Cardiac NM

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Nuclear Cardiology

- RNV
  - Tc-99m labelled RBCs
- MPS
  - Tl-201
  - Tc-99m MIBI
  - Tc-99m tetrofosmin
  - Rb-82
- Others
  - I-123 MIBG
  - C-11 fatty acids
  - Tc-99m HL91
  - F-18 FDG

Is there any money in it

- In E.U. about 300,000 cardiac studies per year
- In USA about 1,000,000 cardiac studies per year
- Turn over of nuclear medicine radiopharmaceuticals $41,000,000 per annum

General priciples

- Use as much activity as you can justify for dosimetry not finances
- Do not exceed recommended maximum activity of Tc-99m added to vial
- Image at correct time post injection

The perfect agent

- High myocardial uptake
- Uptake proportional to blood flow
- Low background
- Good dosimetry
- Washout or no washout? But stable distribution from injection to imaging

Tl-201

- Thallium-201 is a metallic element in group IIIA of the periodic table
- Biological similarities to potassium
- Monovalent cation
- Cyclotron produced
- Decays by electron capture (EC) to mercury
- Physical half-life is 73.1 hours
- Biological half life is 10 days

Tl-201

- Emits predominantly mercury x-rays at 69-83KeV(88%)
- Principle photo peaks at 135 and 167 keV(12%)
- No in-house preparation and no quality control required before injection
- First pass extraction is 60-70% (stress injection), 80-90% (rest injection)
- Maximum myocardial uptake is approximately 3.7-4% of injected dose
- Extraction decreases at higher flow rates

Tl-201

- Accumulation and retention depends on coronary blood flow and cellular viability
- Redistributes
- Critical organs: Ovaries, kidneys, bone surface
- Myocardial uptake has two components: early component (80% with half life of 4hours) and delayed component (20% with half life of 40 hours)
- Disappearance from the blood compartment rapid and has two components: 92% disappears with a half life of 5minutes and 8% with a half life of 40 hours
- Lung uptake proportional to LVEDP

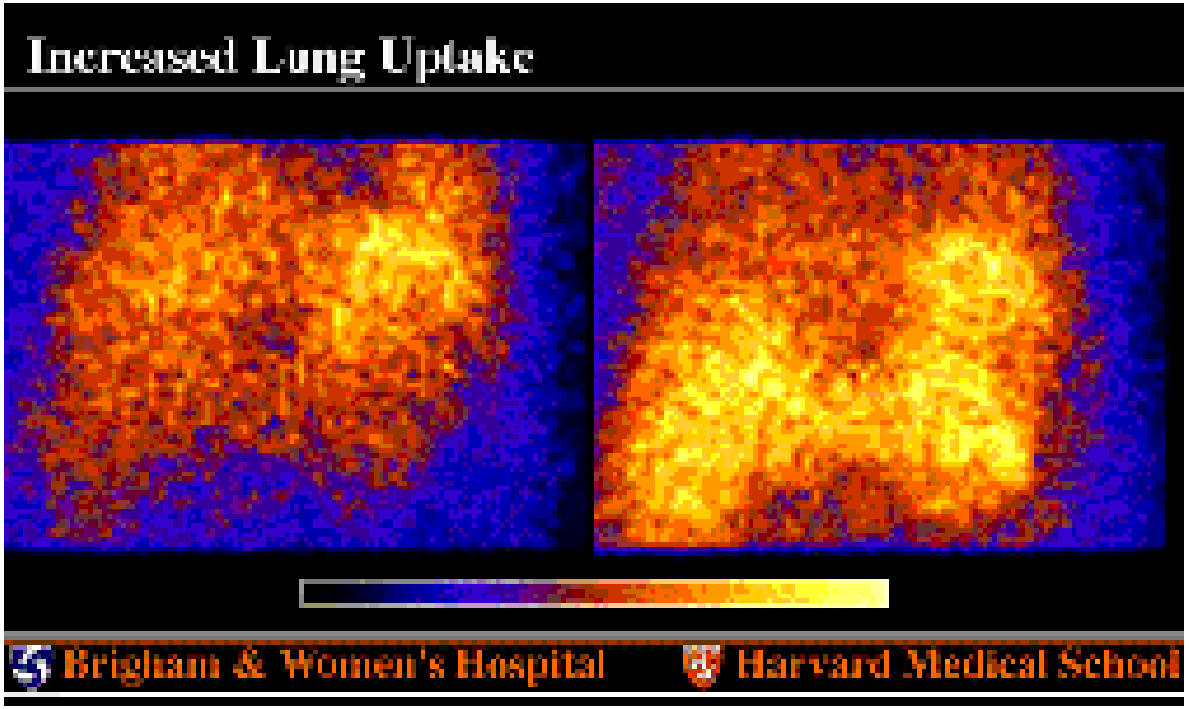
Tl-201

- Requires stringent imaging protocol especially stress images must be started by 5 minute p.i. not to loose sensitivity but at that time patient may not have recovered from stress
- Whole body effective dose is 0.22mSv/MBq (80MBq study =18mSv)
- Excretion: Faeces (80%), urine (20%)

Tl-201

- **Limitations:** Relatively long physical half life [high radiation burden], relatively low injected activity [low-signal to noise ratio, sub optimal images (obese), low counts levels [impairs high quality ECG-gating SPECT], relatively low energy emission [low resolution images and attenuation by soft tissues]

Lung Tl-201 uptake proportional to LVEDP



Tc-99m MIBI

- Lipophilic monovalent cation
- Generator produced
- Emits gamma rays at 140 KeV
- Physical half-life is 6 hours
- The biological half-life is 680 +/- 45 minutes
- Favourable myocardium to background radiation for myocardial imaging

Tc-99m MIBI

- High energy photons decreases the problems of photon attenuation
- Distribution depends on plasma membrane and mitochondrial membrane potentials
- Once accumulated, it is bound in a relatively stable fashion
- Redistribution is negligible or partial [10-15%](does not redistribute to a degree that can be imaged clinically)

Tc-99m MIBI

- First pass extraction fraction is approximately 60%(rest injection), 40% (stress injection)
- 1-2% of the injected dose localizes to the myocardium at rest
- Higher dose compensates for lower extraction
- Flexible imaging protocols
- At higher flow rates there is a plateau in extraction and at low flow rates extraction reduces

Tc-99m MIBI

- Whole body effective dose is 0.009mSv/MBq at rest, 0.008mSv/MBq at stress
- In a 1000MBq study the effective dose will be 8.7mSv
- The primary route of excretion is hepatobiliary (33%). Need to wait 60 mins p.i. for non interference of liver uptake
- Critical organs: Gall bladder, kidneys and colon
- Preparation takes longer (includes boiling in water bath for 20 mins minimum)

Tc-99m tetrofosmin (where different from Tc-99mMIBI)

- Hepatic uptake is lower than with Tc-Sestamibi and it also clears more quickly therefore can start imaging at 30mins pi
- First pass extraction fraction is about 54%
- The myocardial extraction plateaus at higher flow rate
- Overestimates flow at low flow rates

Tc-99m tetrofosmin

- Whole body effective dose is 0.008 mSv/MBq at rest, 0.007 mSv/MBq at stress
- In a 1000MBq study the effective dose will be 7.5 mSv
- Preparation requires no boiling in water bath

Other agents

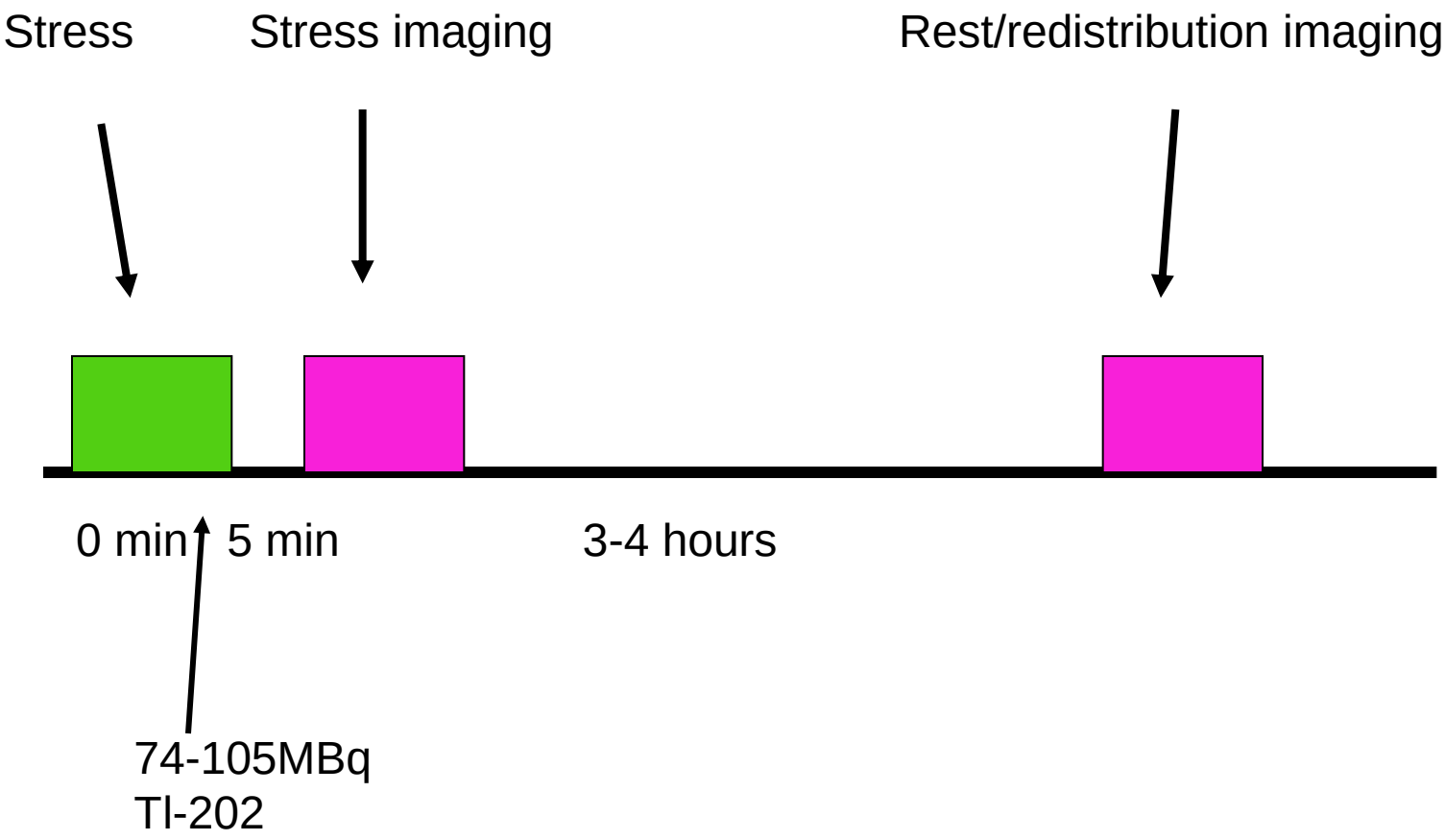
- Tc-99m Teboroxime
  - Rapid uptake and clearence imaging must be finished within 12 minutes p.i. needs triple headed camera
- Tc-99m Neot
  - Like MIBI but killed rats!!
- Tc-99m furifosmin
  - Rumoured to be even more deadly than Neot

Practical differences

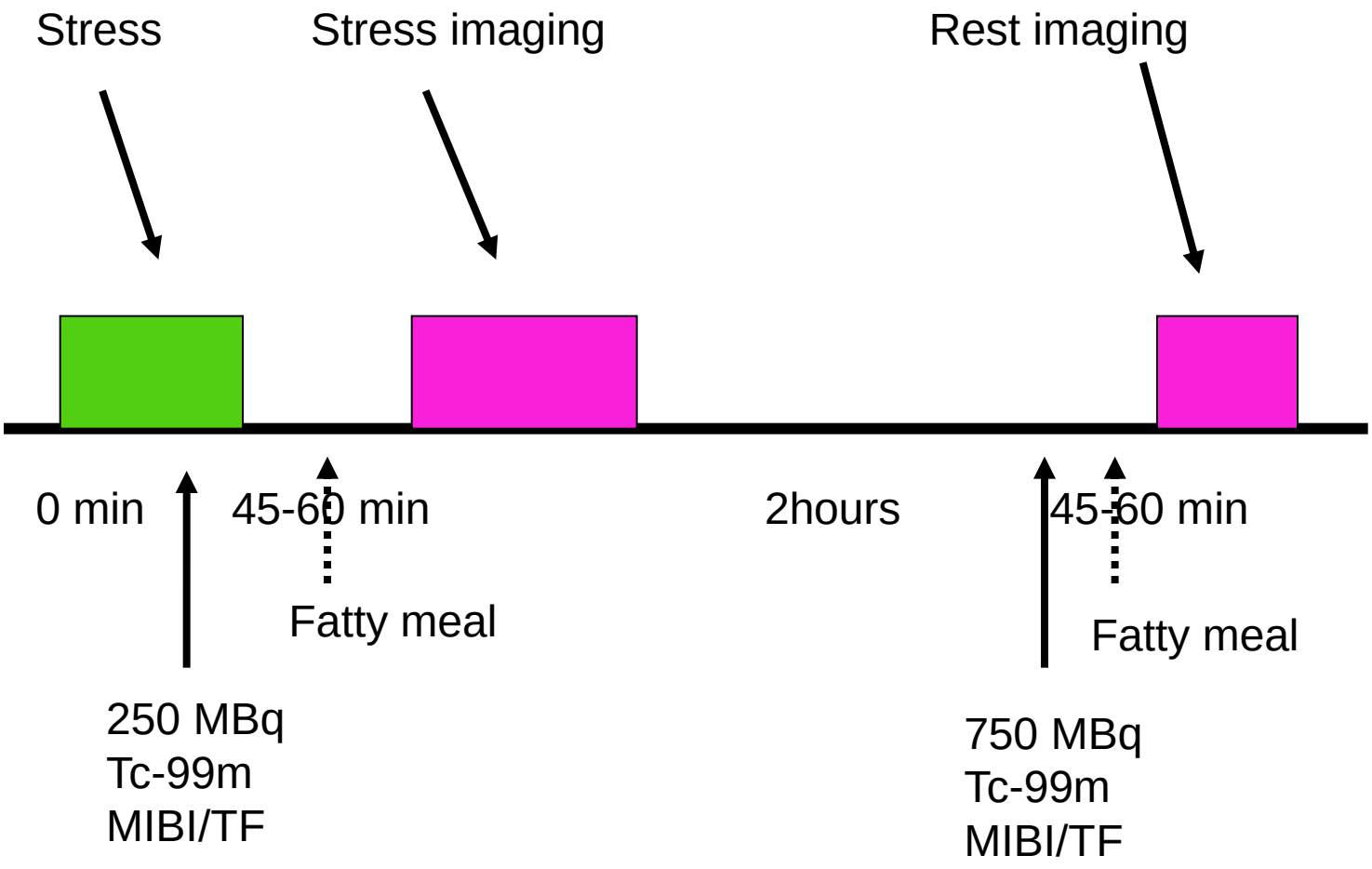
- Tl-201
- Single injection
- Low energy X-rays
- Patient must be stressed next to camera
- Maybe better looking at viability

- Tc-99m MIBI/TF
- Double injection
- Higher energy gamma rays
- Patient can be stressed away from camera
- Better for gating

