</sup>  | 0.28                    | 0.68                  | NR                |
| Leberich et al. | 26                 | N <sup>13</sup>  | 0.27                    | 0.81                  | 0.25              |
| Leberich et al. | 16                 | N <sup>13</sup>  | 0.36                    | 0.75                  | 0.19              |
| Leberich et al. | 16                 | Rb <sup>82</sup> | 0.37                    | 0.78                  | 0.19              |
|                 |                    | Weighted average | 0.34                    | 0.75                  |                   |

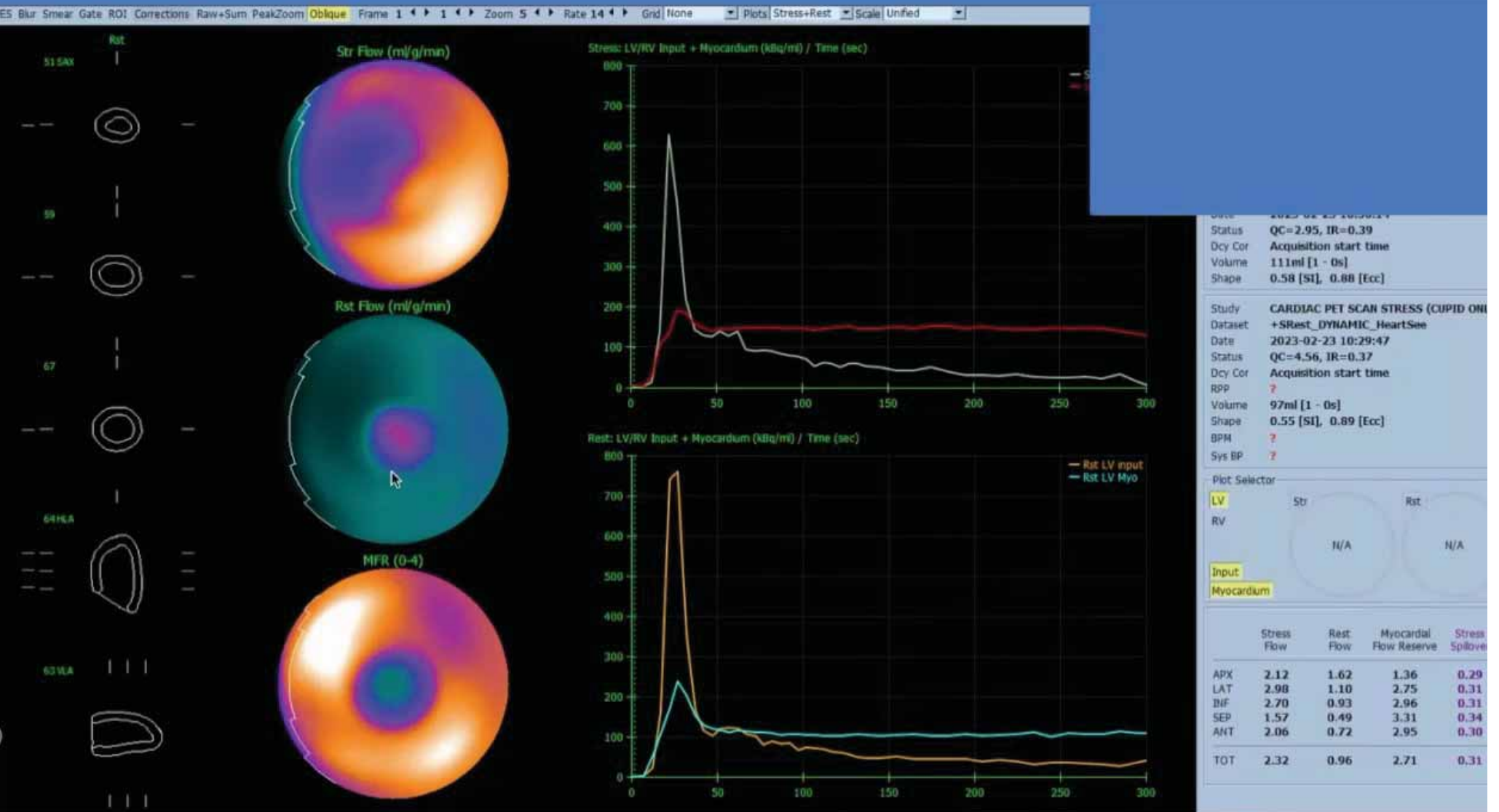
absolute flow in MRI-verified scars

- transmural =  $0.32 \pm 0.07$  cc/min/g  
(relative uptake  $41 \pm 6\%$  max)
- non-transmural =  $0.45 \pm 14$  cc/min/g  
(relative uptake  $55 \pm 8\%$  max)