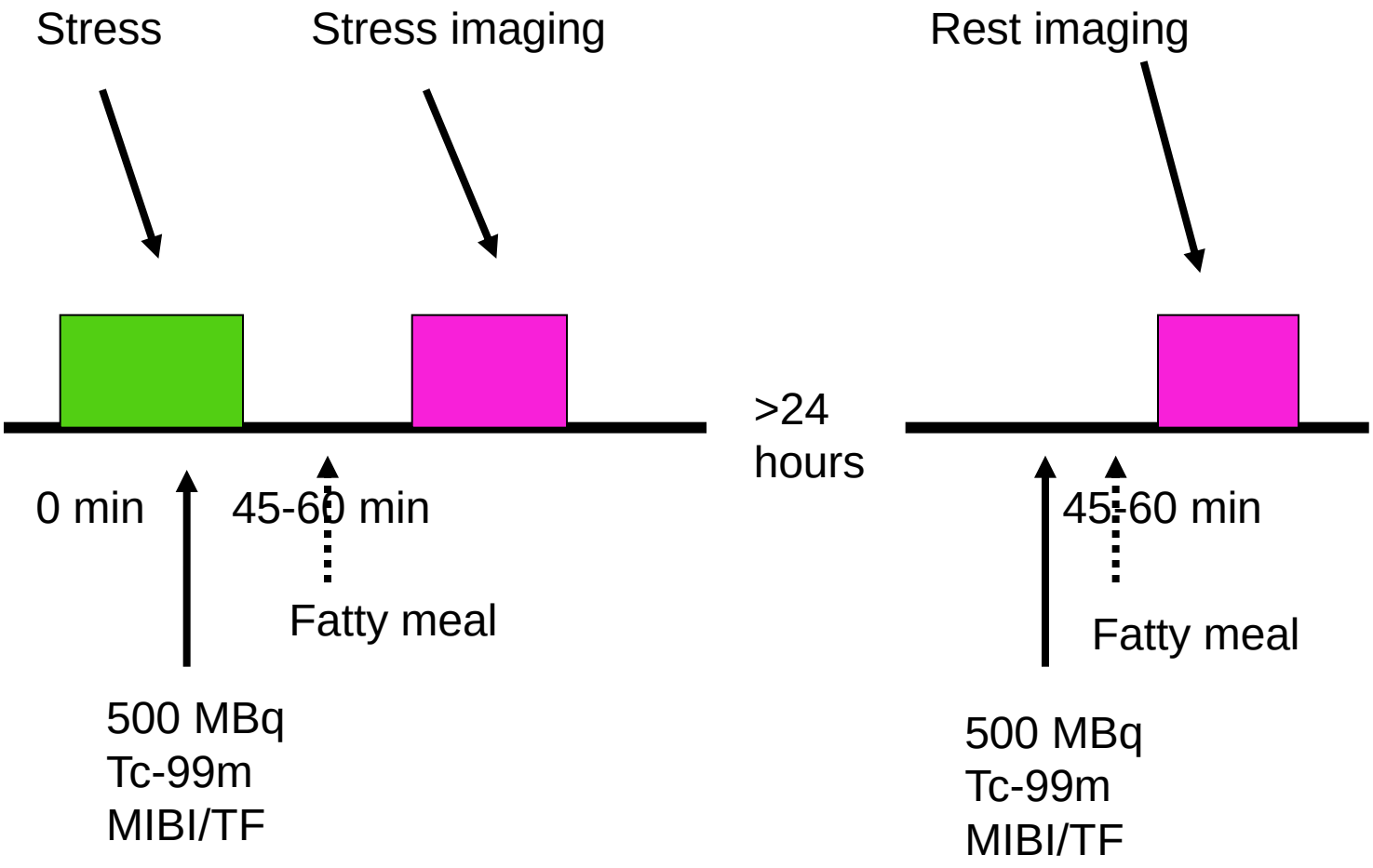
Protocol for Tl-201



Protocol for Tc-99m MIBI/TF one day

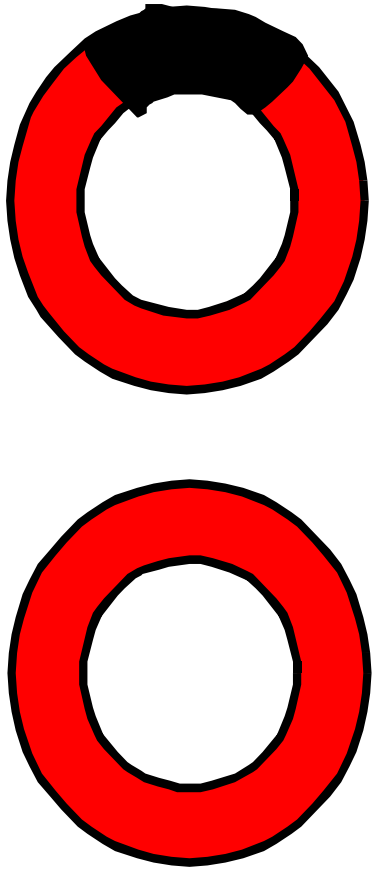


Protocol for Tc-99m MIBI/TF two days

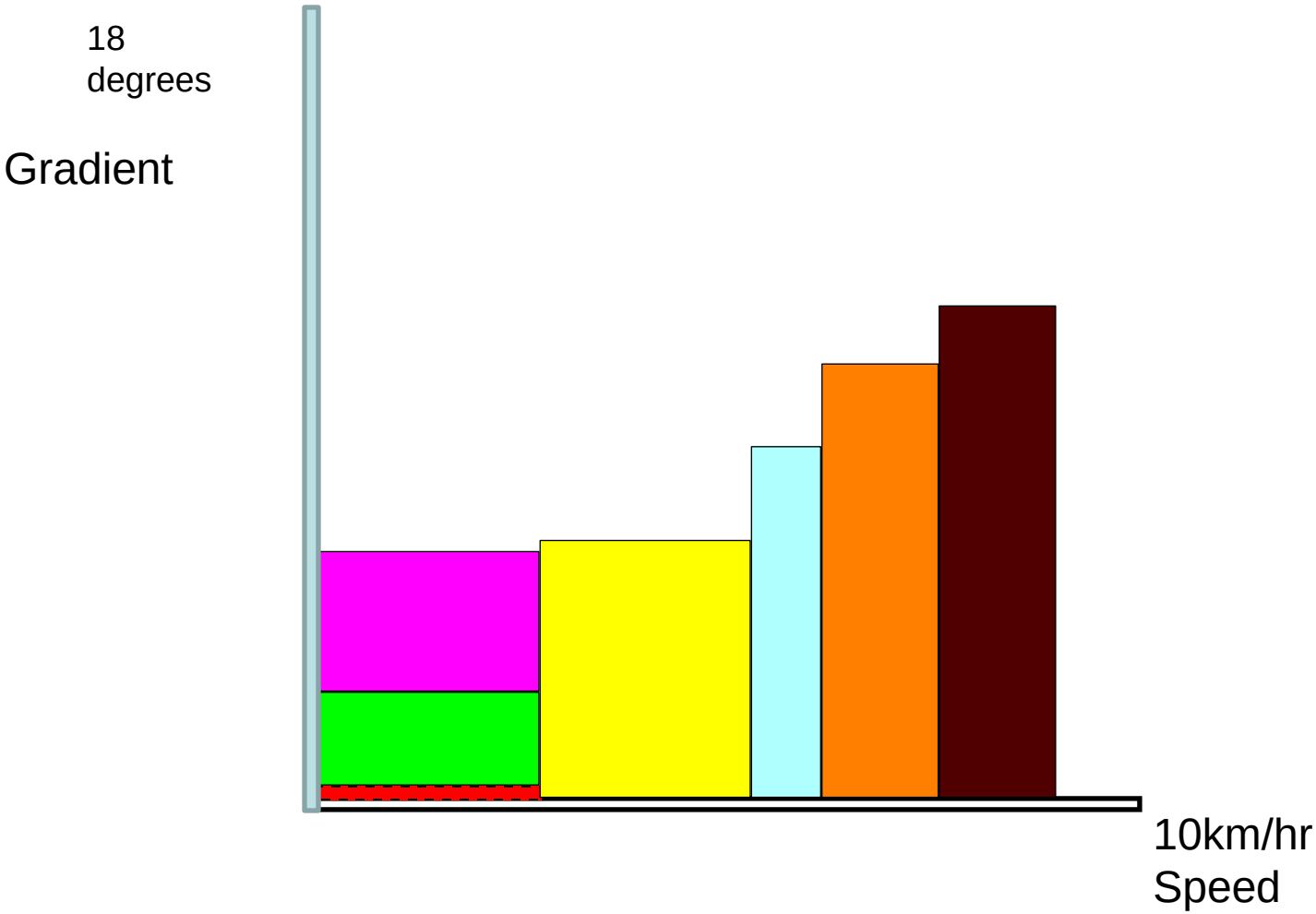


Why perform a stress test

- At stress blood flow in heart increases
- Cannot occur in stenotic vessels
- Less flow down these arteries (defect on scan)
- Returns to normal at rest (no defect on scan)



Stages of the Bruce protocol



Pharmacological stress

- Why might pharmacological stress be so useful?
- Not all patients can perform physical stress
  - The elderly
  - Arthritic
  - PVD, diabetes
  - Anaemic
  - Unfit

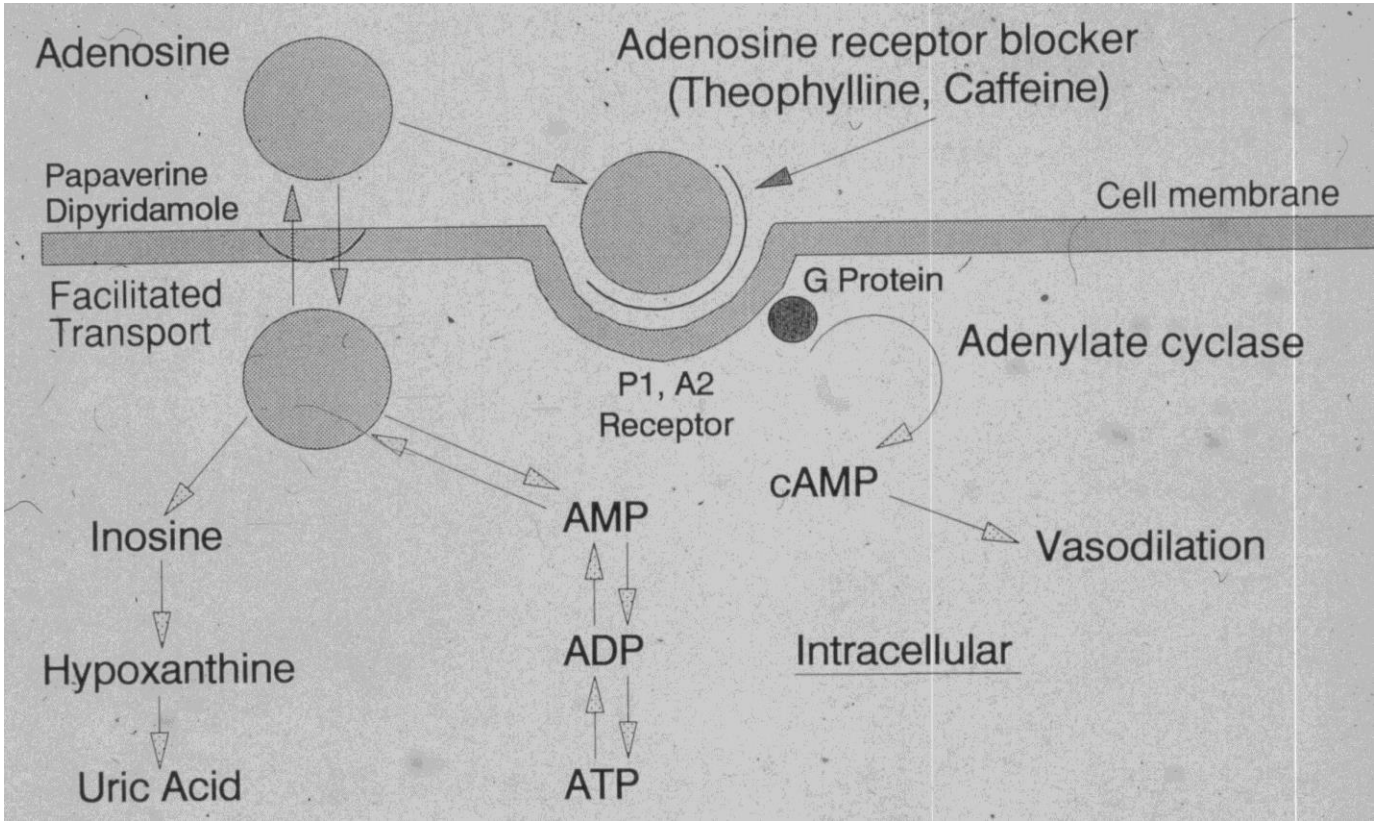
Pharmacological stress

- Main agents used
- A2 receptors
  - Dipyridamloe
  - Adenosine
- B1 receptors
  - Dobutaomine
  - Arbutamine

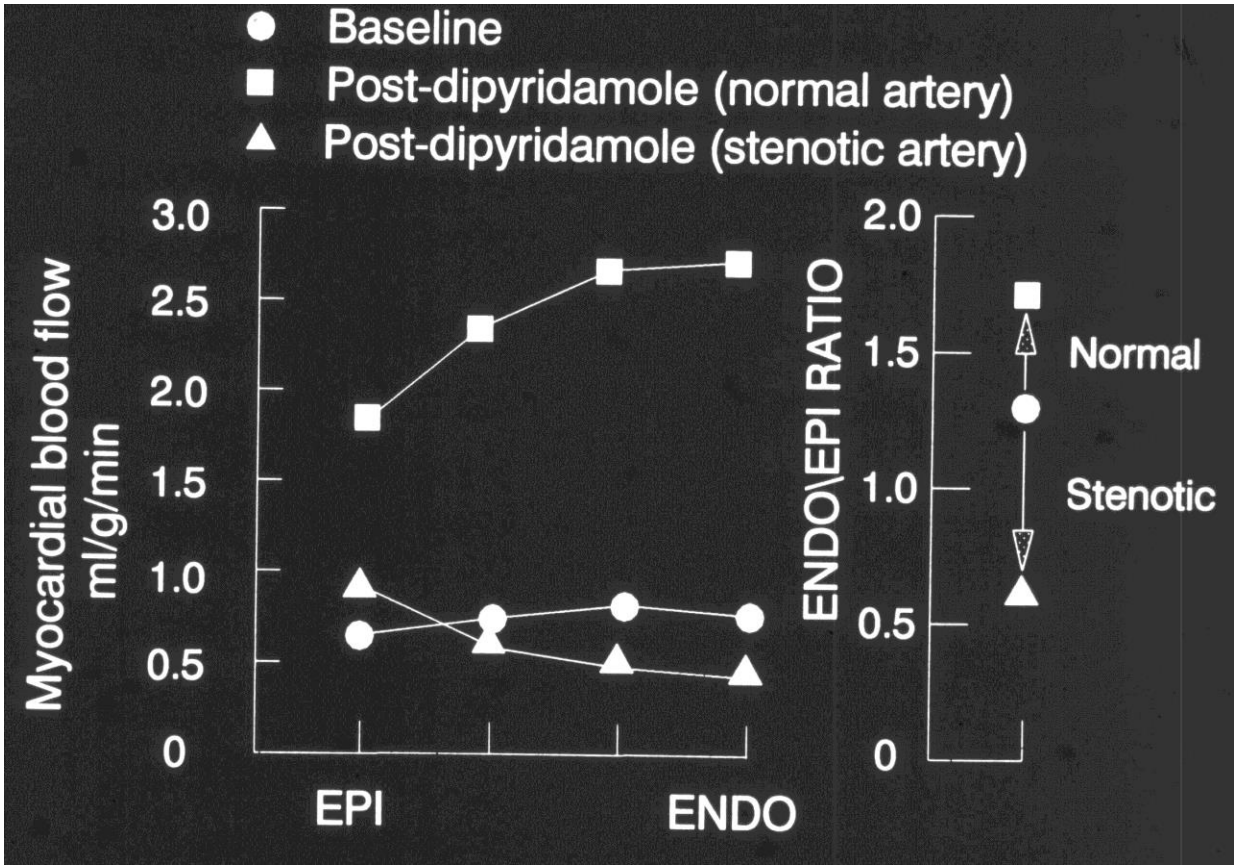
Why do vasodilators work

- Coronary artery vasodilataion is normal response to stress
- Increases flow during short diastole
- Mediated via cAMP
- Atherosclerotic vessels do not dilate
- Steal of blood from these vessels
- >50% drop in perfusion seen on SPECT (>90% needed for ecg)

How Vasodilators work



Effect of Dipyridamole on blood flow



Adenosine

- Works on A2 recepotrs directly
- Plasma half life 20-60 seconds
- Vasodilates via cAMP
- Contraindications
  - Asthma
  - 3rd degree heart block
- Relative contraindications
  - Wheezy bronchitis
  - 2nd degree heart block

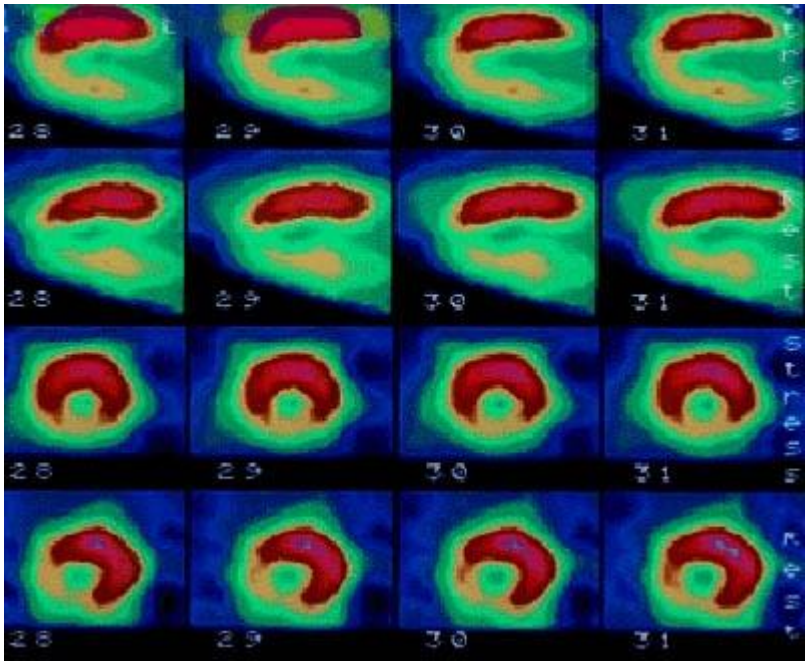
Dobutamine

- Works at beta 1 receptors
- Increase stroke volume > HR
- No need to reach Max predicted HR
- Contra-indications
  - Recent VF
  - Allergy to dobutamine
  - Critical aortic stenosis
- Relative contra-indications
  - Recent VT

Acquiring the image

- Remember need to have good quality image for diagnosis
- Look for patient movement correct or re-scan
- Look for attenuation
  - Breast-ant wall women
  - Diaphragm inf wall men

Inferior attenuation in a man



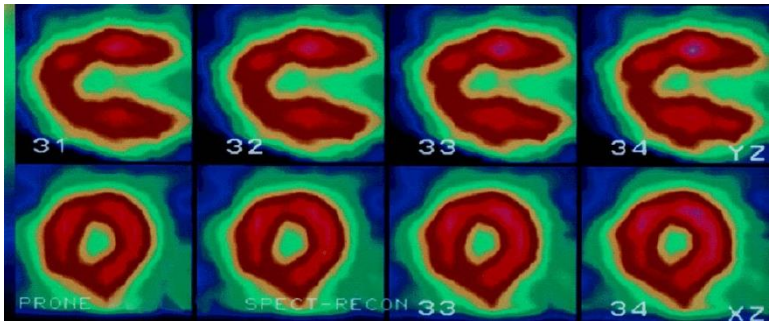


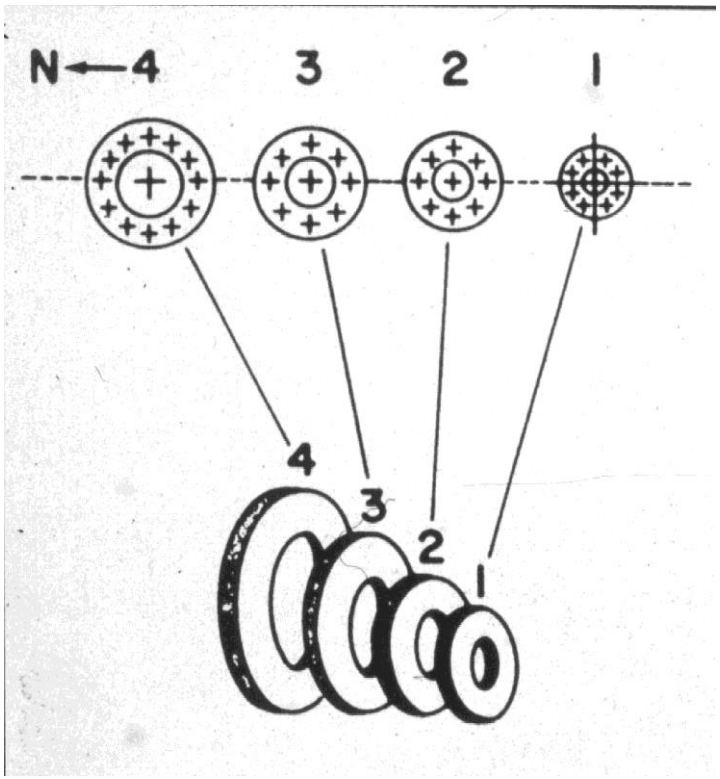
Image to left shows un attenuated image with apparent inferior defect in inferior wall. Above is the same patrent after attenuation correction.

Quantitative cardiac SPECT

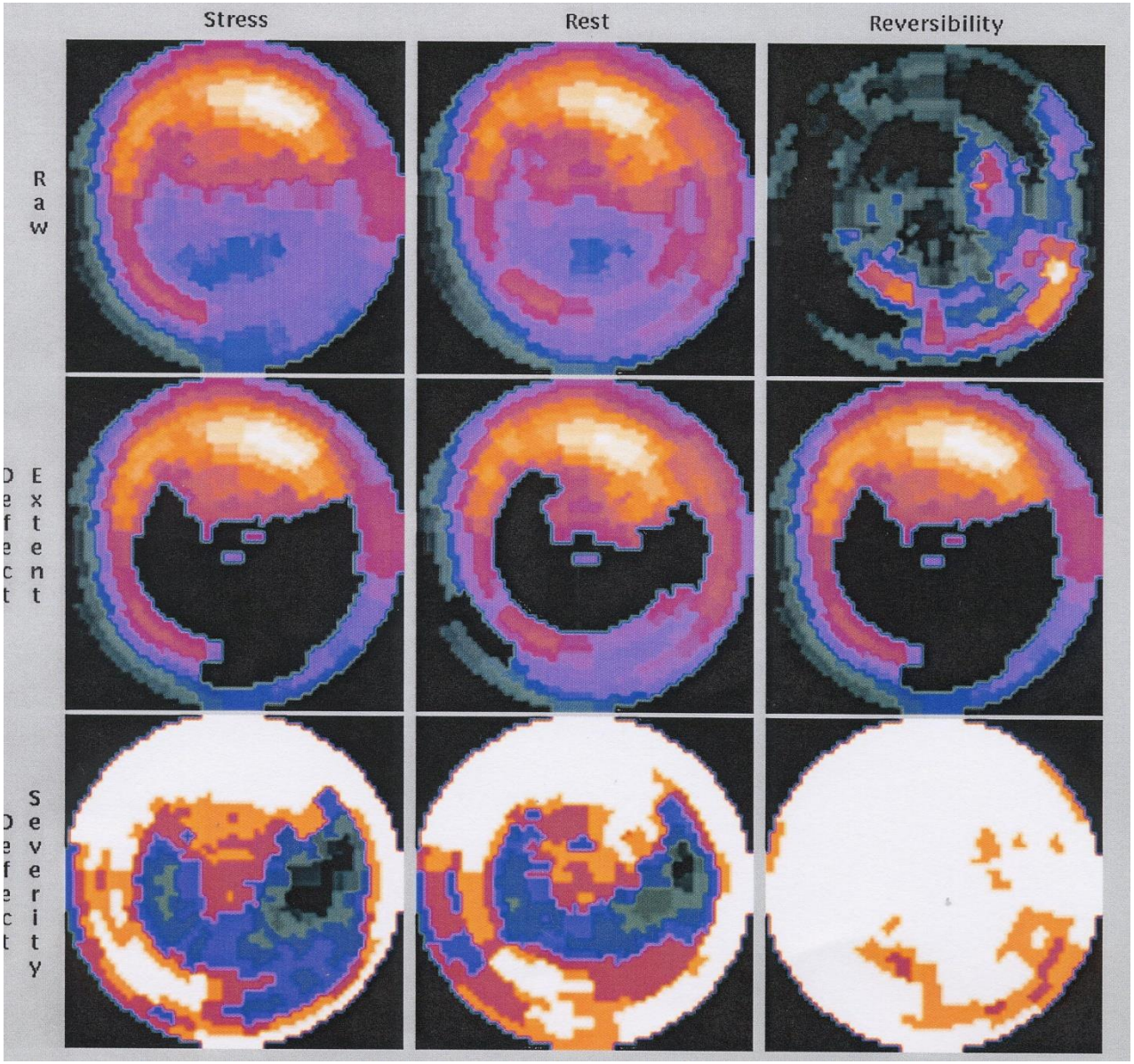
- Compares results of patient's scan with normal data base
- Controlled for gender, age, (occ race) tracer injection time and activity, also stress/rest
- Assigns >-2.5 s.d as defect
- Assigns improvement of >+1.5 s.d as reperfusion

Smei-quantification: Forming a bulls eye plot

Sequential rings of data used to build the bulls eye plot



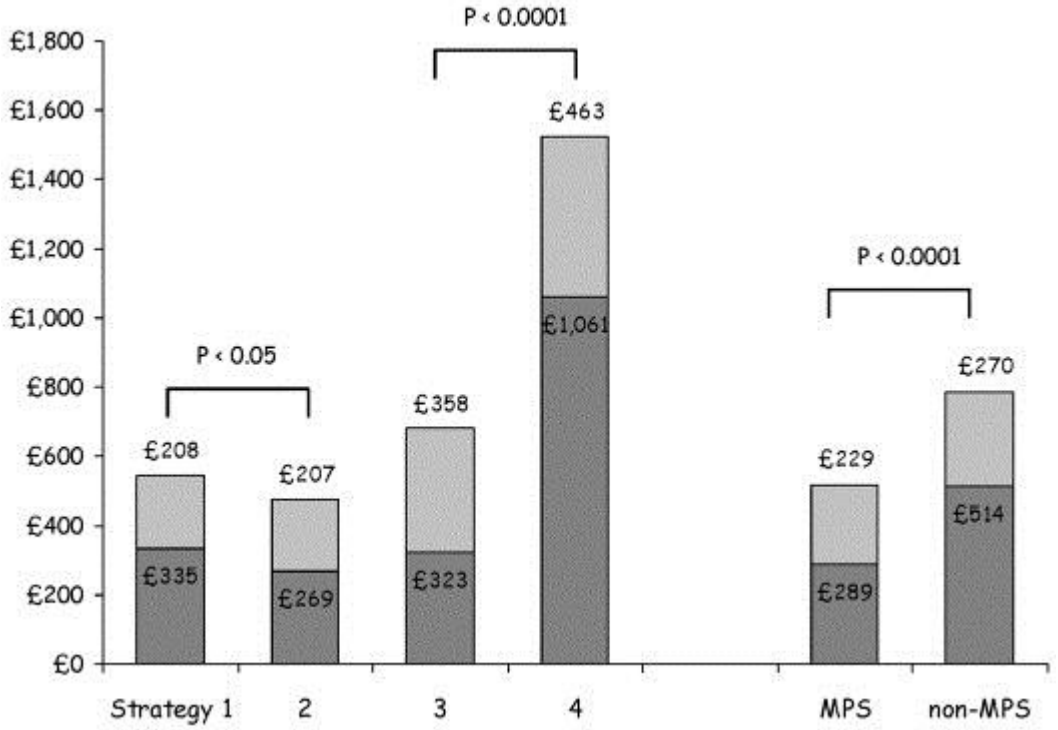
Polar “bullseye” plots-Emory



MPS has high NPV

- Myocardial perfusion scintigraphy has a high negative predictive value
- Even if stenosis on angiography a normal MPS means low risk
- Therefore MPS can be used to determine who gets treatment
- If MPS used in all patients in EU savings would be 4 billion Euros/year-EMPIRE

Costs of investigating chest pain- EMPIRE



1=eecg, 2=eecg+MPS, 3=MPS+angio, 4=angio

Risk stratification

- Men more at risk than women at any age
- Smokers more at risk
- High cholesterol at risk
- Diabetics at high risk (may also be without symptoms)
- Poor haemodynamic response to stress

Risk stratification

- Advanatges of MPS
  - Gives good information on function
  - Accurate
  - Reproducable
  - Understandable
  - Quantifiable (Bullseye)

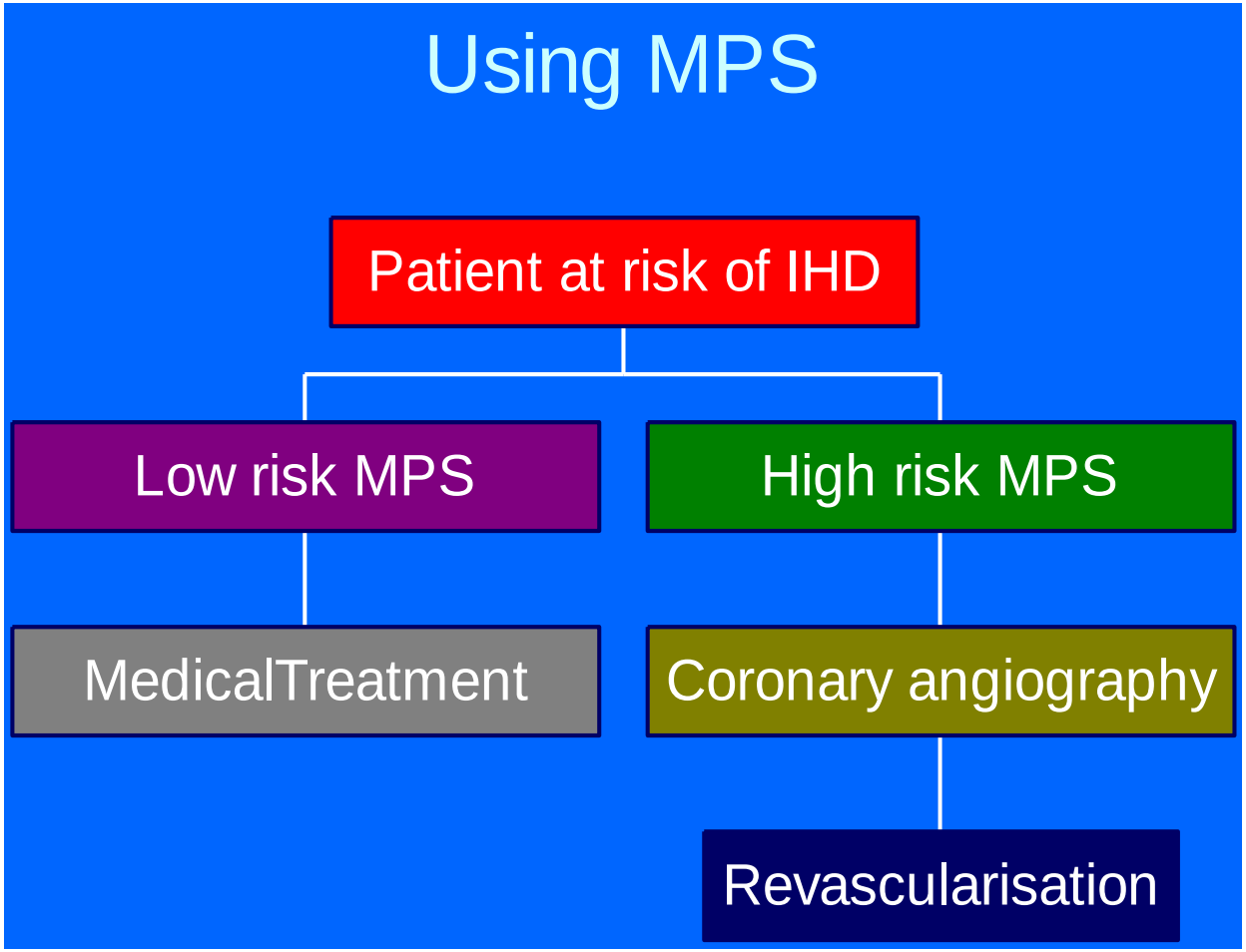
Risk stratification-MPS

- The risk of cardiac event is linked to volume of myocardium at risk
- If more than 1 coronary artery territory involved, greater the risk
- If LVEF reduced the greater the risk
- LV dilatation increase risk
- Lung uptake increases risk

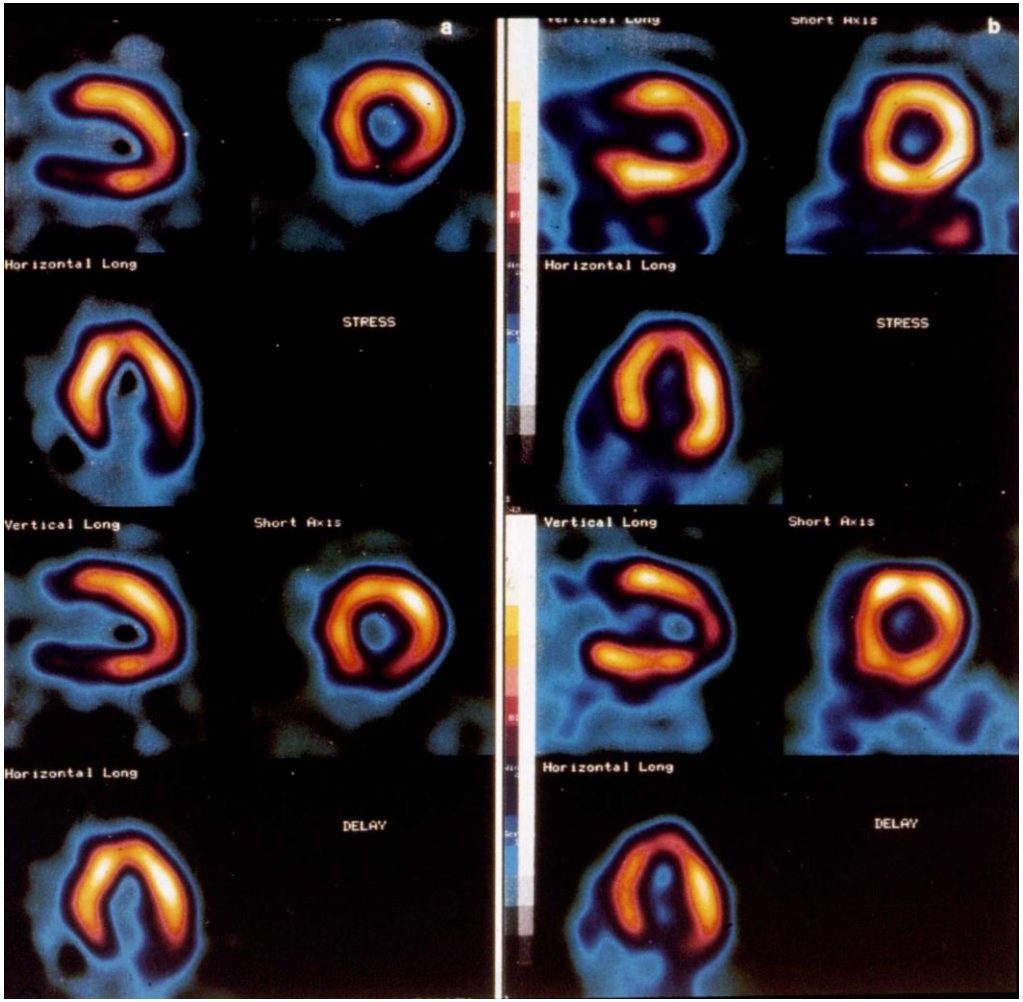
Risk assessment using Tl-201

- Kaul et al JACC, 1988
- Identified main risk factors from Tl-201 MPS
  - Highest risk Inc lung activity
  - Then > 1 coronary art ter involved
  - Then reduction in LVEF
  - Then size of defects

Using MPS in practice



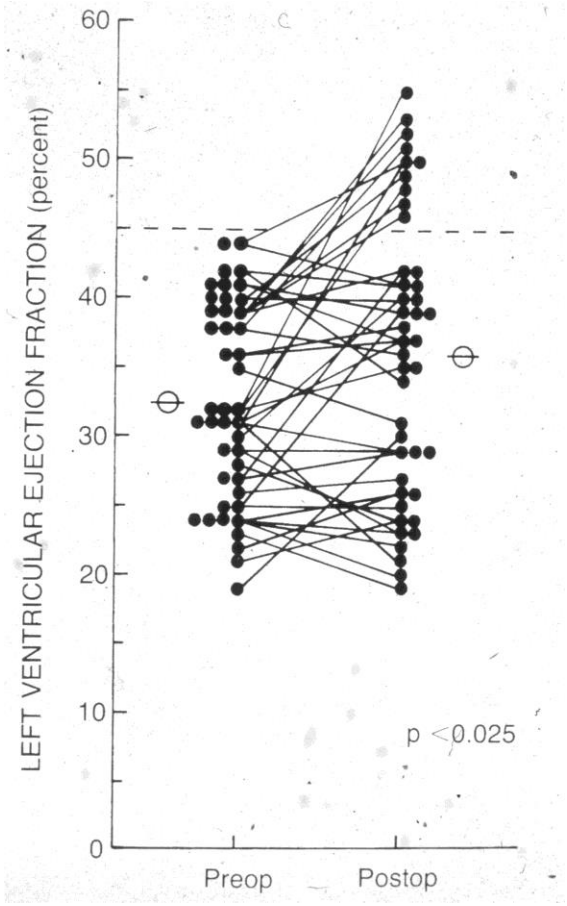
Showing improvement in ischaemic myocardium



Change in LVEF after CABG

Use of Gated LVEF before and after CABG

New work looking at gated SPECT un same context



Where is nuclear cardiology best?