# Variation in infarct flow among software packages

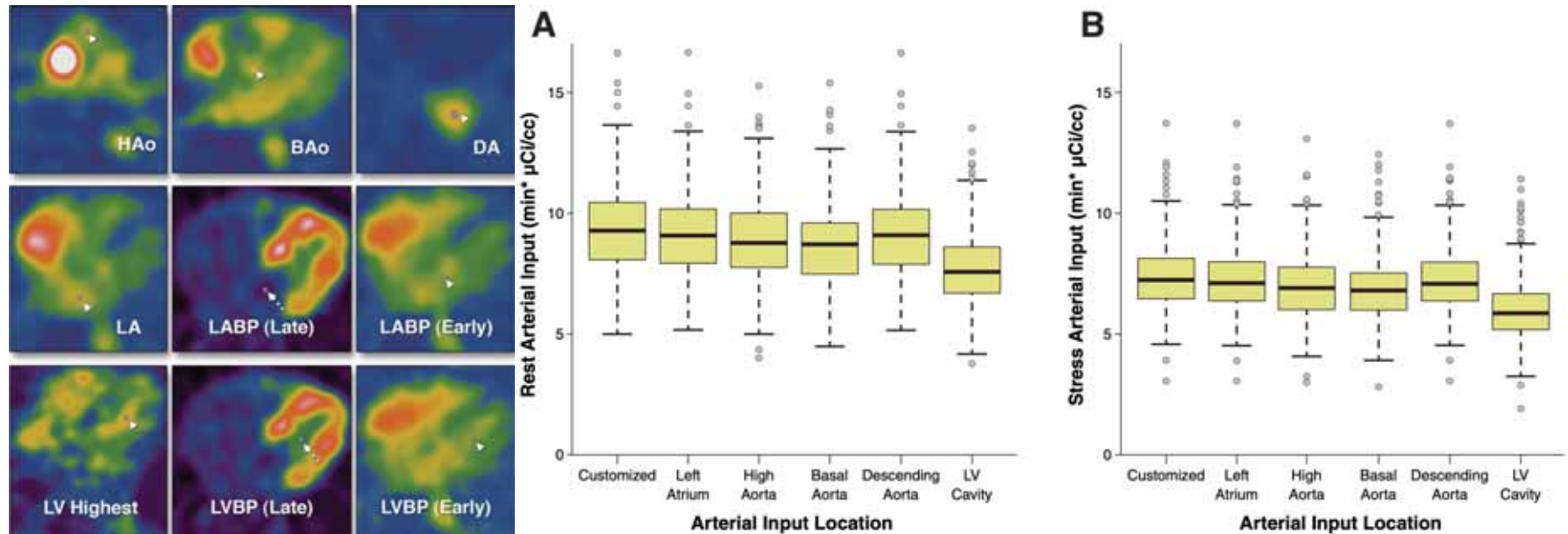


# Motion correction

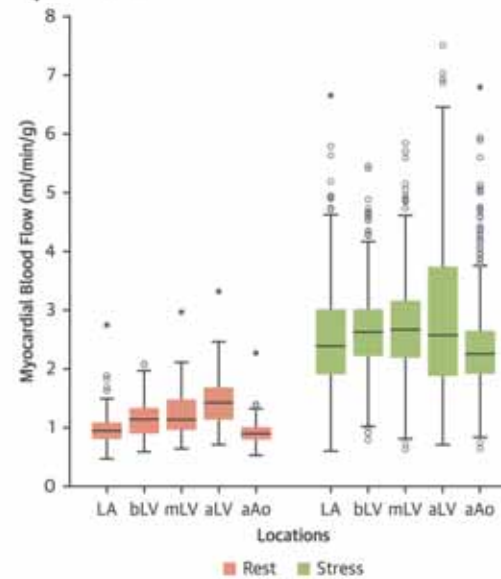
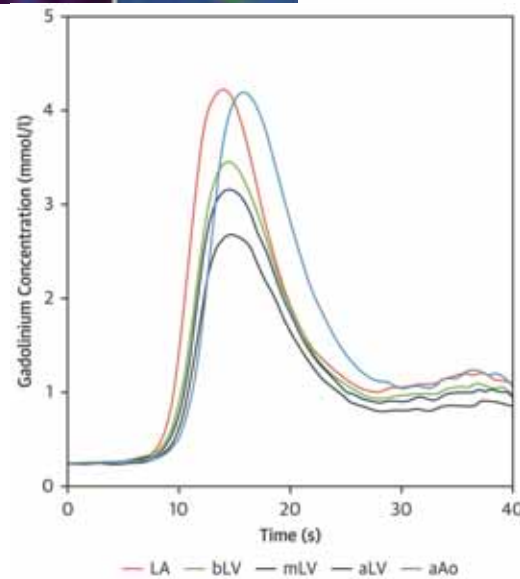


courtesy of Dr. Robert Bober (Ochsner, New Orleans)

# Location of arterial input

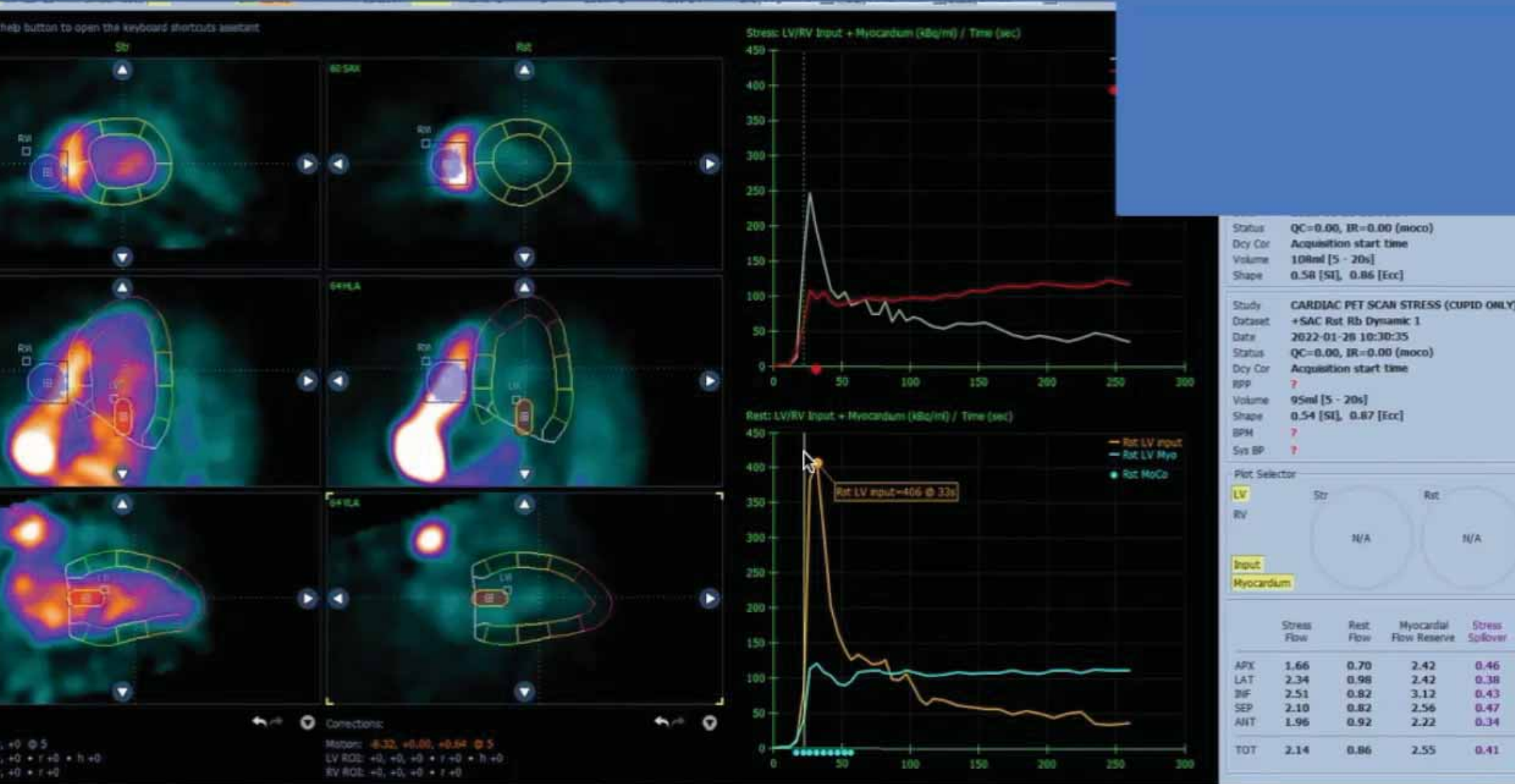


cardiac MRI



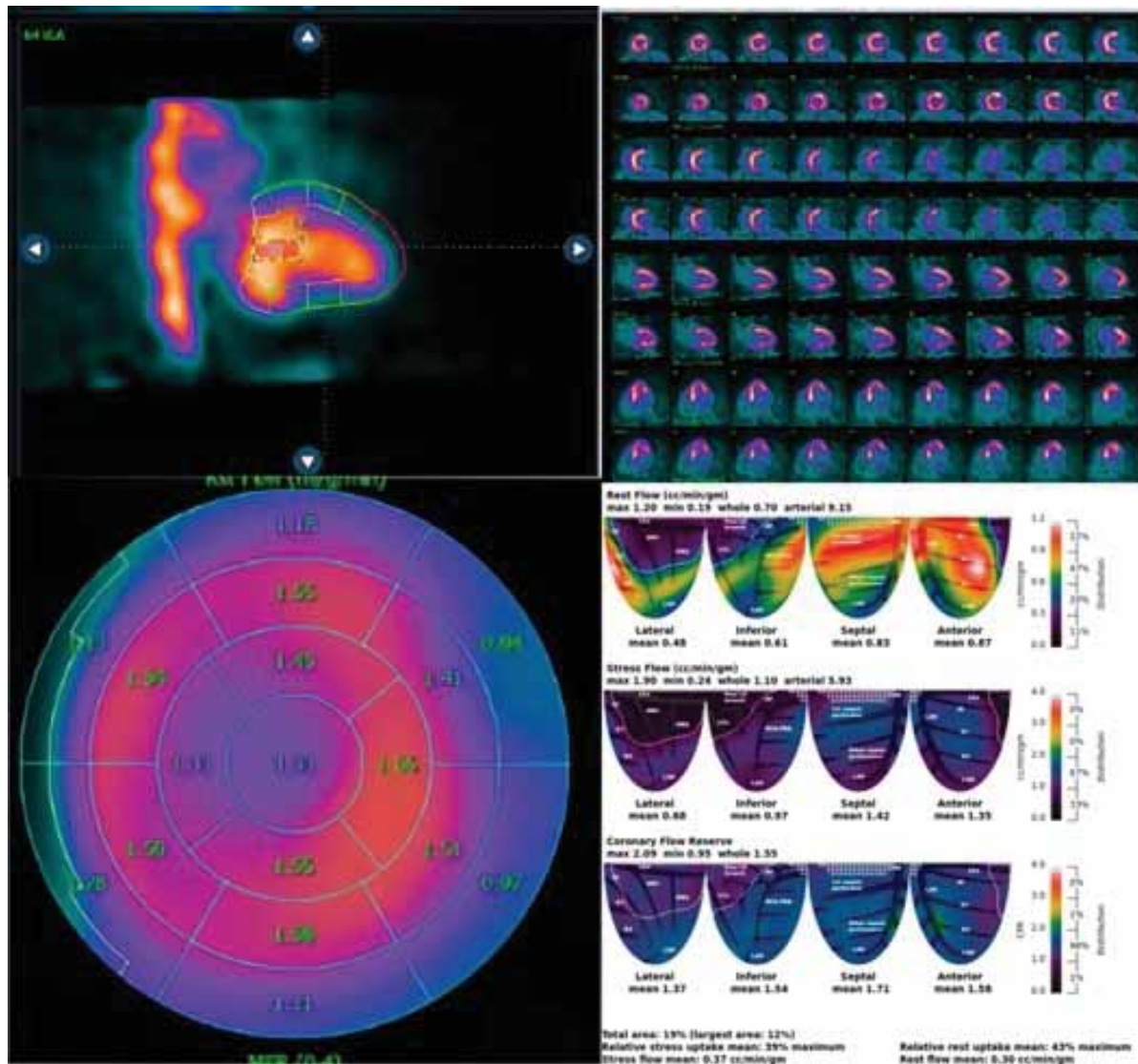
o = Vasquez AF, *JACC Cardiovasc Imaging*. 2013 May;6(5):559-68. (Figures 2 and 3)  
 ttom = Franks R, *JACC Cardiovasc Imaging*. 2020 Dec;13(12):2693-2695. (Figure 1)