- Gate keeper for angiography
- Diabetes
- Women

Diabetes and silent ischaemia

- Araz et al Acta Diabet 20004
- Reviewed 116 type II diabetics
- 15% had ischaemic changes on MPS
- 10% patients no chest pain
- Recommended screening all type II diabetics with HBA1> 9%

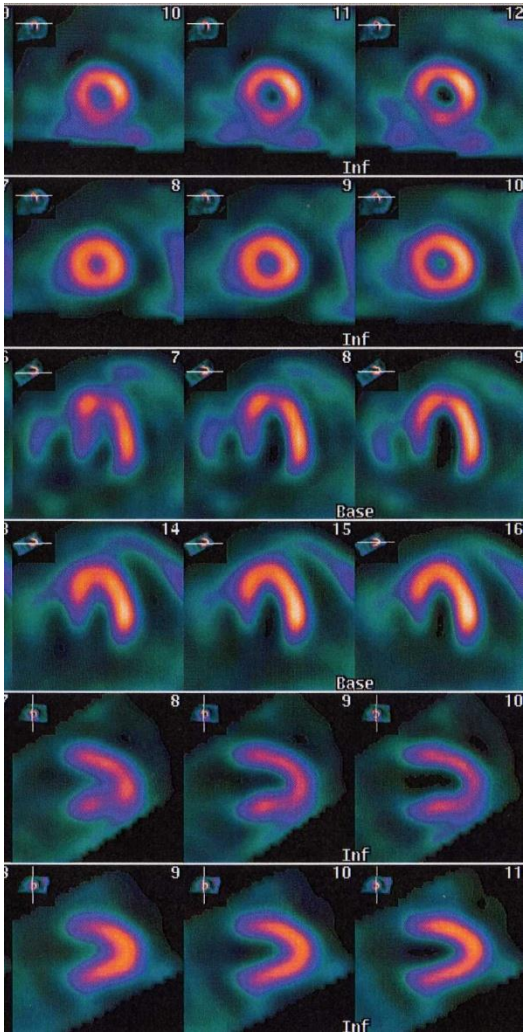
Women

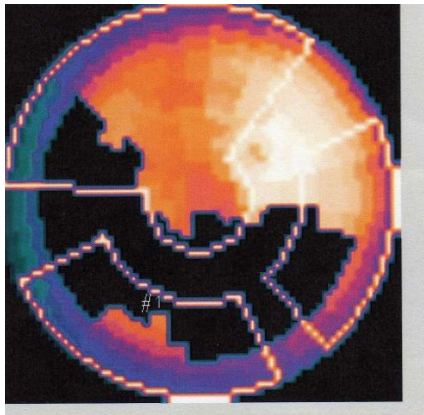
- In 1970 Common belief women did not have IHD
- Did not explain major cause of death in women in Europe
- Symptoms atypical (may be food related)
- Risk factors diabetes, hypertension, obesity
- Racial factors – Africans & South Asians worse if then more to Europe or North America

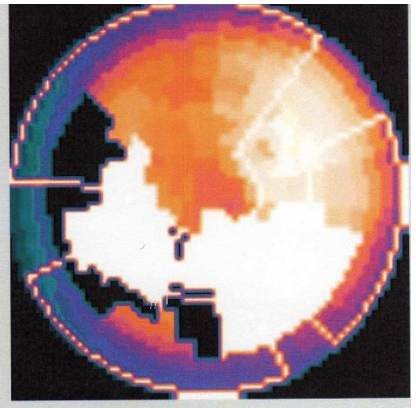
Women and heart disease

- Not able to do physical stress so easily
- Problems of breast attenuation in MPS
- Despite this clear evidence that a normal MPS in women= low risk of cardiac event and abnormal MPS = rate of cardiac event similar to men (Hachamovitch et al JACC 1996, Berman et al JACC 2003)

A women with extensive ischaemia







	Def 1	Def 2	Def 3	Def 4	Def 5	Totals
Stress Defect (as % of total myocardium or of coronary territory):						
Total:	38%	0%	0%	0%	0%	38%
LAD:	20%	0%	0%	0%	0%	20%
LCX:	27%	0%	0%	0%	0%	27%
RCA:	47%	0%	0%	0%	0%	47%
Reversibility (as % of total defect or of defect in coronary territory):						
Total:	76%	0%	0%	0%	0%	76%
LAD:	59%	0%	0%	0%	0%	59%
LCX:	100%	0%	0%	0%	0%	100%
RCA:	56%	0%	0%	0%	0%	56%

There are 182 pixels blacked out (38%), of 481 total pixels

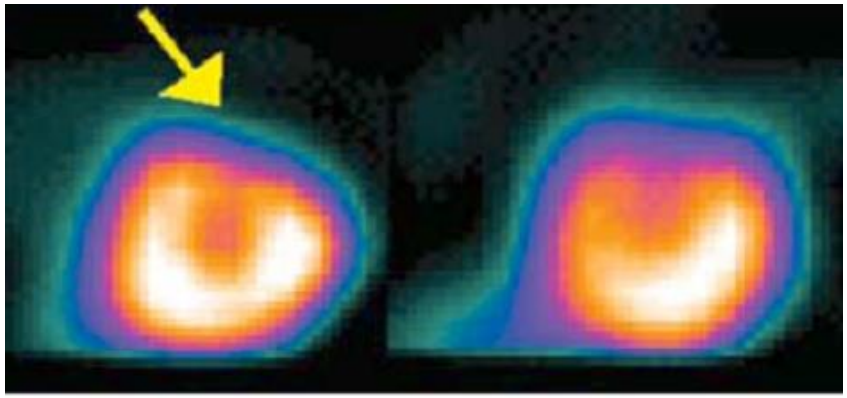
Stress Total Severity Score = 647

Probability of Survival: 1 yr: 81% 2 yr: 77% 3 yr: 63% 4 yr: 42%

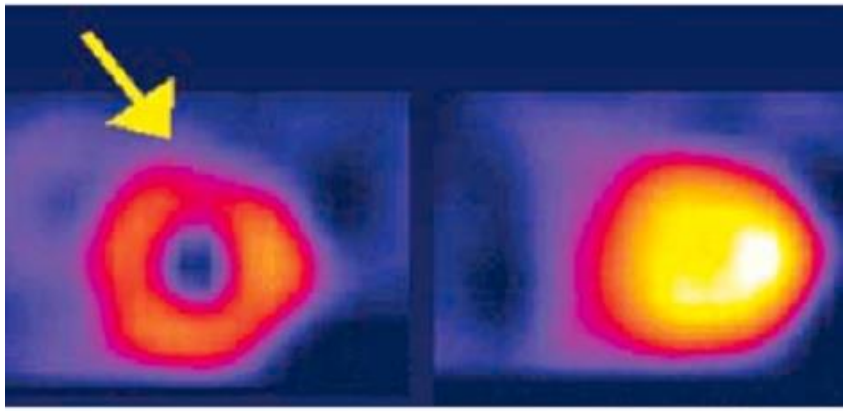
Looking at attenutaion

- Review the cine mode planar acquisition
- See if attenuation obvious from some angles
- Also should affect the same site at stress and rest (in women breast must be in same position)
- Differential of a fixed defect MI or attenuation
- A-C does appear to introduce mew artefacts
- However gated study if moves it was attenuation if akinetic MI most likely

Gated SPECT MPS ?attenuation

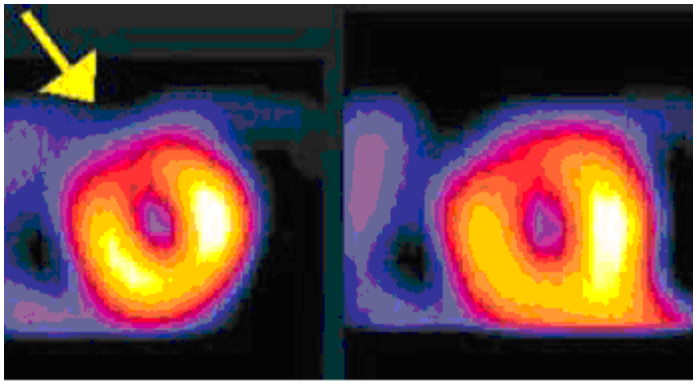


Stress Rest

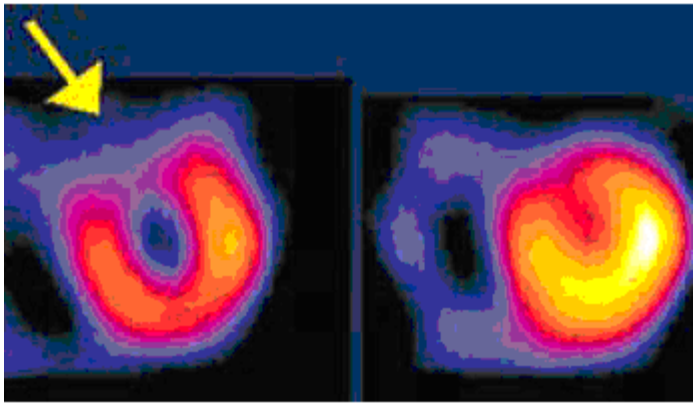


Diastole Systole

Gated MPS SPECT ischaemia



Stress Rest

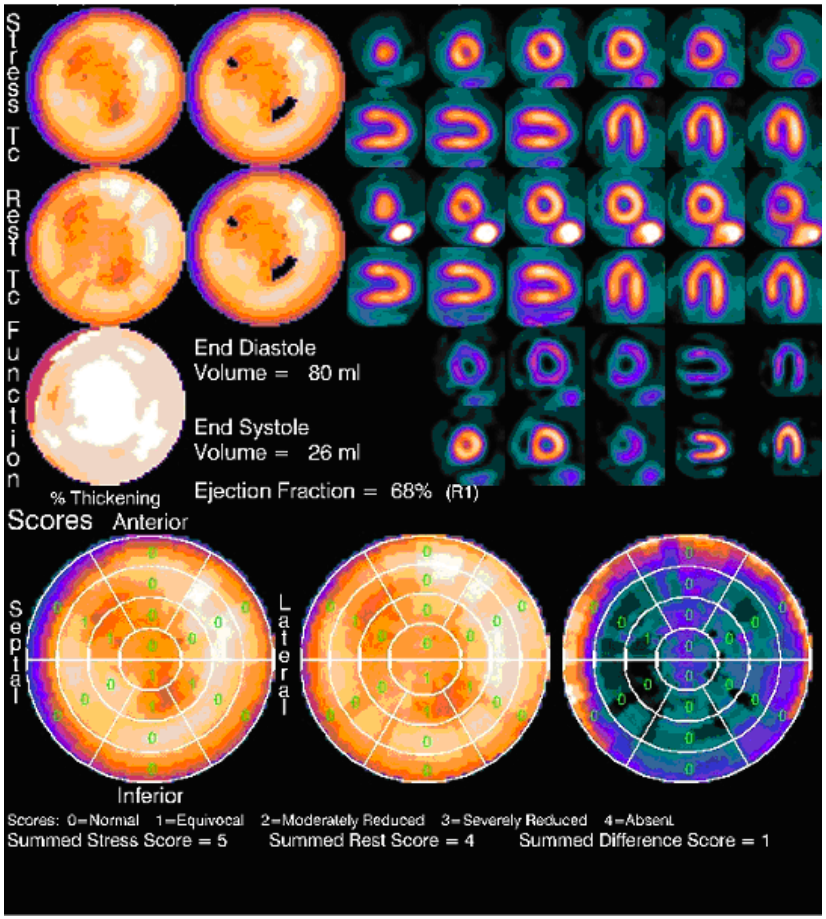


Diastole Systole

Quantitative gated studies

- Programmes such as QGS
- Used to analyse LVEF, EDV and ESV
- Also can provide imaging of wall motion
- Reduced regional wall motion can be due to
  - Severe ischaemia
    - Hibernating
    - Stunning
  - Infarct

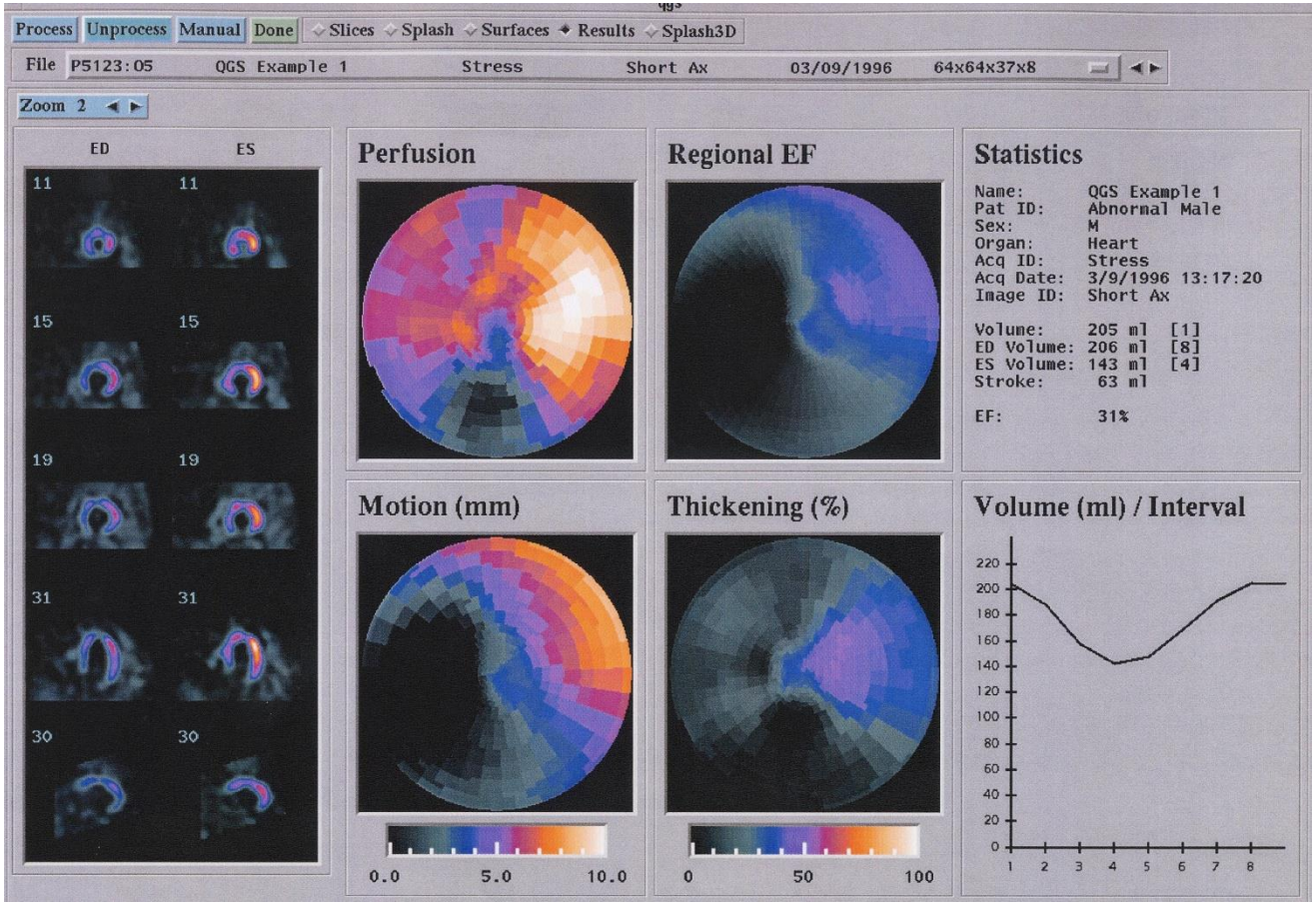
Problems of plotting 4D on 2D



Hibernation

- Defined as chronic severe ischaemia
- Hypoxic tissue
- Not able to burn lactate through Kreb cycle
- Able to survive on phosphorylation of glucose alone
- Cannot contract
- So (especially in delayed imaging) some perfusion but no movement seen on gated SPECT

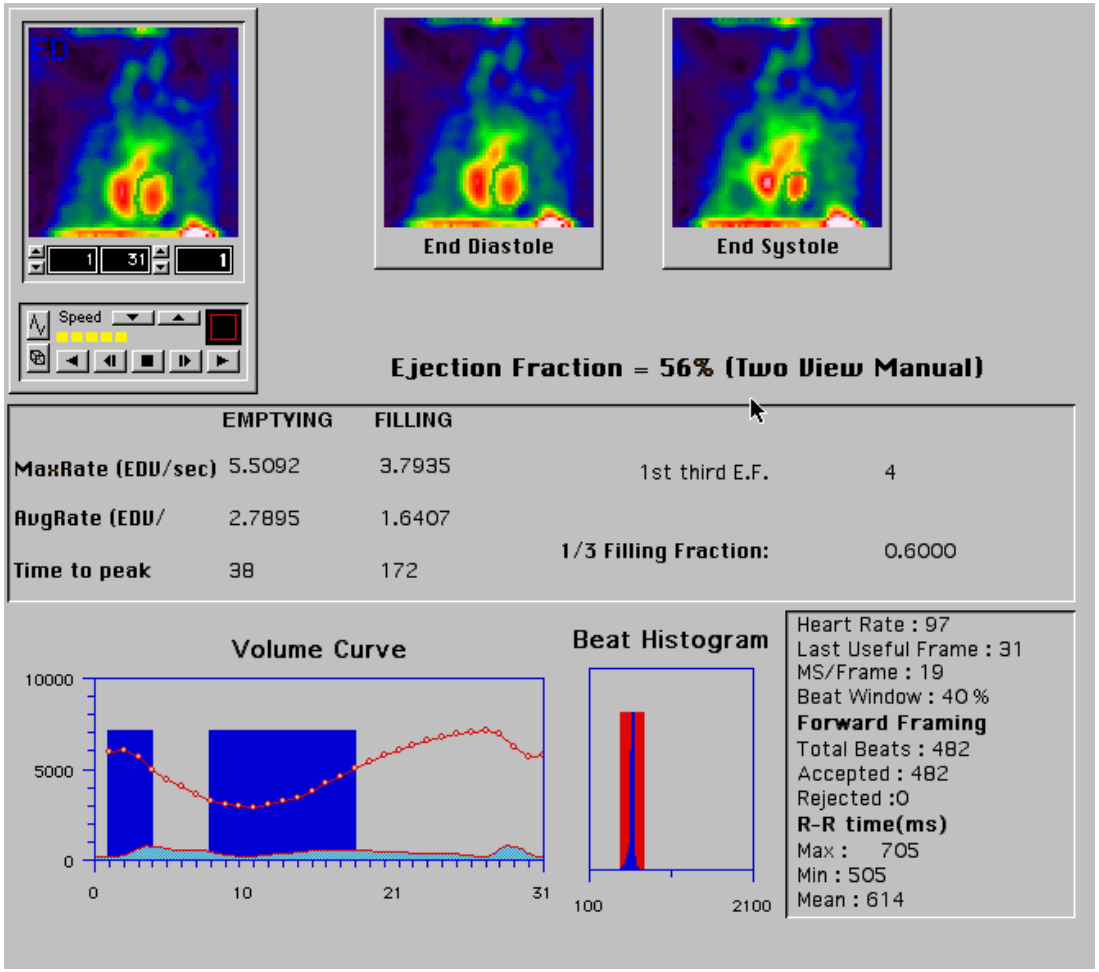
Antero-septal hibernation



Assessment of cardiac function

- Use of gated studies
- Can be done on RNV and MPS
- Improve specificity of MPS scans
- Look for wall motion abnormalities-Infarct, ischaemia, stunning and hibernation
- Look for dyskinesia – ventricular aneurysm
- Global function to look at prognosis

Cardiac MUGA



MUGA vs ECHO

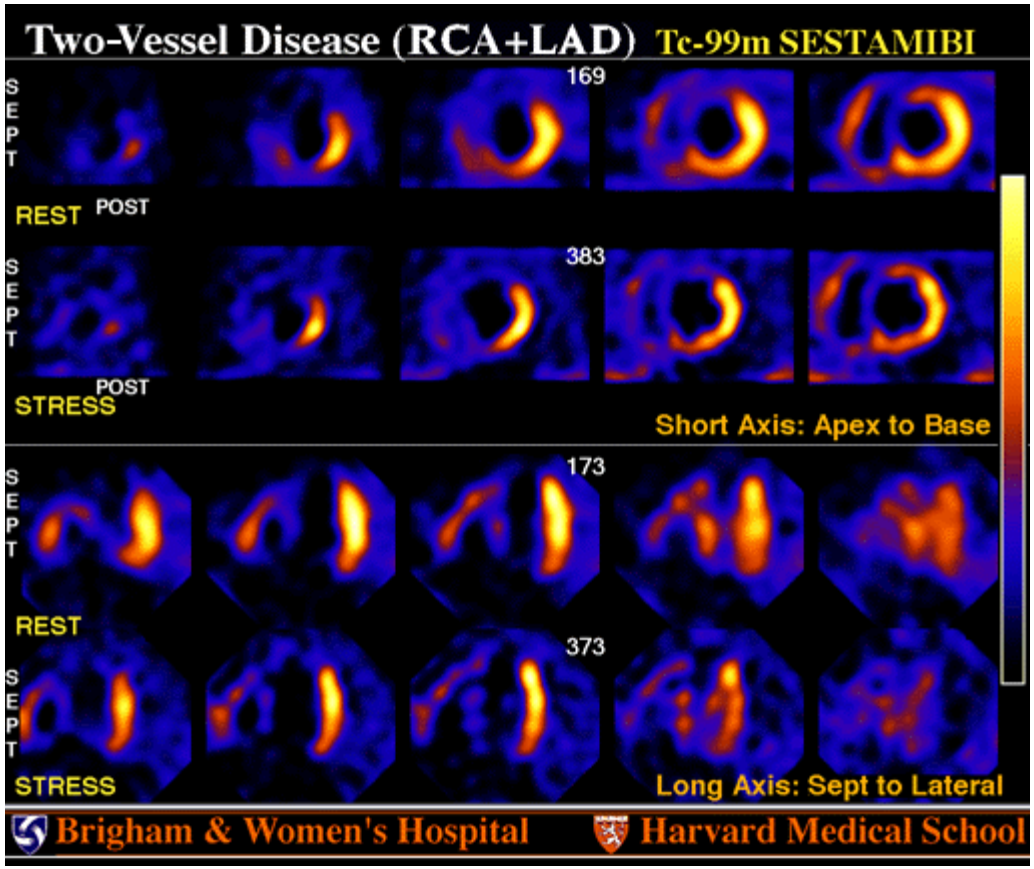
- MUGA
- Accurate LVEF
- Need special equipment and trained staff
- Reproducable
- Uses radiation

- ECHO
- Needs special equipment and trained staff
- No radiation
- Can see valves as well
- LVEF not so accurate

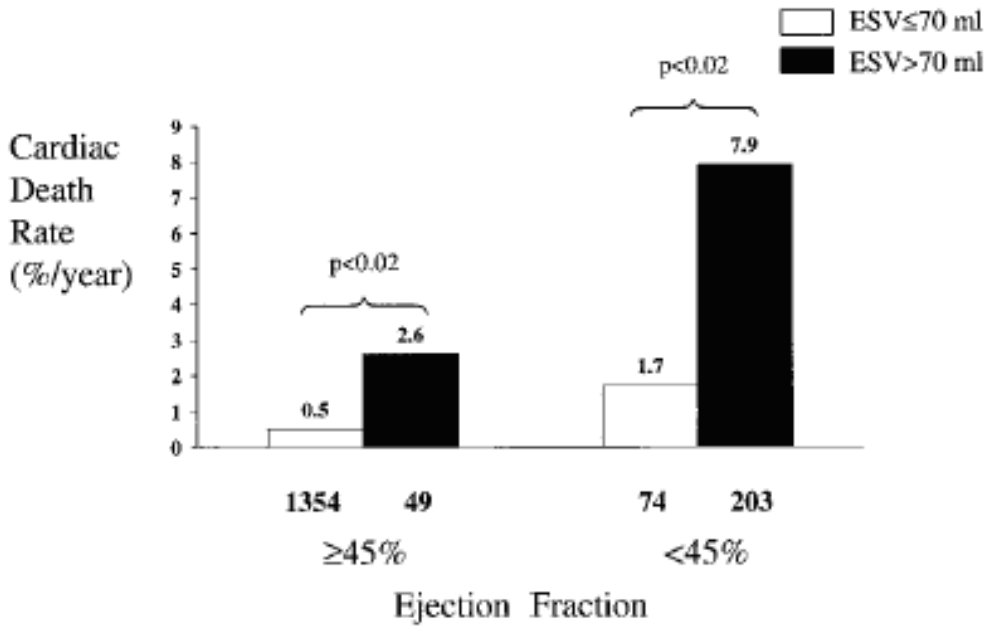
Prognostication with gated studies

- Reduction of LVEF below 50% is abnormal
- Reduction of LVEF below 40% means significant reduction in LV function
- Reduction of LVEF below 30% means symptoms
- Reduction of LVEF below 20% means symptoms at rest
- Reduction of LVEF below 10% means transplant or death
- If ventricular aneurysm all these are worse

Note large defect and spalying of walls to apex suggesting aneurysm

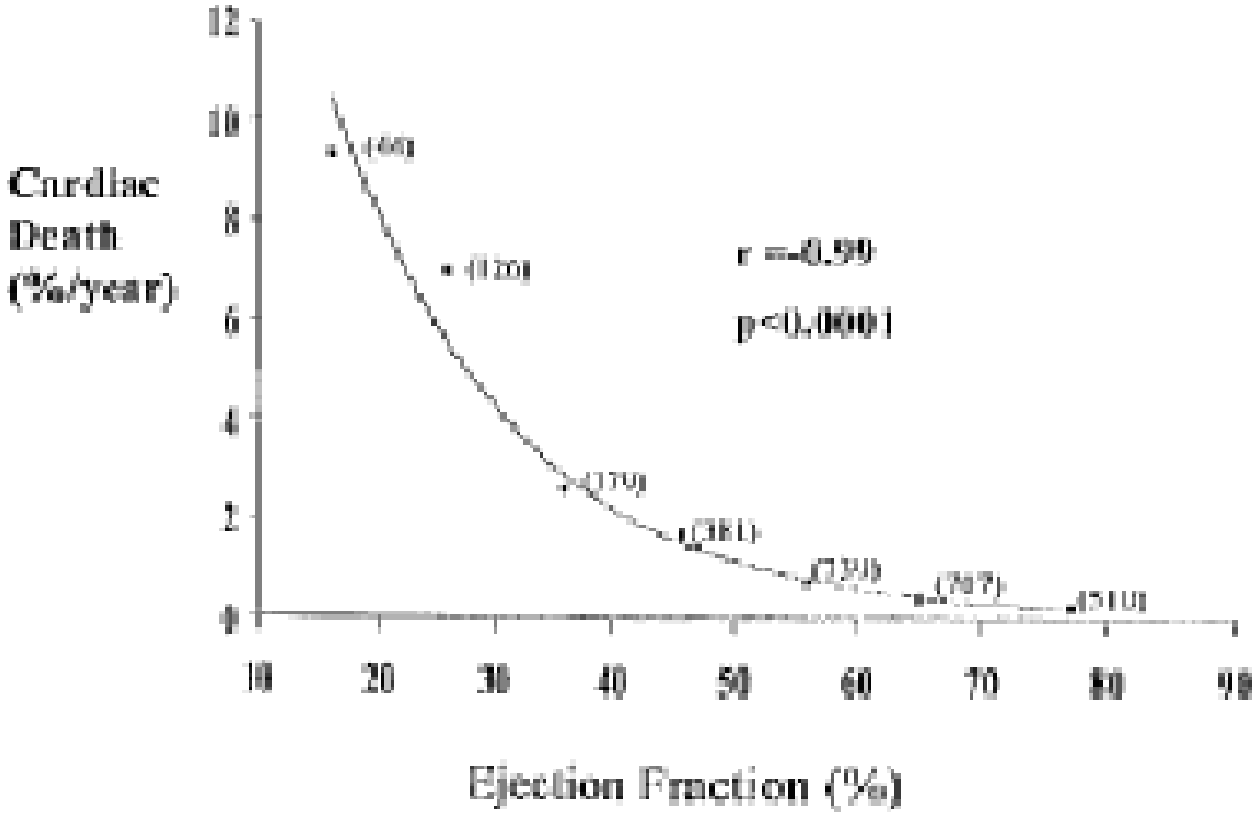


Both LVEF and LV size predicts survival



Cardiac death rate (%/year) as a function of EF and ESV (Source: SharirT, Germano G, Kabanaugh PB, et al: Incremental prognostic value of post-stress left ventricular ejection fraction and volume by gated myocardial perfusion single photon emission computed tomography. Circulation 100 (10): 1035-1042, 1999).

Death rate by LVEF



Sharir T, Germano G, Kang X et al. J Nucl Med 2001; 42:831-837

Why PET?

- Improved resolution-not really required in cardiology
- Improved sensitivity – this may be important-financially as reduced acquisition time
- Improved attenuation correction-good
- Look at metabolism-could be very good

F-18 FDG

- Most commonly available PET radiopharamceutical
- Uptake dependent on glucose drive in cells
- Related to hypoxia
  - Glucose to lactate (no O_2) = 4ATP per molecule
  - Glucose to Krebs cycle =32 ATP per molecule
- So ischaemic tissue needs lots of glucose but remember in diabetics competitive uptake so need blood glucose <6mmol/l

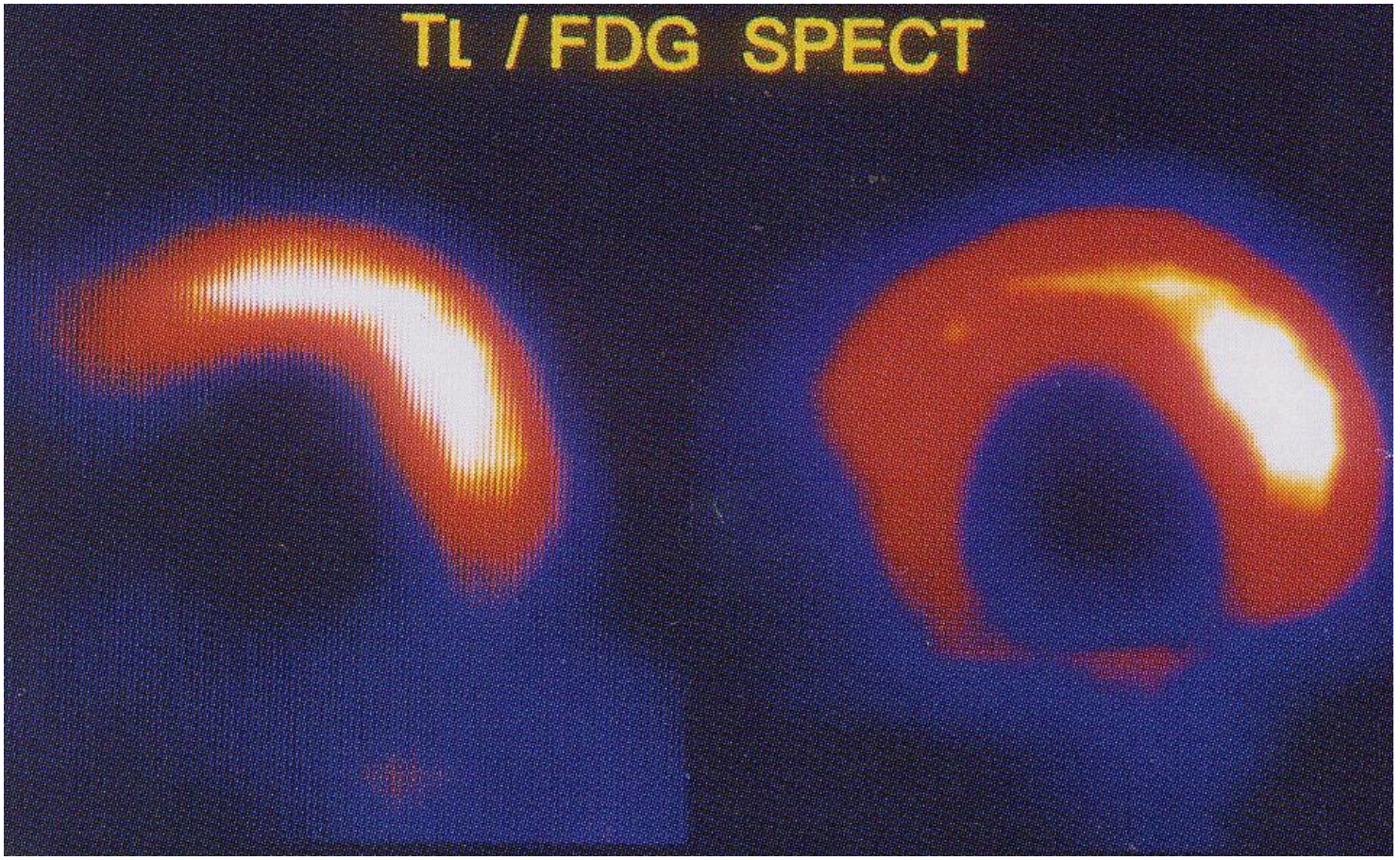
Viability

- In patients with severe ischaemia identification of viable heart very important
- Revascularisation may result in improvement in flow and over time return of function
- Prognosis dependent on LVEF in these patients is viable myocardium not improved 32% 1 year survival vs 7% if improved (Dy Carli et al JTCS 1998)
- F-18 FDG can find that viability