# Arterial input location



Courtesy of Dr. Robert Bober (Ochsner, New Orleans)

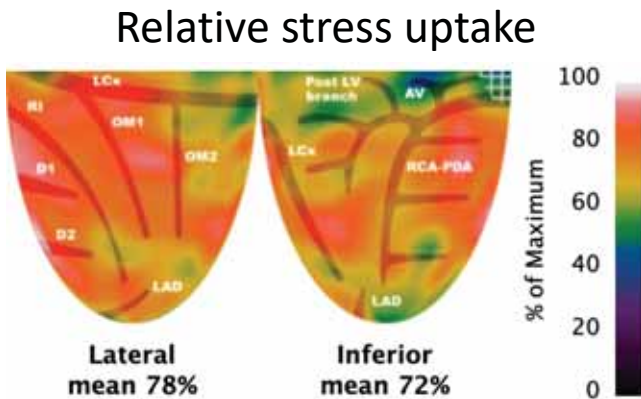
# Inferior infarct with aneurysm.



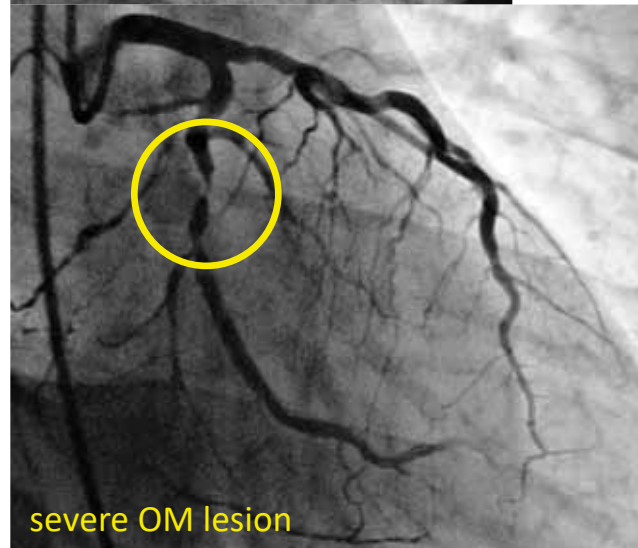
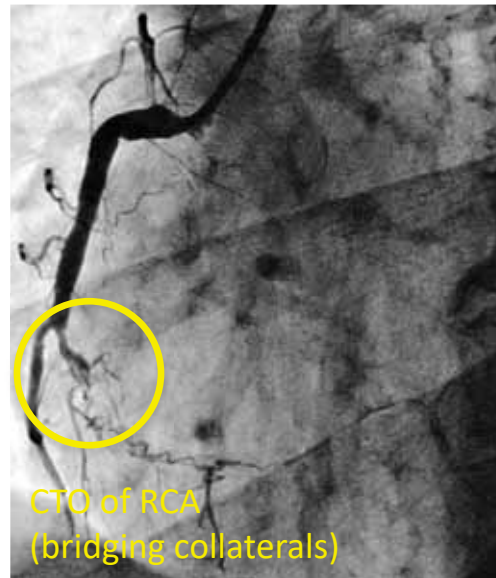
0.97  
cc/min/gm

0.3  
cc/min/gm

# How can PET miss these severe lesions?

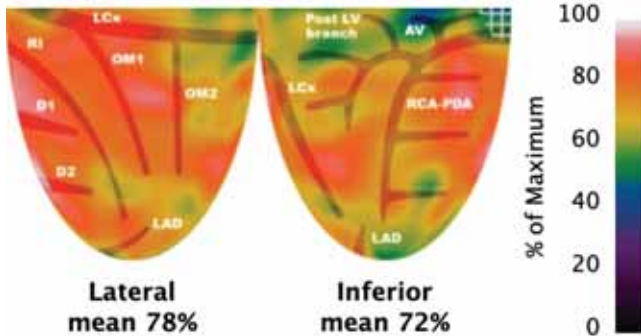


Invasive angiogram



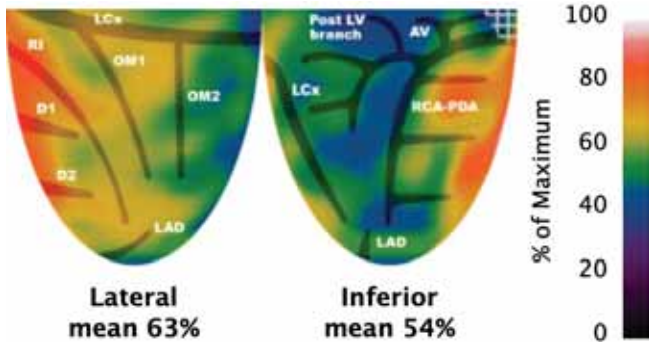
# Caffeine can blunt hyperemia

Relative stress uptake



PET #1

caffeine *1.2 mg/L*

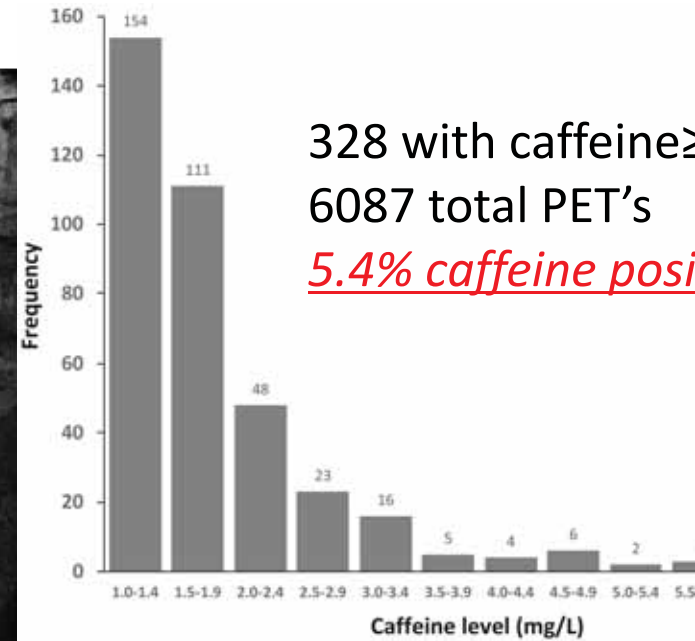
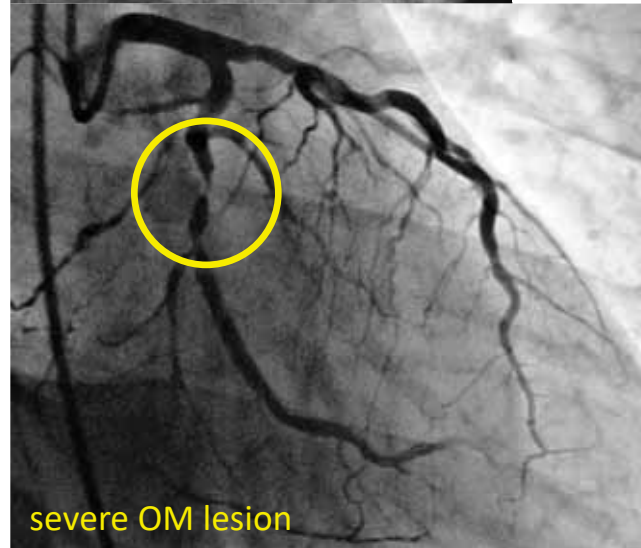
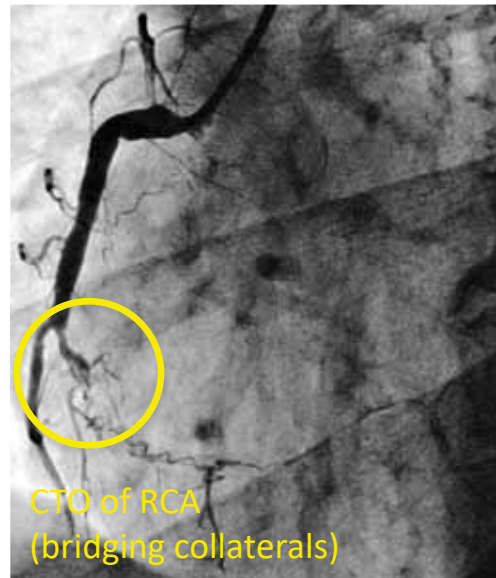


PET #2

caffeine *<1 mg/L*

(28 days later)

Invasive angiogram



328 with caffeine  $\geq$  1.5 mg/L  
6087 total PET's  
*5.4% caffeine positive*



# But do we really need flow?

10556 rest/stress PET  
(Apr 2007 to July 2022)

- exclude
- 1080 non-dipy
  - 508 caffeine (+)
  - 65 dipy timing

8903 dipy scans

2904 (32.6%) abnormal uptake  
( $\geq 5\%$  rest or stress %LV $<60\%$ )

- 882 ischemia
- 728 ischemia + infarct
- 901 infarct only
  
- 186 endothelial dysfxn
- 207 infarct + endo

5999 (67.4%) normal uptake

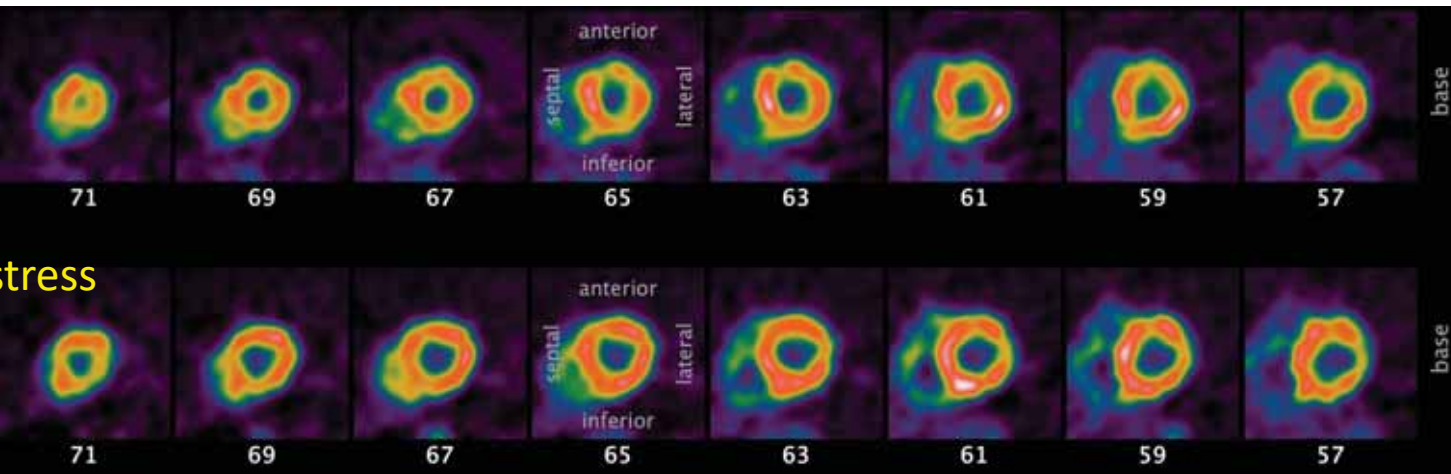
330 (6%) green/blue CFC

4320 (72%) reasonable CFC

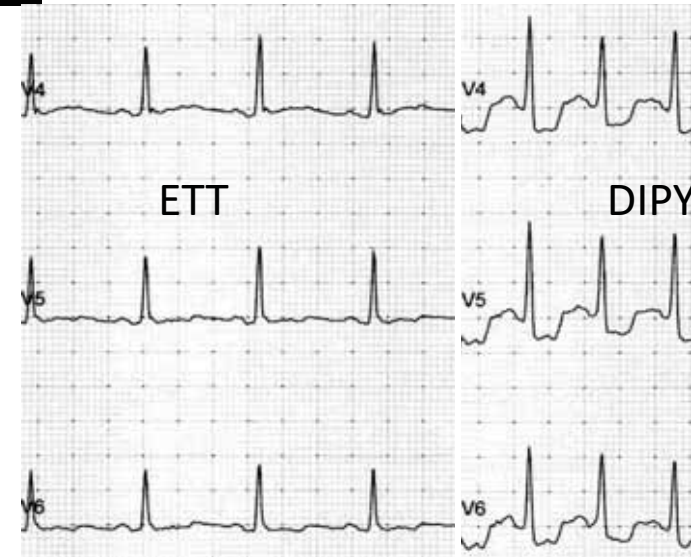
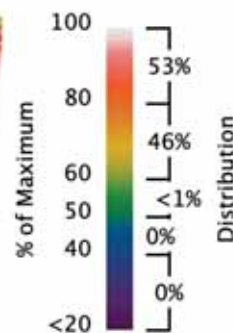
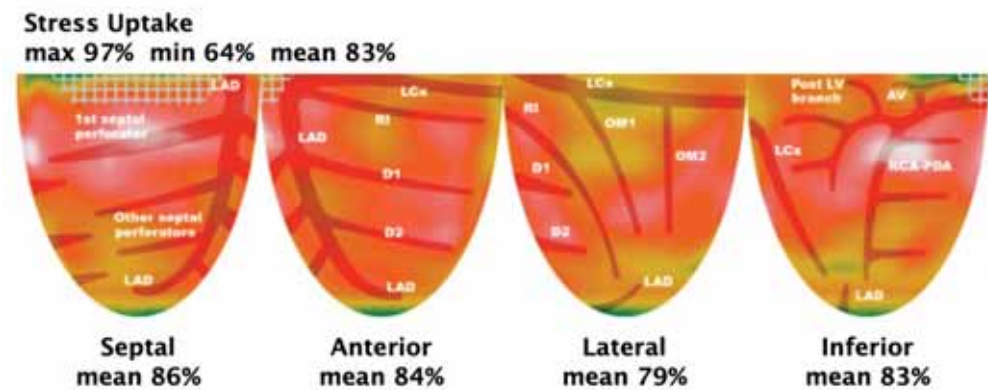
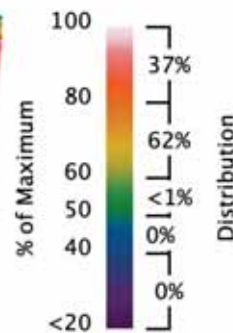
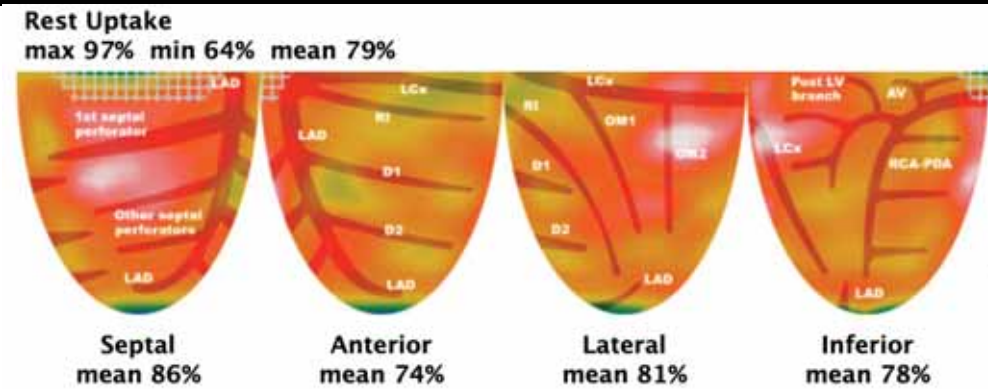
1349 (22%) yellow CFC