Perfusion and viability

- Viability found with F-18 FDG (where uptake may be increased in severe ischaemia)
- How about perfusion
  - N-13 H_3
  - Rb-82
- However though not perfect can use single photon for perfusion

SPET and PET



FDG in action

- Wu et al Kyoto JNM 2007
- Looked at 41 patients with severe IHD
- Using Tl-201/FDG PET mismatches identified (heart divided into 17 segments)
- 394 viabible segments per heart were identified in 31 patients
- 29 had CABG, 76% of these had an improvement of >5% in LVEF

FDG in viability

- Slart et al Groningen JNC 2006
- 213 segments in 31 patients (17 segments per patient) were imaged with F-18 FDG before and just after CABG
- An increase in F-18 FDG uptake of more than 50% post surgery predicted improvement in LVEF in 93% of cases (specificity 85%)

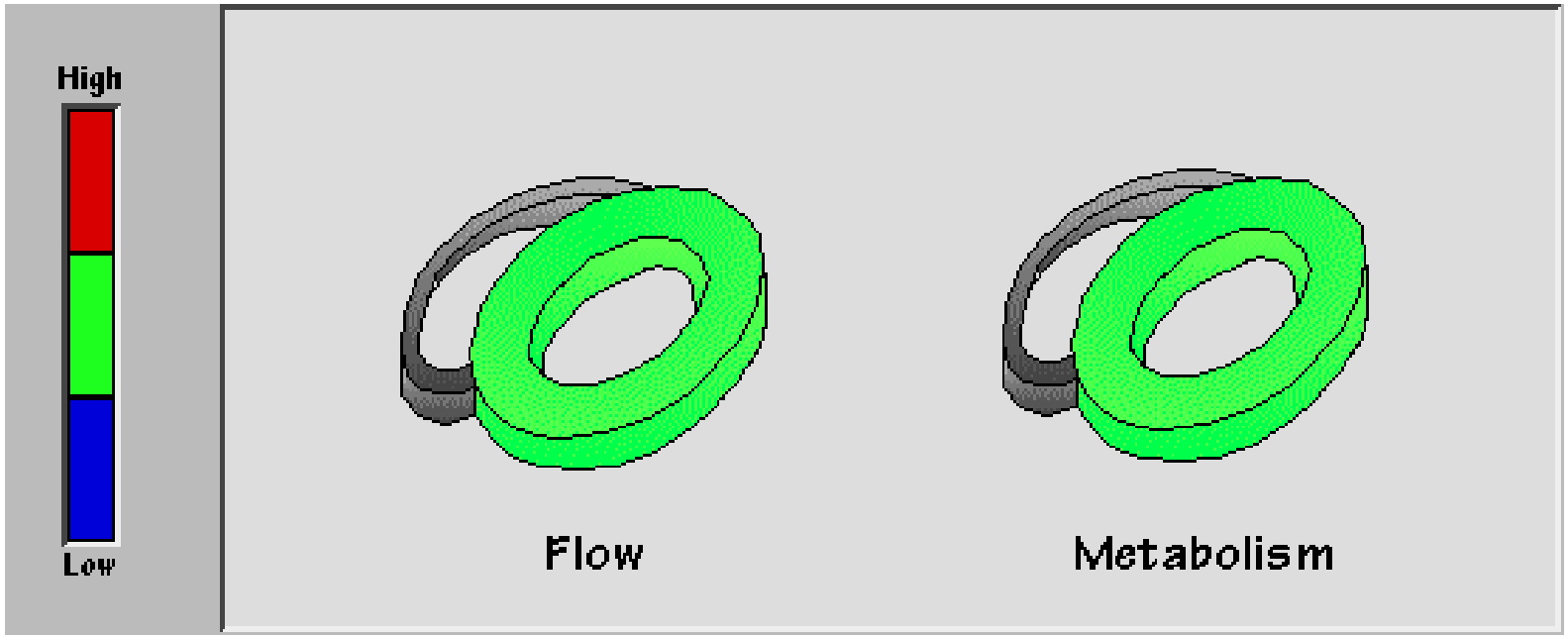
Comparing NH_3 and F-18 FDG

- Slart et al Groningen EJNMMI 2006
- Used combination of NH3 and F-18 FDG PET to determine areas of viability (reduced NH_3 with normal or raised F-18 FDG) or normal NH_3 but raised F-18 FDG)
- 47 patients with severe IHD
- In 90% of these PET predicted an improved LVEF post surgery

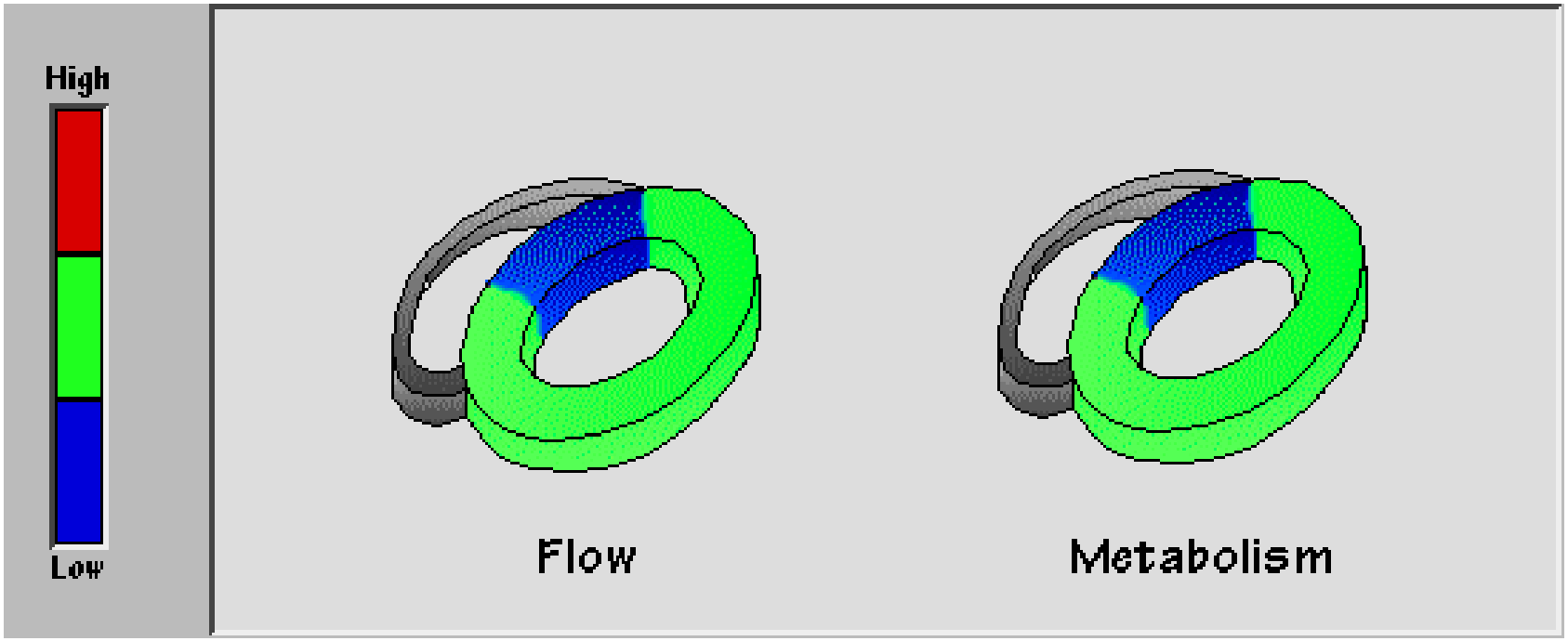
What can we see

- What follows is a series of perfusion maps of perfusion and viability
- Available on line from Bringham and Womens's hospital in Boston
- Only illustrative examples