28% with normal  
have reduced C

# 56 year-old man with severe angina

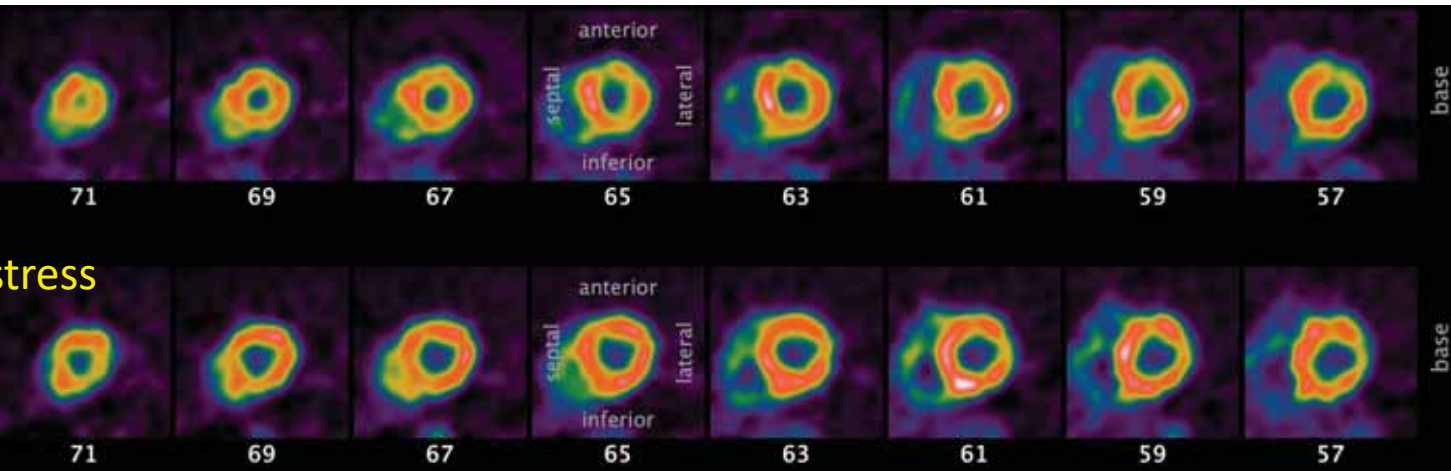


- diabetes, dyslipidemia
- dense CAC on CT
- Bruce treadmill
  - 5:12 minutes
  - reached 164/min (164 bpm)
  - 5-6/10 angina near end

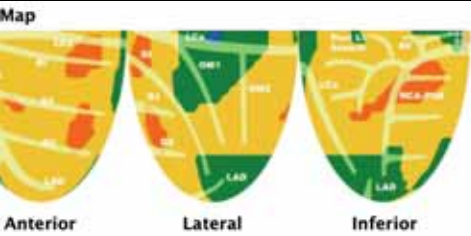


stress EF 66%  
angina, ST depression  
with dipyridamole

# 56 year-old man with severe angina

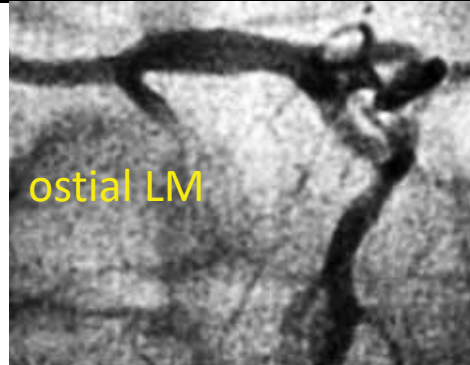


stress

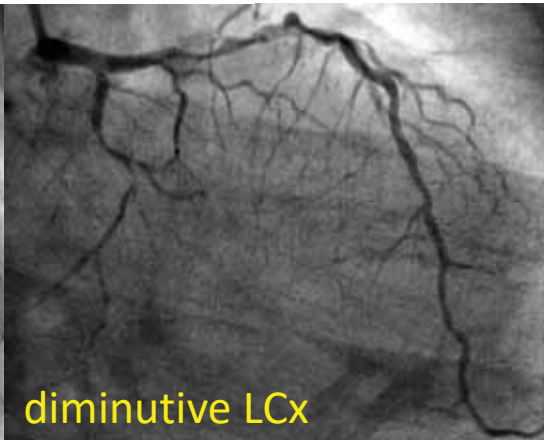


Map  
 Anterior Lateral Inferior  
 healthy young volunteers  
 risk factors only  
 definite ischemia

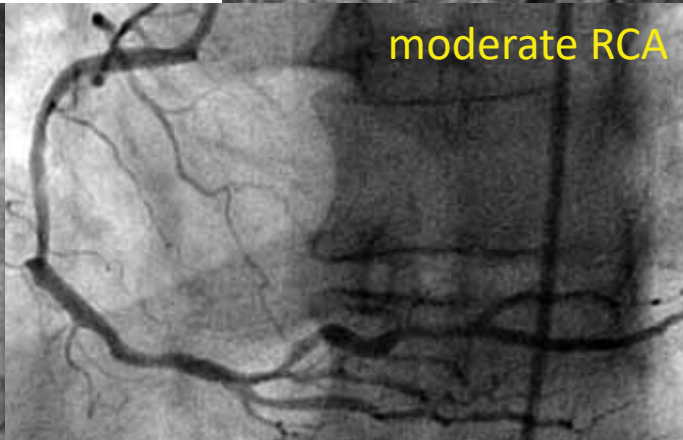
rest = 0.69  
 stress = 1.24  
 CFR = 1.84  
 <1%LV < 60% max  
 caffeine negative  
 angina, ST depression



LAD

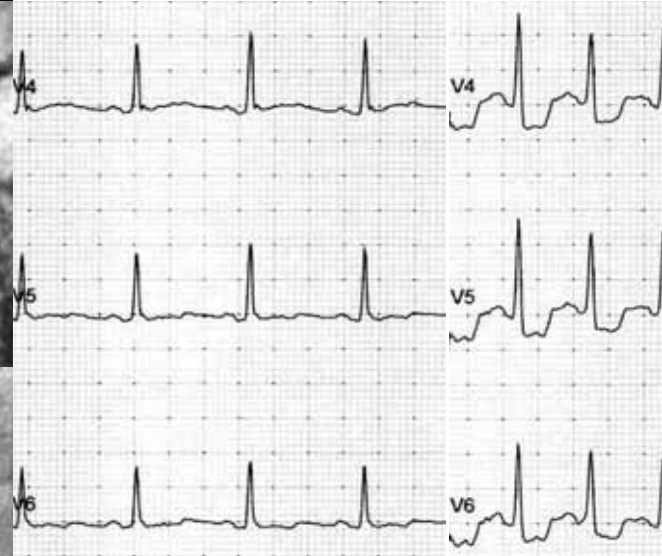


diminutive LCx

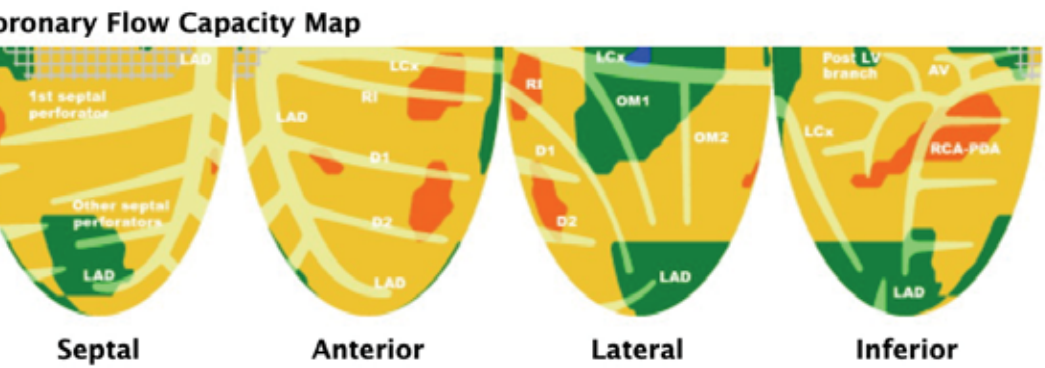
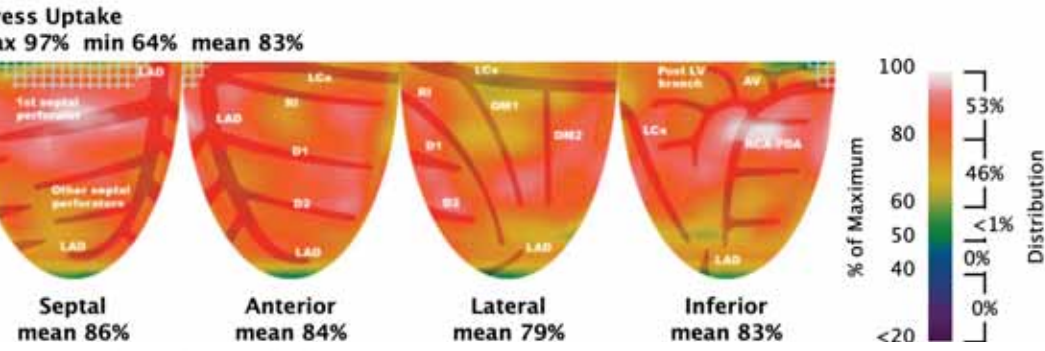
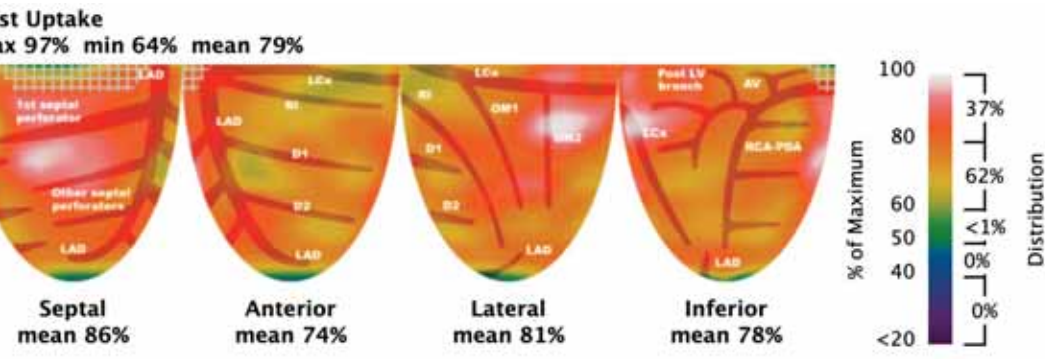


moderate RCA

- diabetes, dyslipidemia
- EF 66% with dense CA
- Bruce treadmill
  - 5:12 minutes
  - reached 164/min
  - 5-6/10 angina near

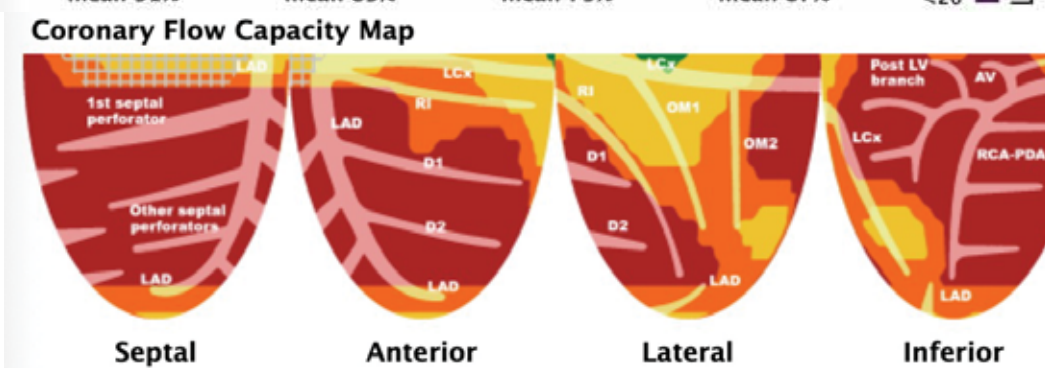
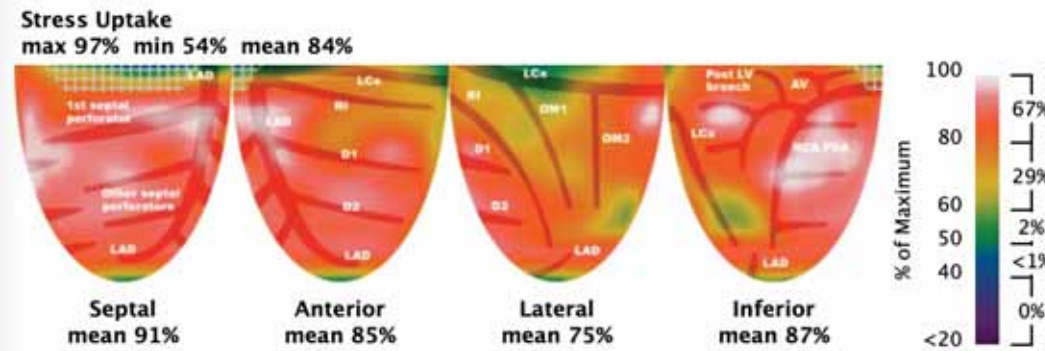
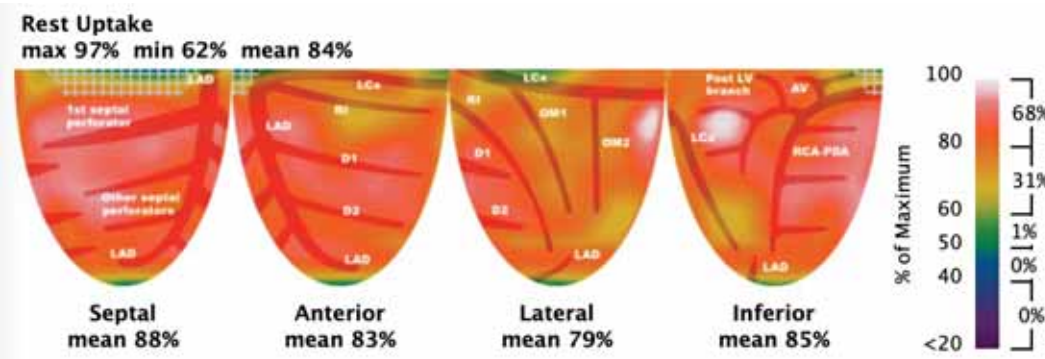