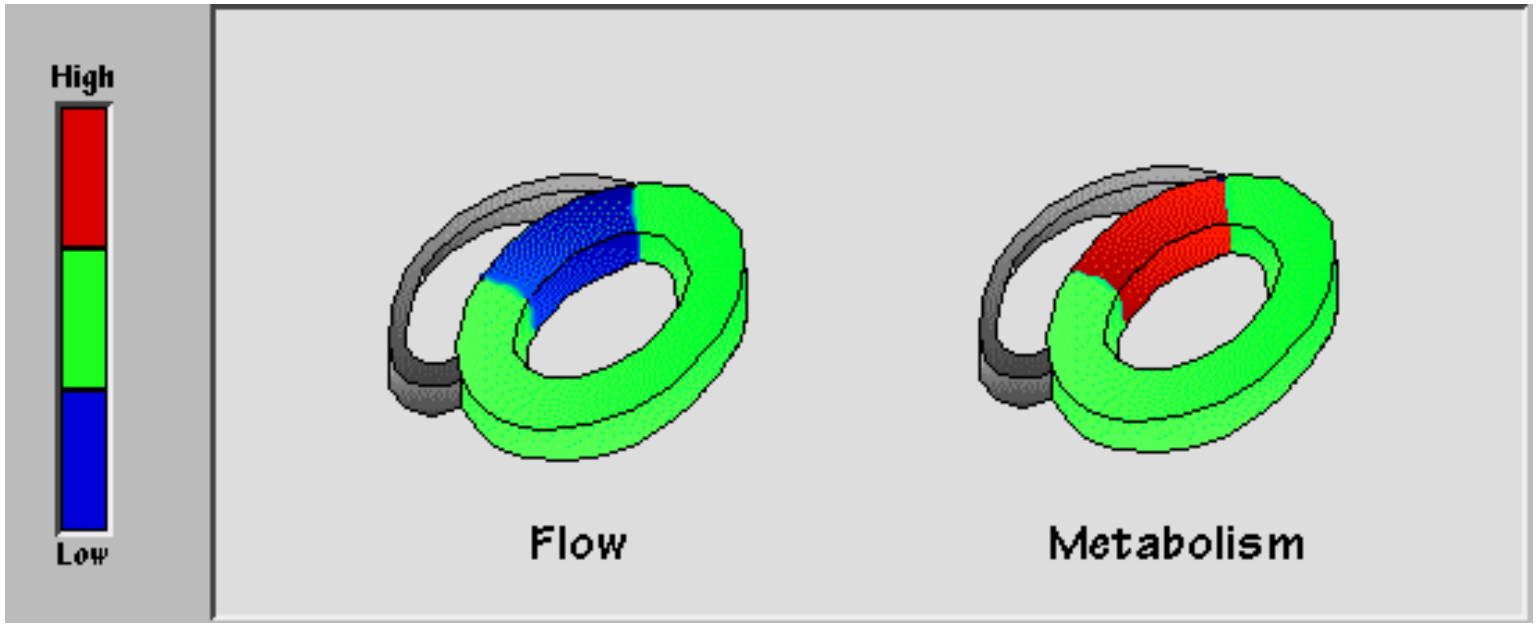
Normal



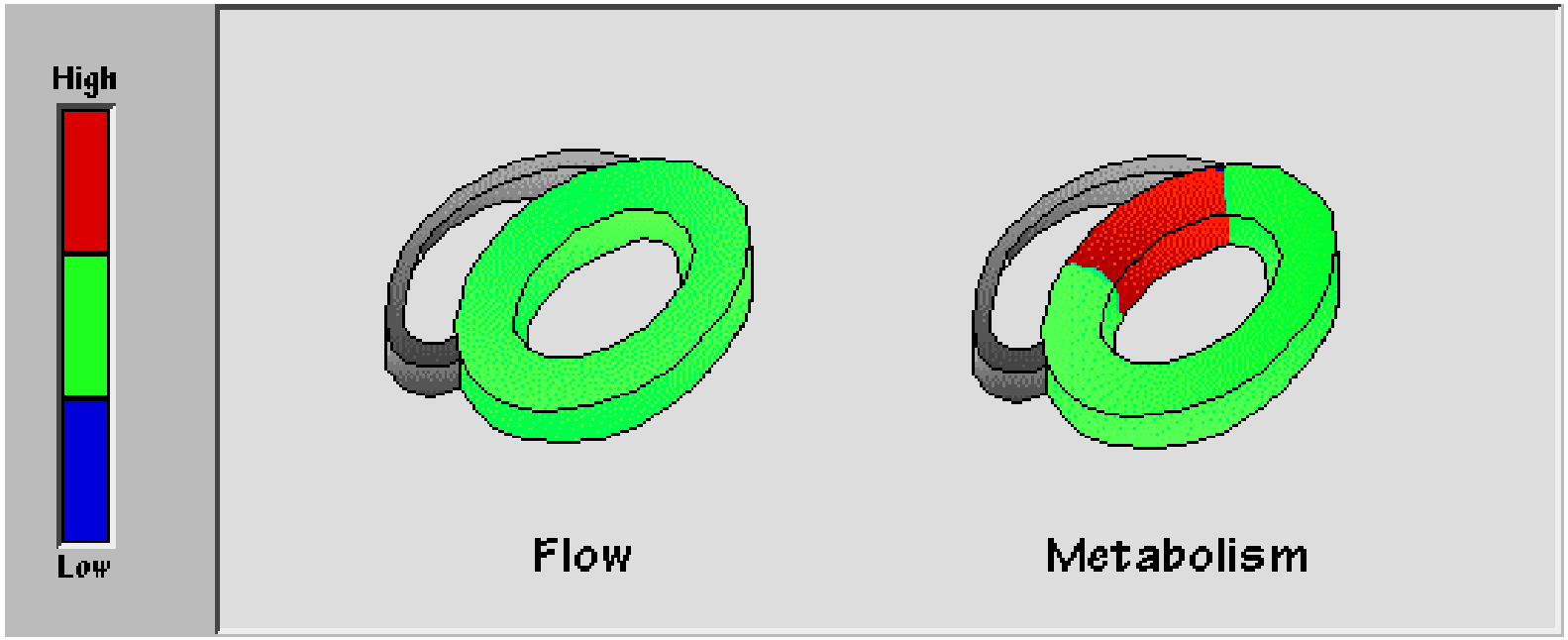
Infarct



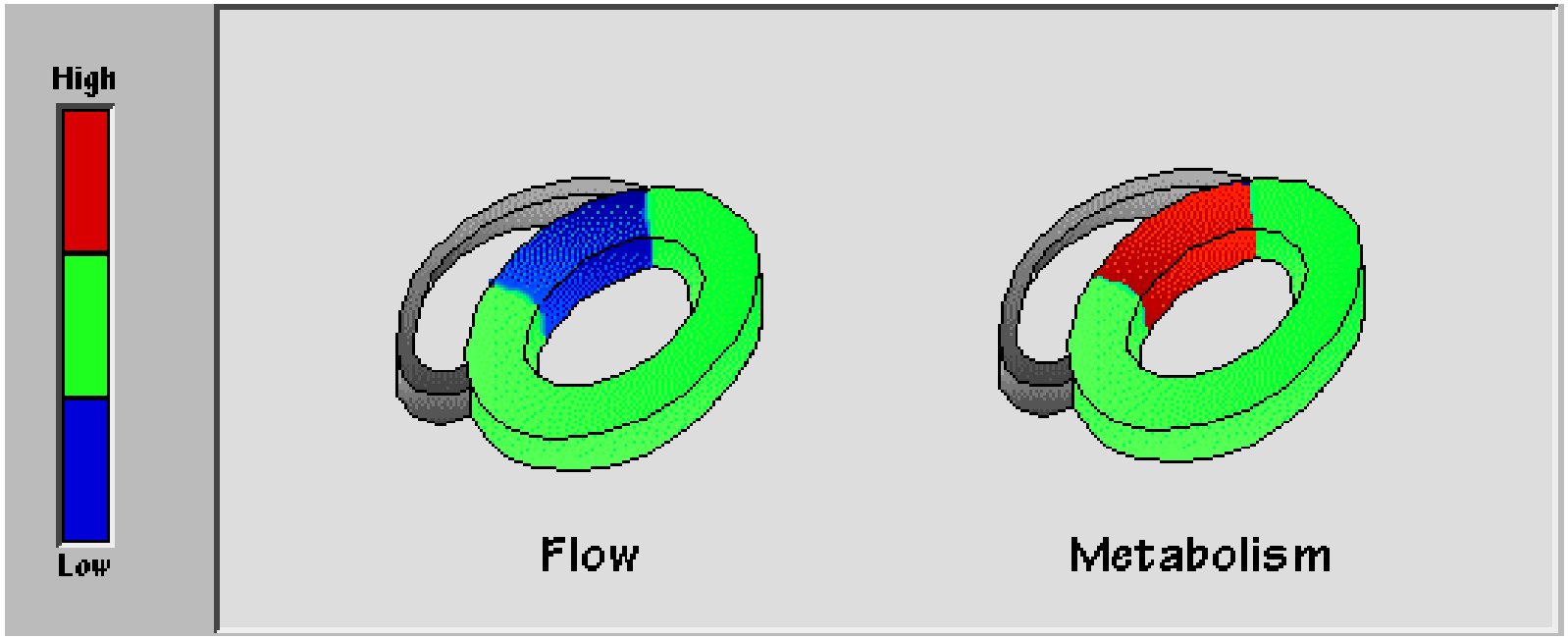
Viability



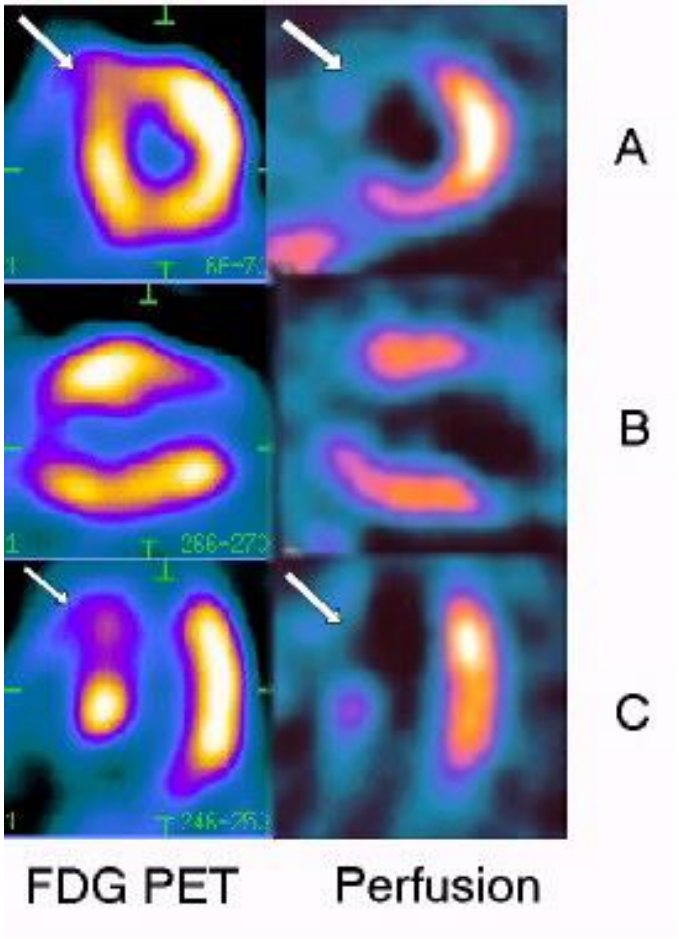
Hibernation



Cardiomyopathy



In reality what it looks like

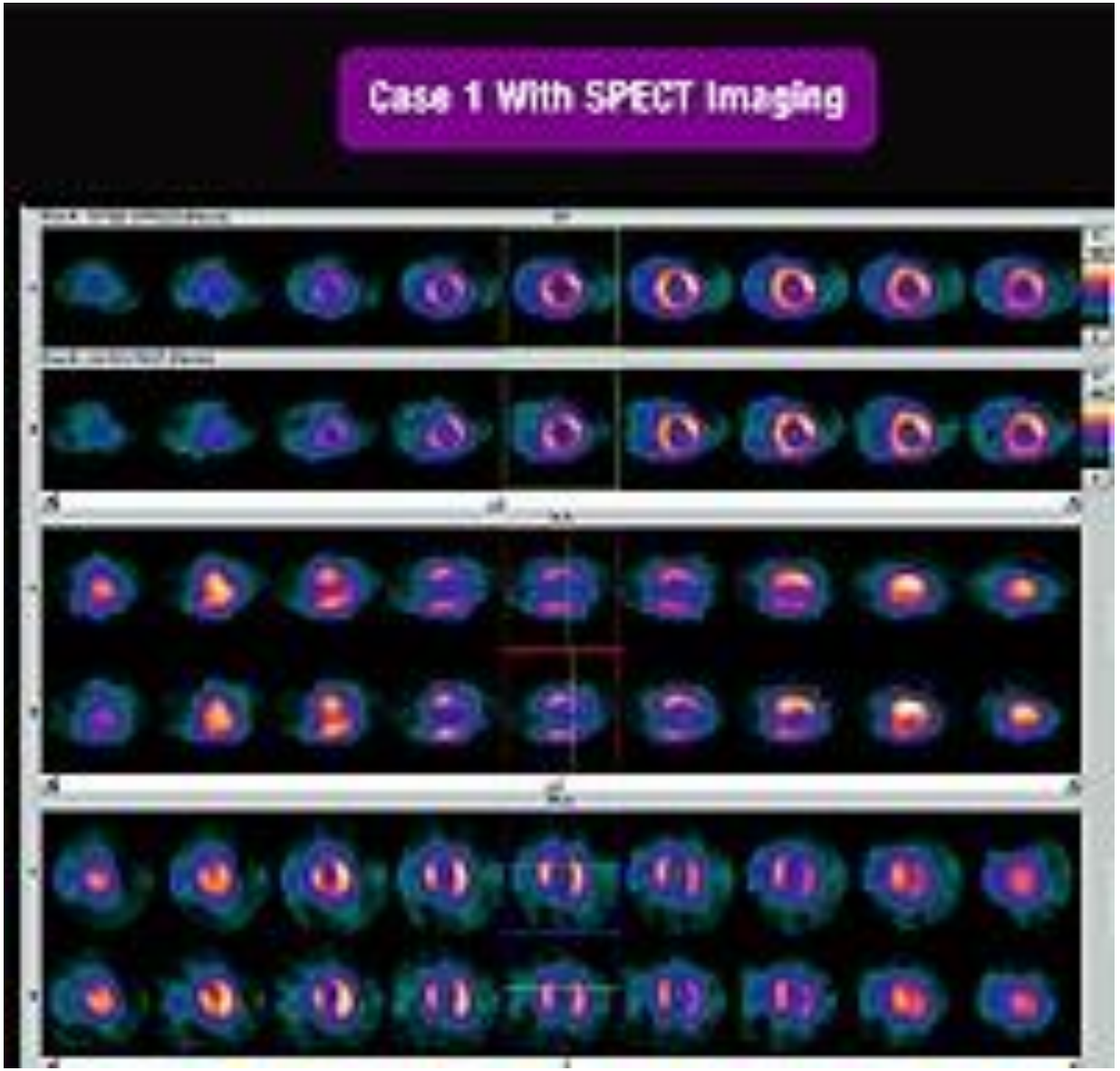


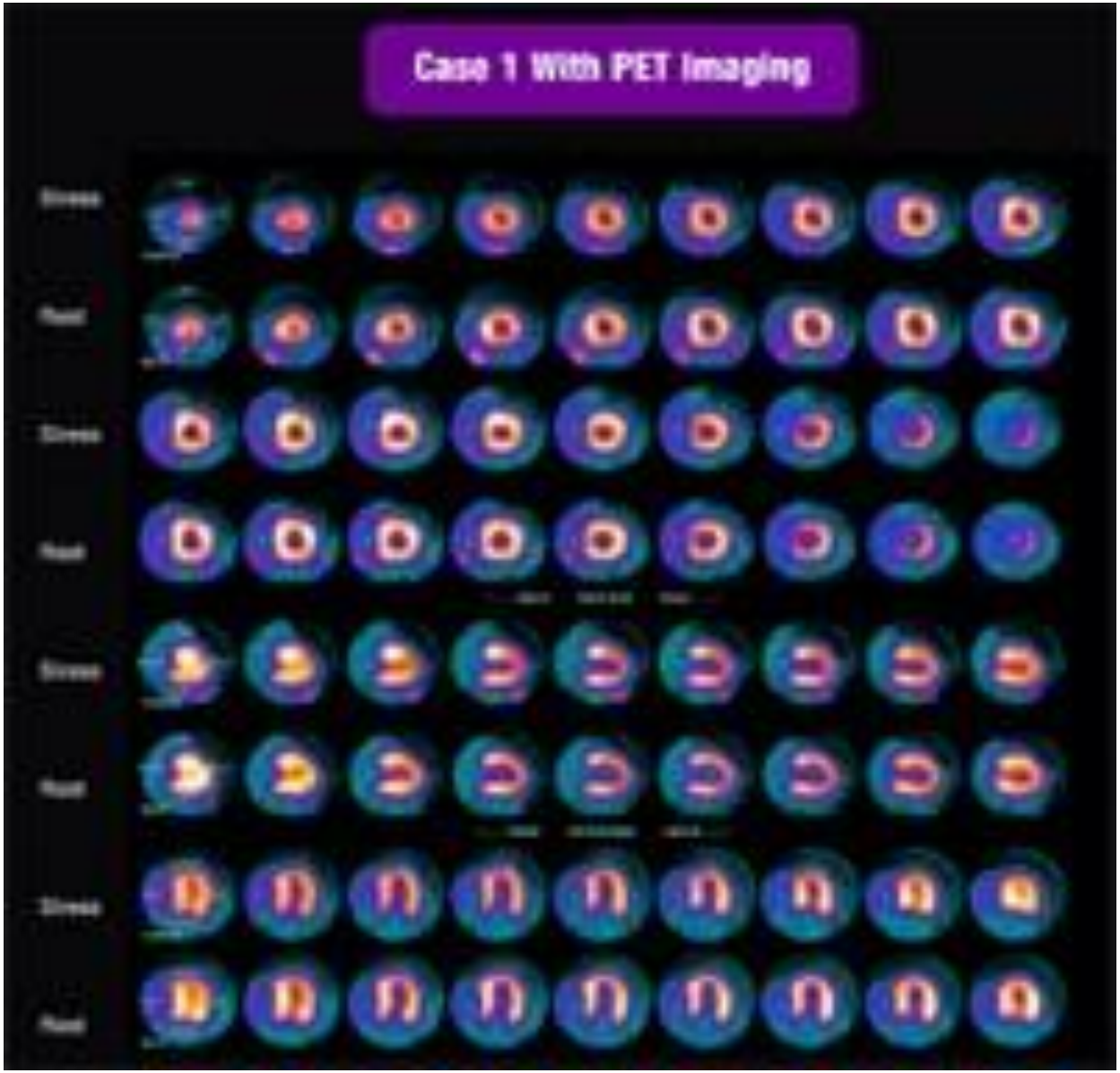
Improving the system

- Can we use PET to provide a better service
- Rb-82 may allow for faster more accurat imaging
- Possibly all can be performed in a (one stop shop)
- Especially with 64 or 128 slice CT

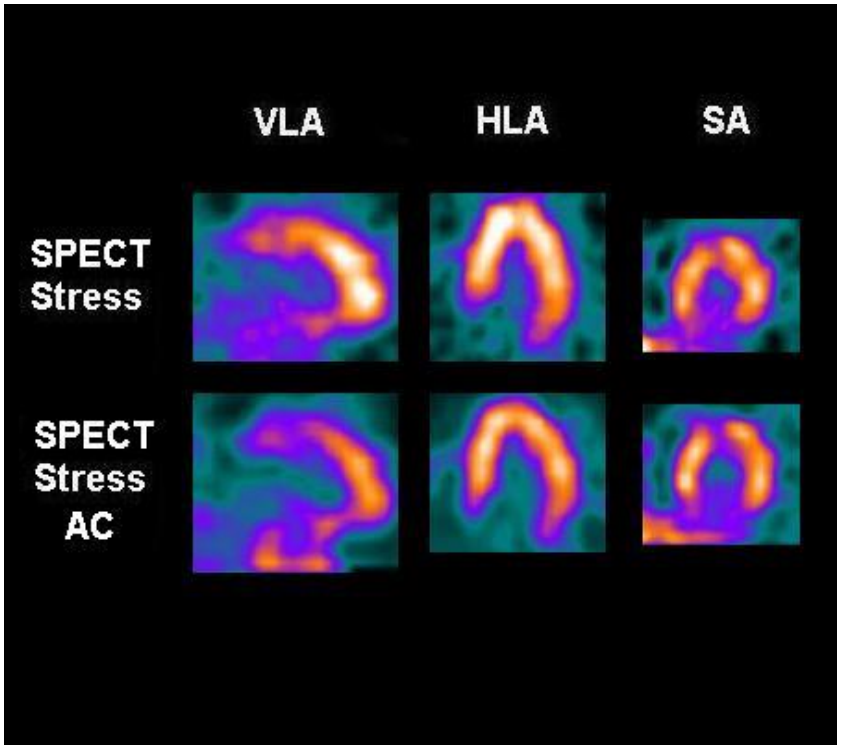
Rb-82 for perfusion

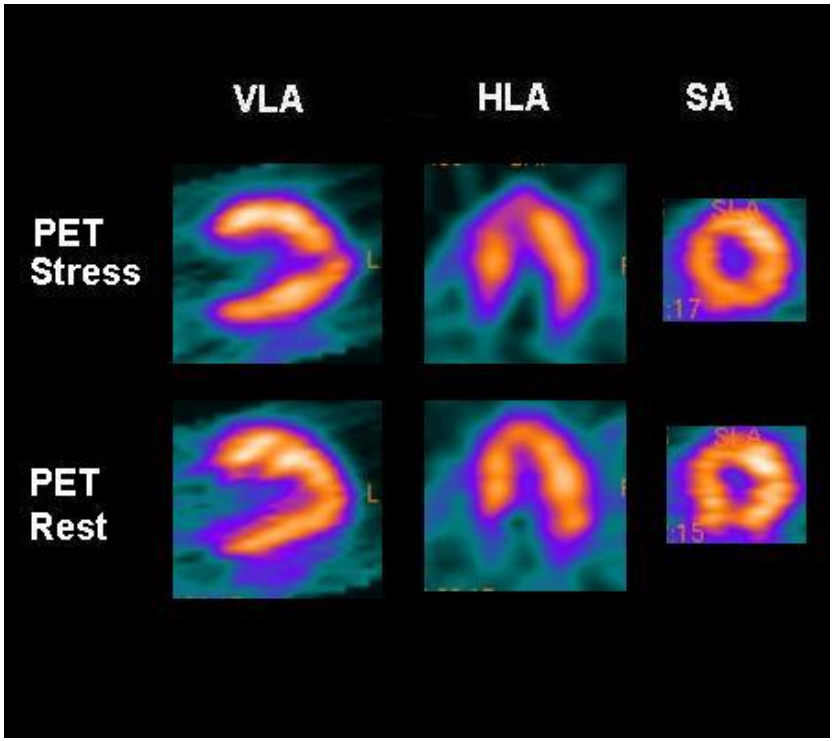
- Bateman et al Kansas JNC 2006
- 112 patients had Tc-99m MIBI and Rb-82 perfusion studies
- 4 blinded readers compared results with CABG (stenosis of 70%)
- Rb-82 had accuracy of 89% compared with 79% for SPECT (p=0.003)
- Rb-82 better in men and the obese