# Underwent CABG (LIMA-LAD, SVG-DIAG, SVG-RCA)



0% Normal, from healthy young volunteers  
6% Minimally reduced, risk factors only  
72% Mildly reduced  
22% Moderately reduced  
<1% Severely reduced, definite ischemia

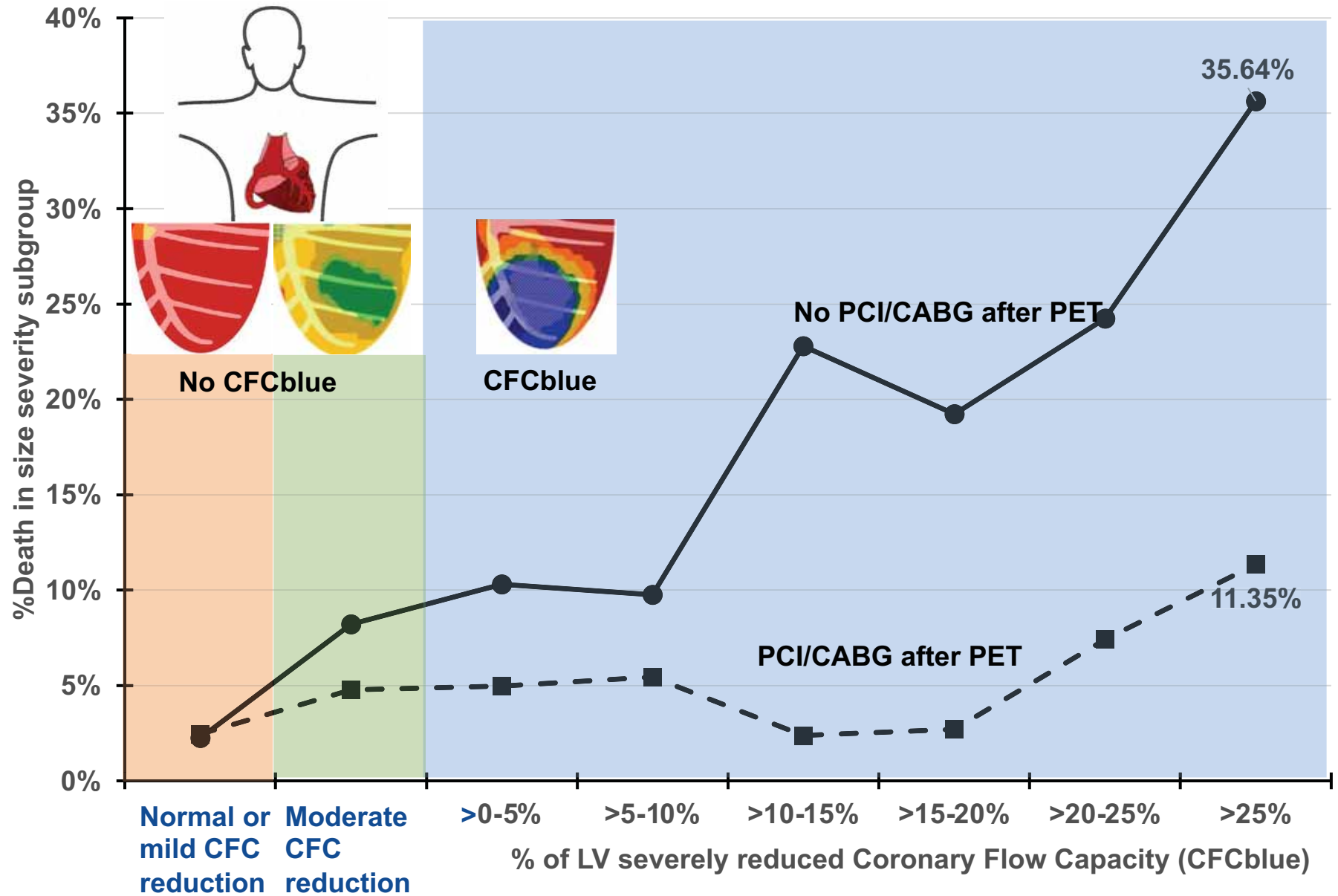
rest 0.69  
stress 1.24  
CFR 1.84



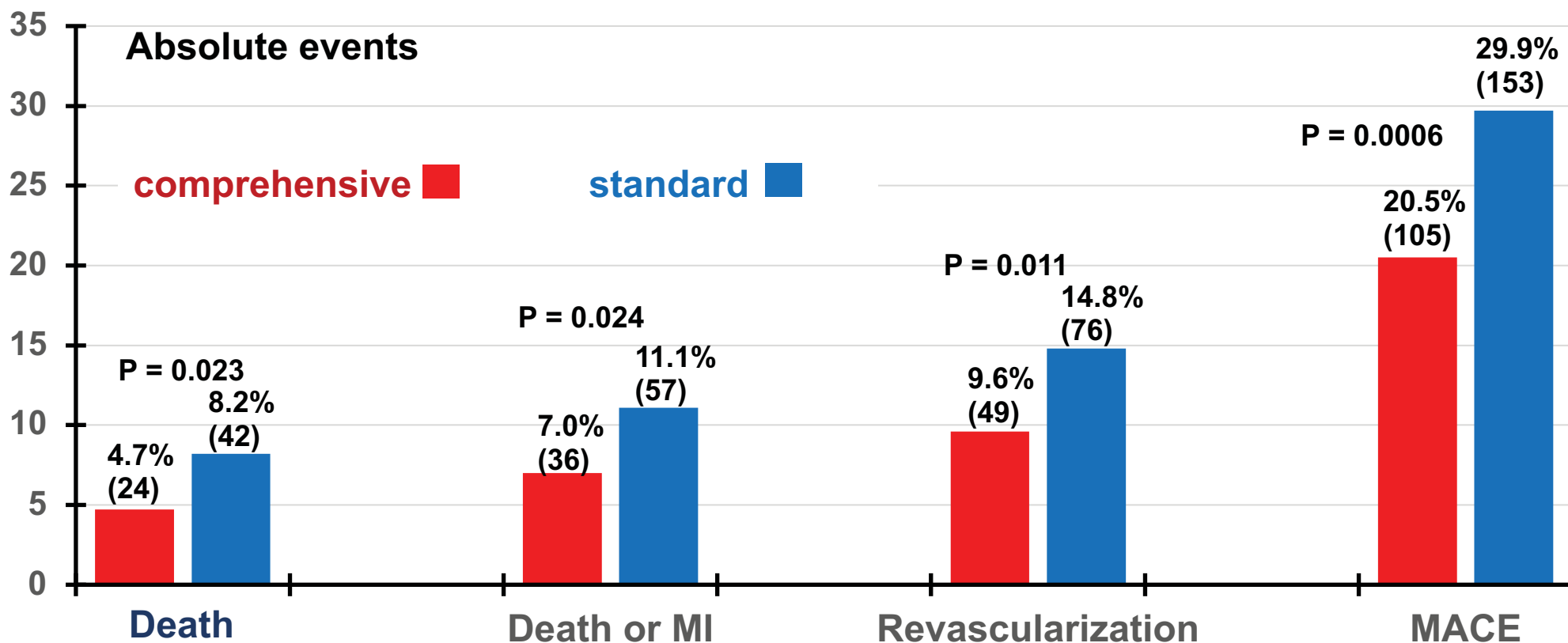
62% Normal, from healthy young volunteers  
24% Minimally reduced, risk factors only  
14% Mildly reduced  
<1% Moderately reduced  
0% Severely reduced, definite ischemia

rest 1.21  
stress 2.41  
CFR 1.98

## Mortality over 10 years after rest-stress PET

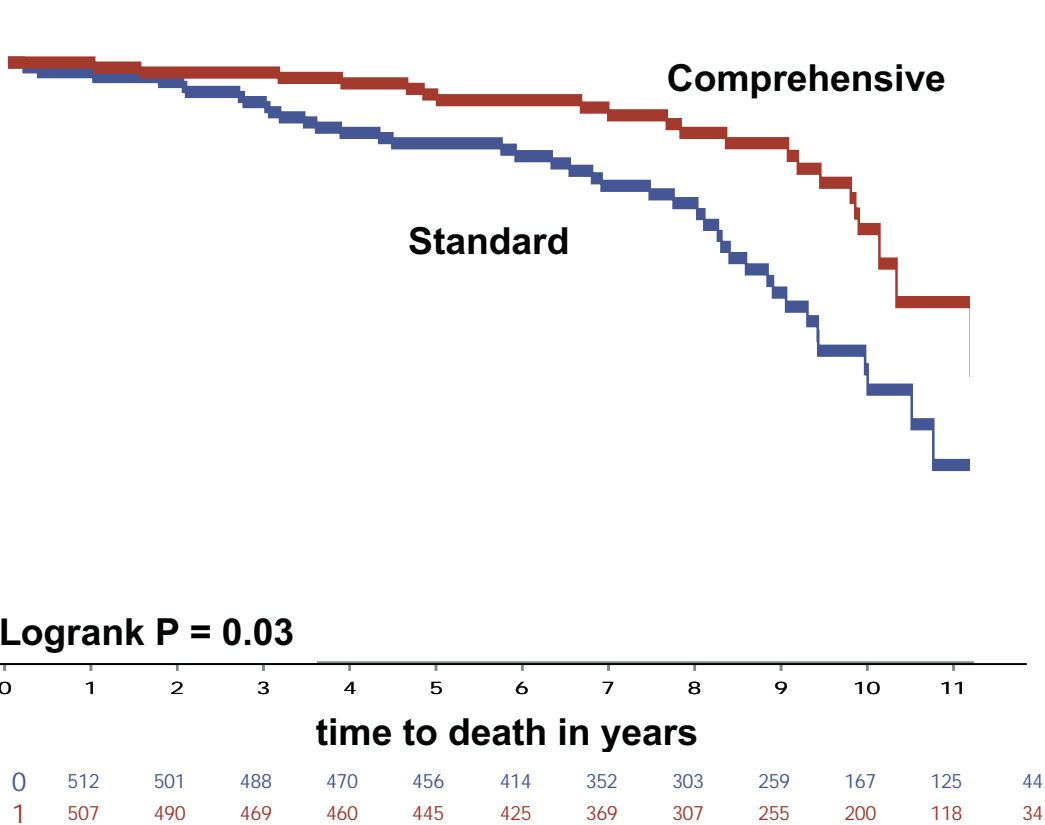


# Randomized CENTURY Trial of Intense Lifestyle, Medical Treatment To Goals And PET Guided Interventions

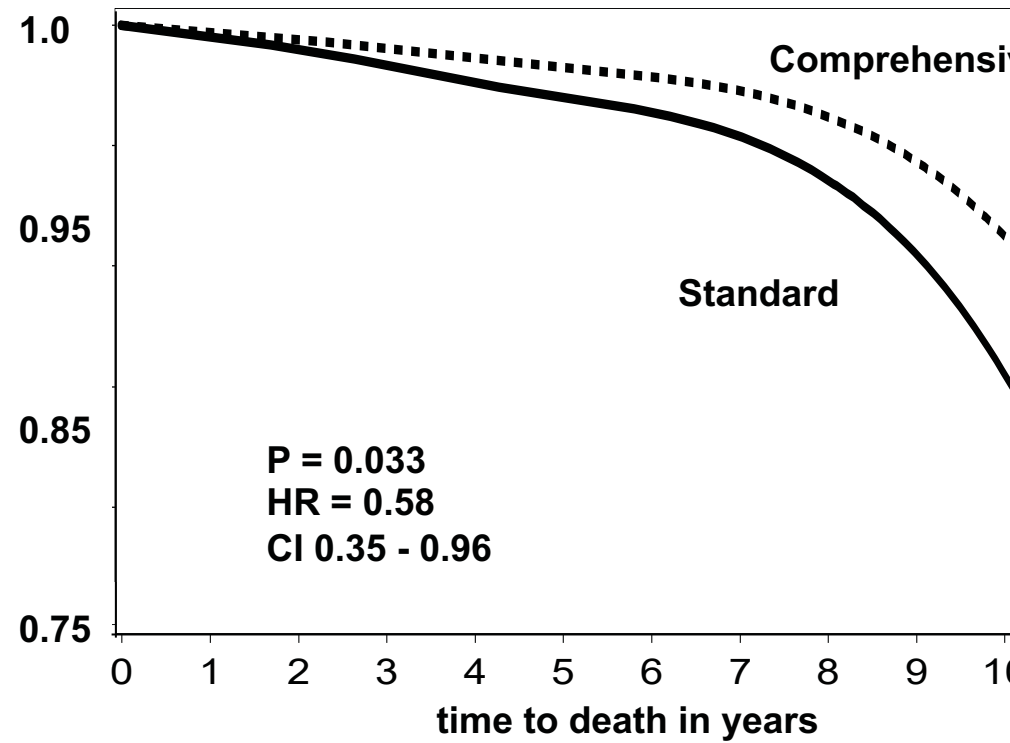


# Randomized CENTURY Trial of Intense Lifestyle, Medical Treatment To Goals And PET Guided Interventions

Kaplan Meier Plot for death extended follow-up



Cox Regression Modeling for death extended follow-up



# Accurate data into a validated flow package=

Better precision and lower failure rate than  $FFR_{CT}$

Fewer contraindications than  $FFR_{CT}$ , CMR, or ICA

More information than CMR

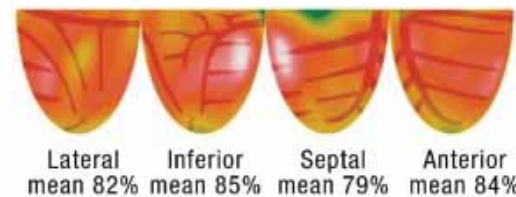
Artery specific diagnosis

Predicts ICA- $FFR$  and predicts PCI/CABG best outcomes

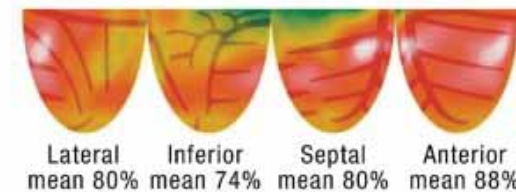
Fig. 2

## Pre-Revascularization

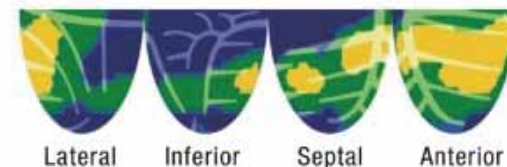
**Rest Uptake**  
max 98% min 54% mean 83%



**Stress Uptake**  
max 97% min 56% mean 81%

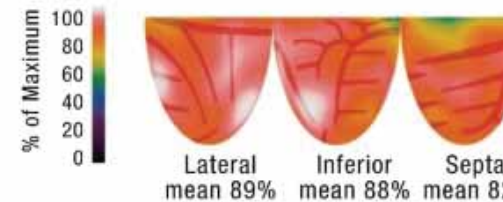


## Coronary Flow Capacity Map

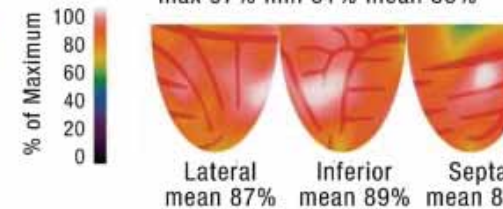


## Post-Revascularization

**Rest Uptake**  
max 97% min 61% mean 87%



**Stress Uptake**  
max 97% min 61% mean 86%



## Coronary Flow Capacity Map