Case 1 With SPECT Imaging


Case 1 With PET Imaging

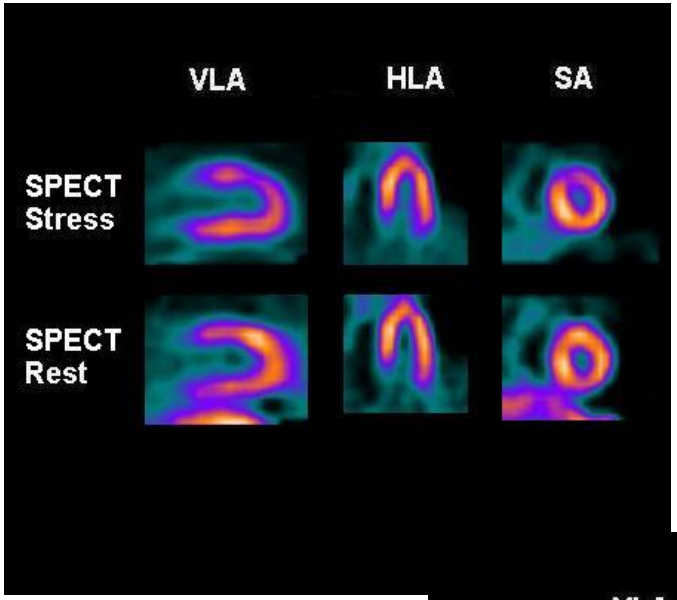
SPECT vs Rb-82 PET

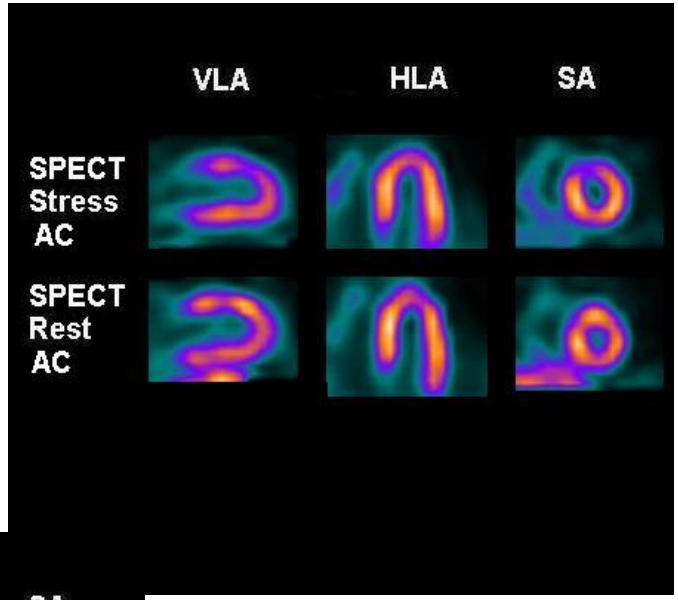


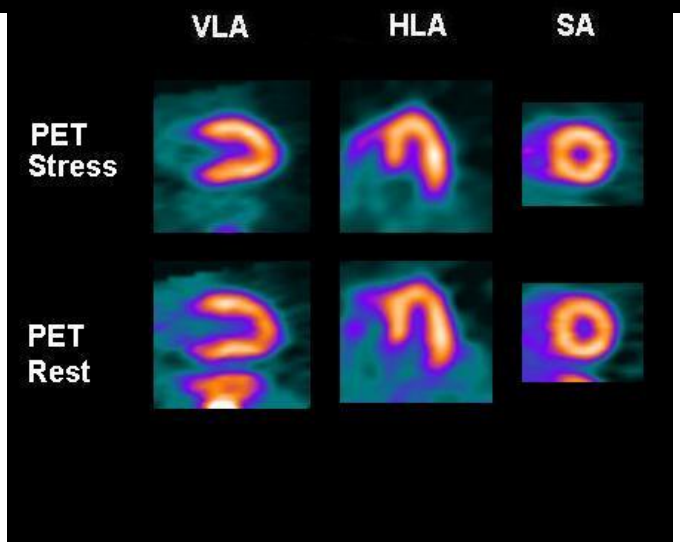


J Machac NYU

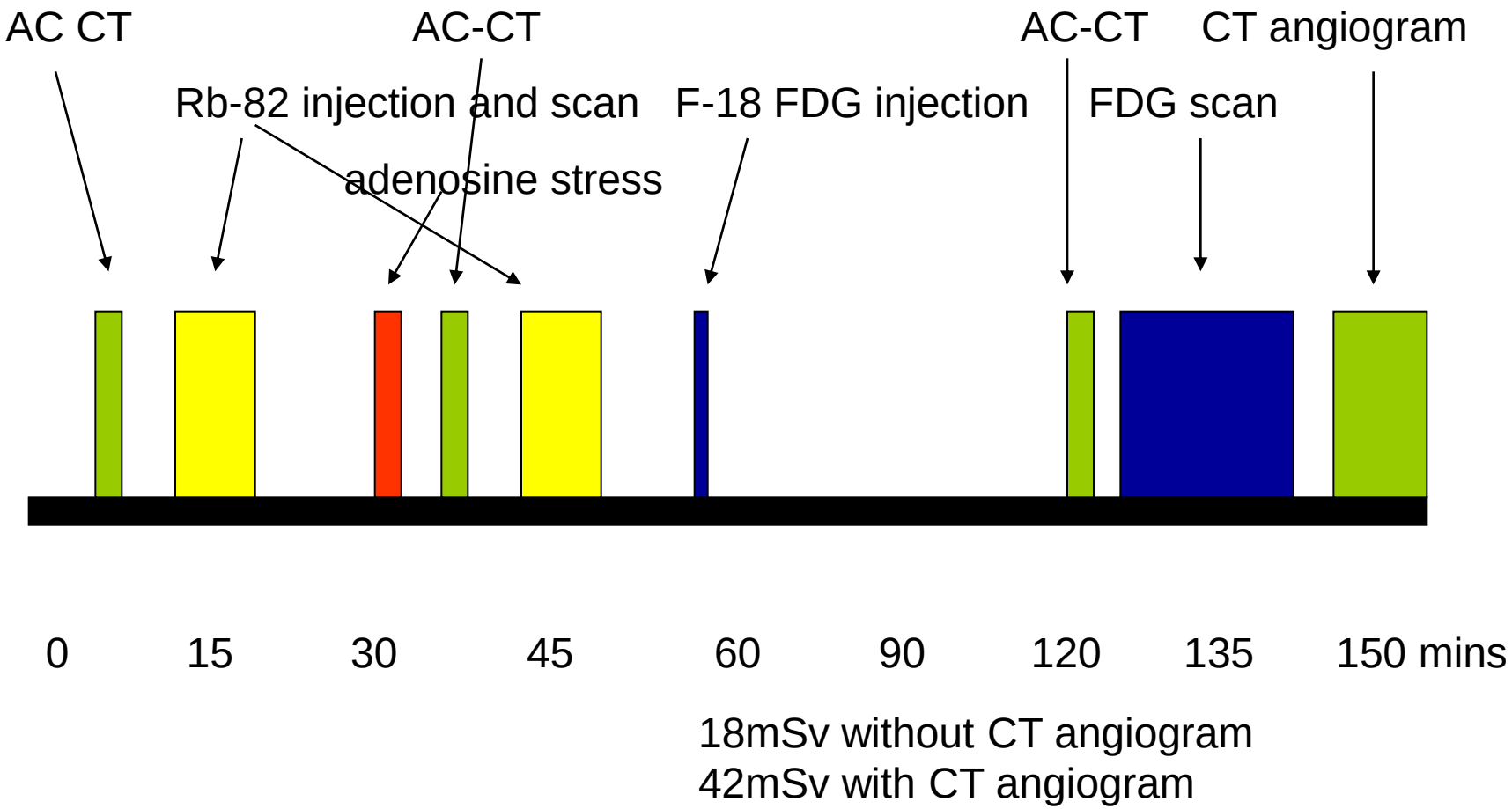
AC vs PET


VLA
HLA
SA
SPECT Stress
SPECT Rest


VLA
HLA
SA
SPECT Stress AC
SPECT Rest AC


VLA
HLA
SA
PET Stress
PET Rest

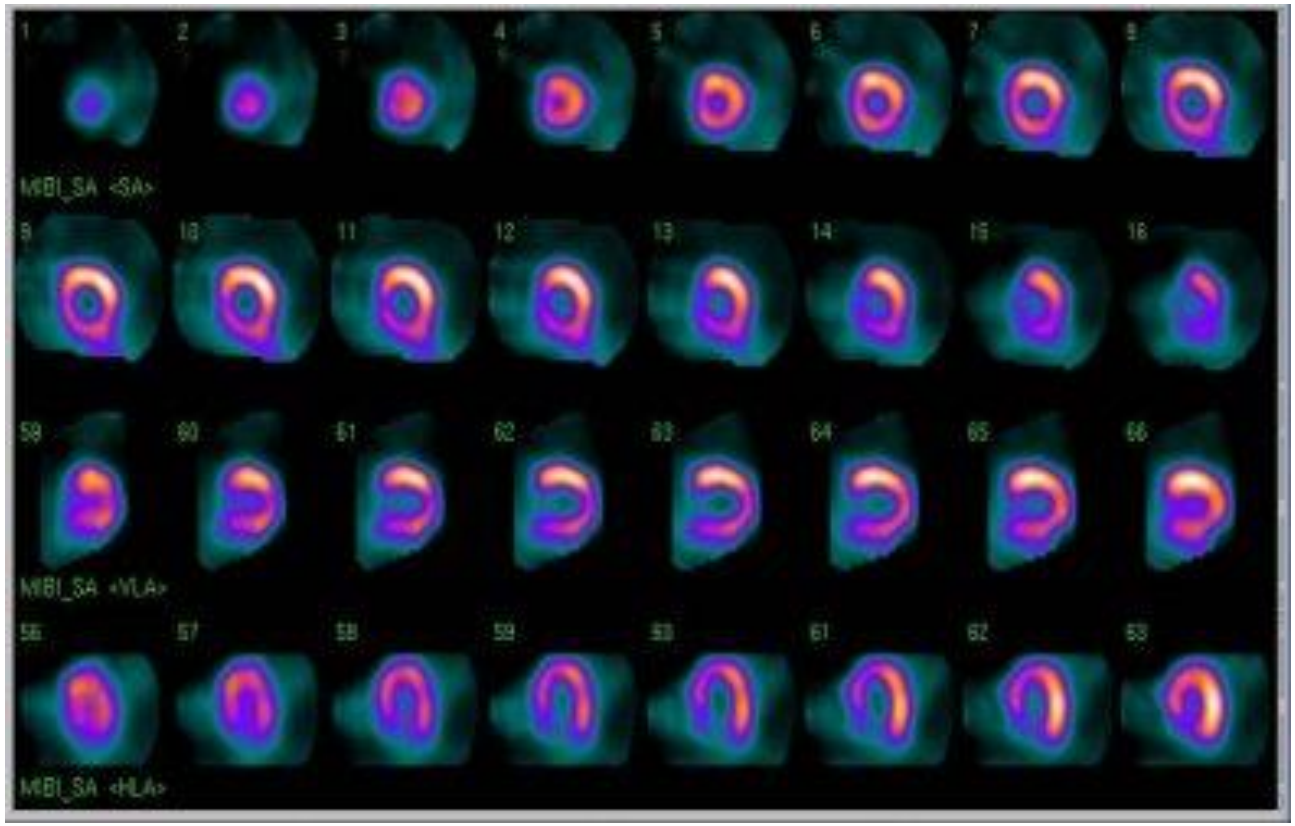
Proposed scheme for viability



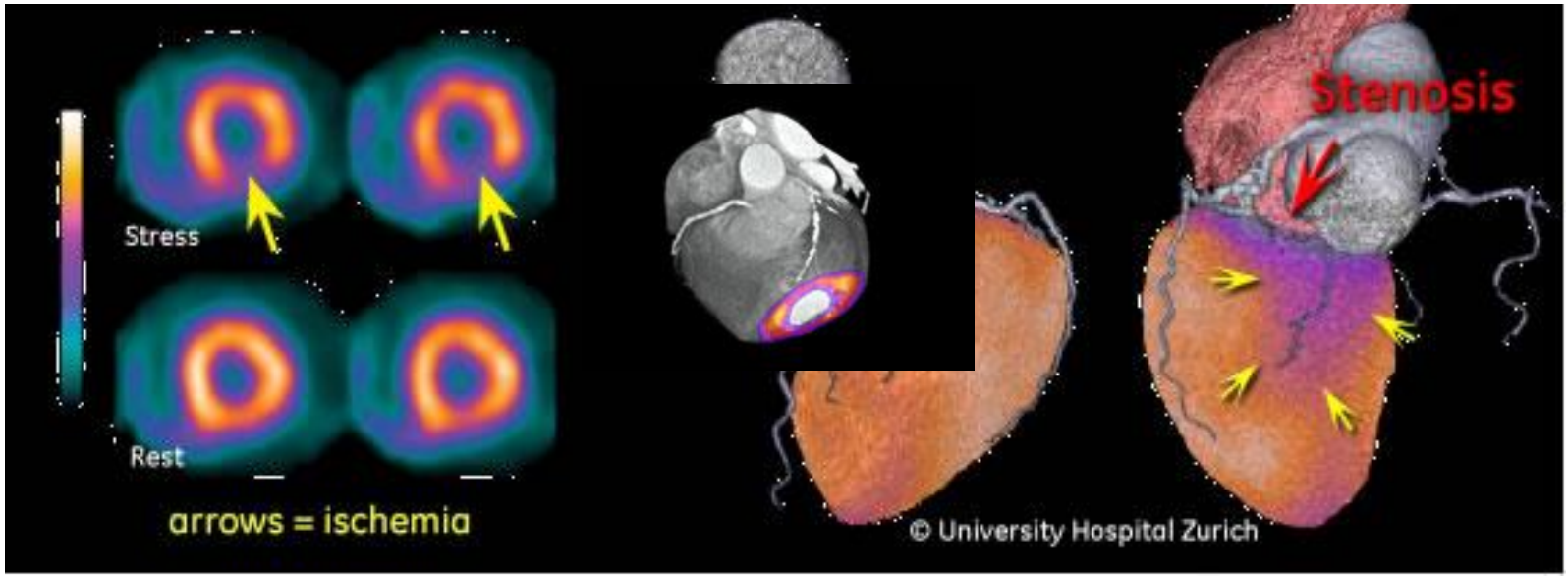
Dedicated cardiac SPECT-CT camera

New digital technolgy

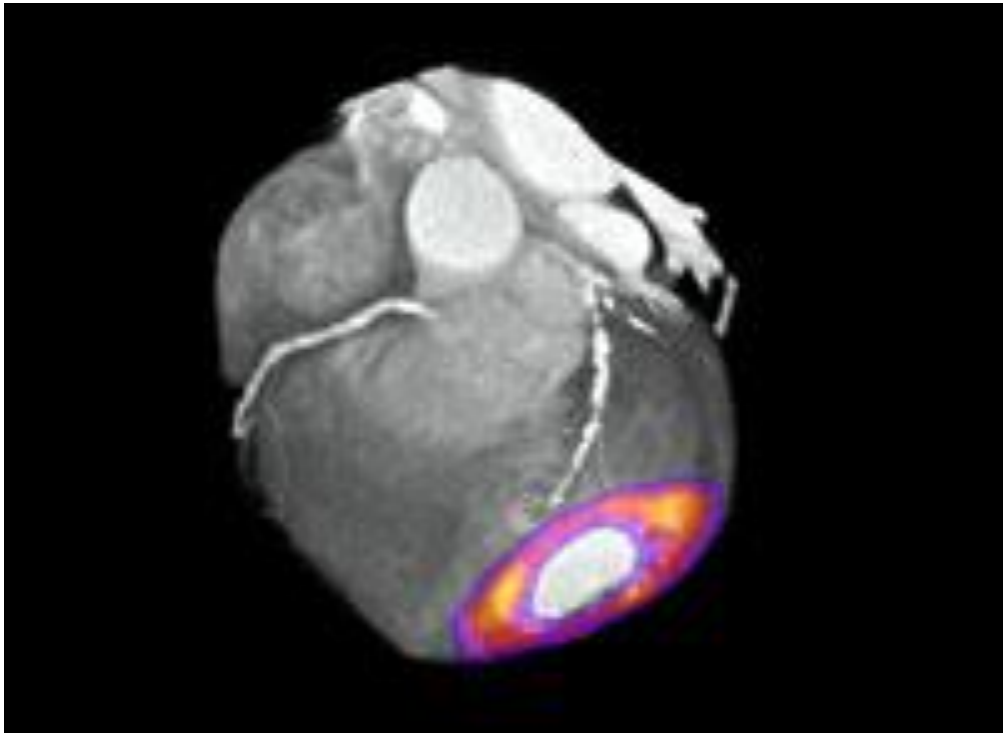
D-SEPCT 2 minute acquisition 400MBq Tc-99m MIBI



SPECT-CT


Stress
Rest
arrows = ischemia
Stenosis
© University Hospital Zurich

Cardiac PET-CT



FDG PET in the CVS

- F-18 FDG used in imaging cancer for 25 years
- Since the earliest days of PET uptake seen in vasculature
- Often seen as annoying artefact
- Then in early 2000s F-18 FDG started to be used to look for inflammation
- This included identification of vasculitis

Patient with renal cell cancer

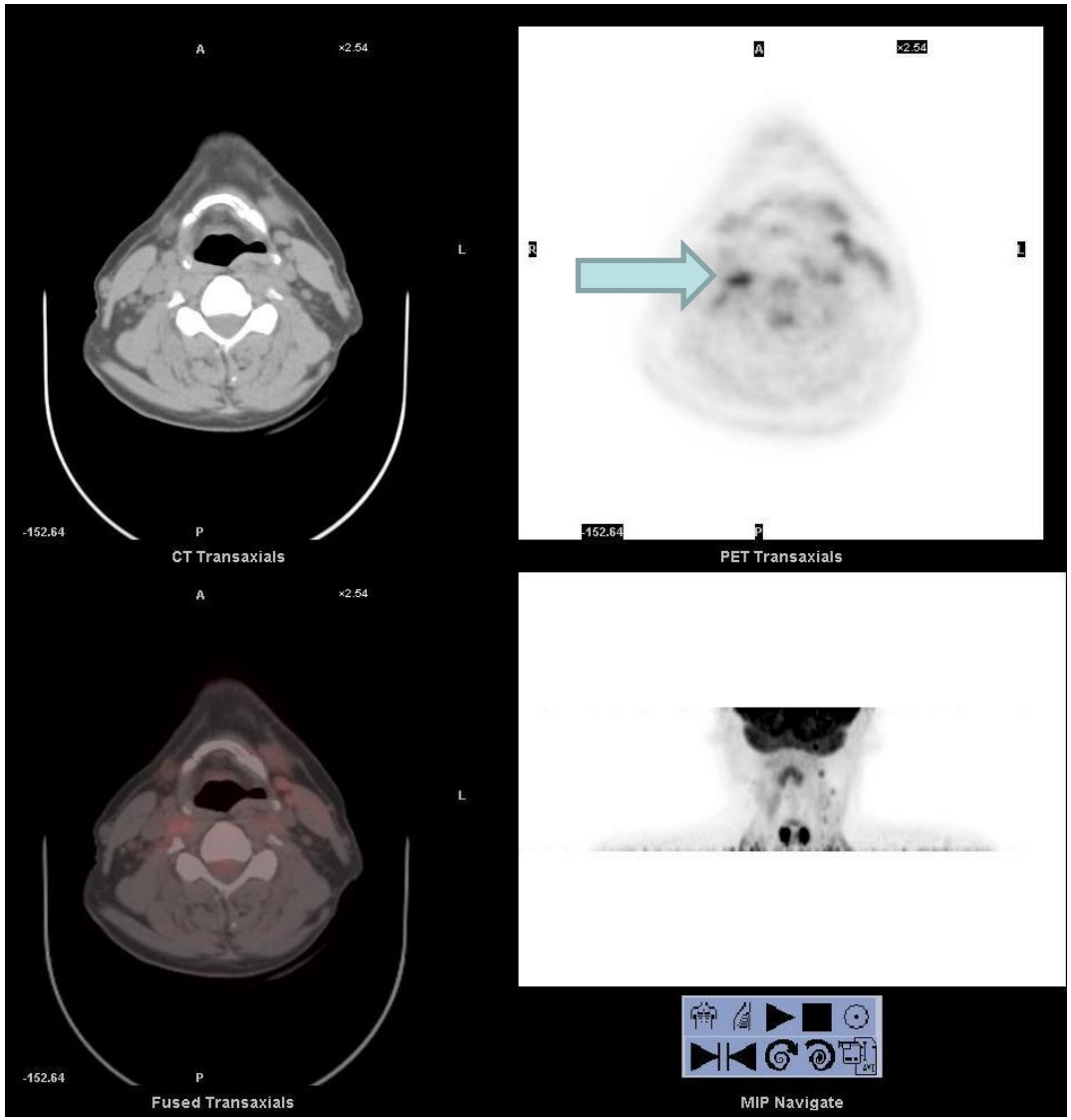
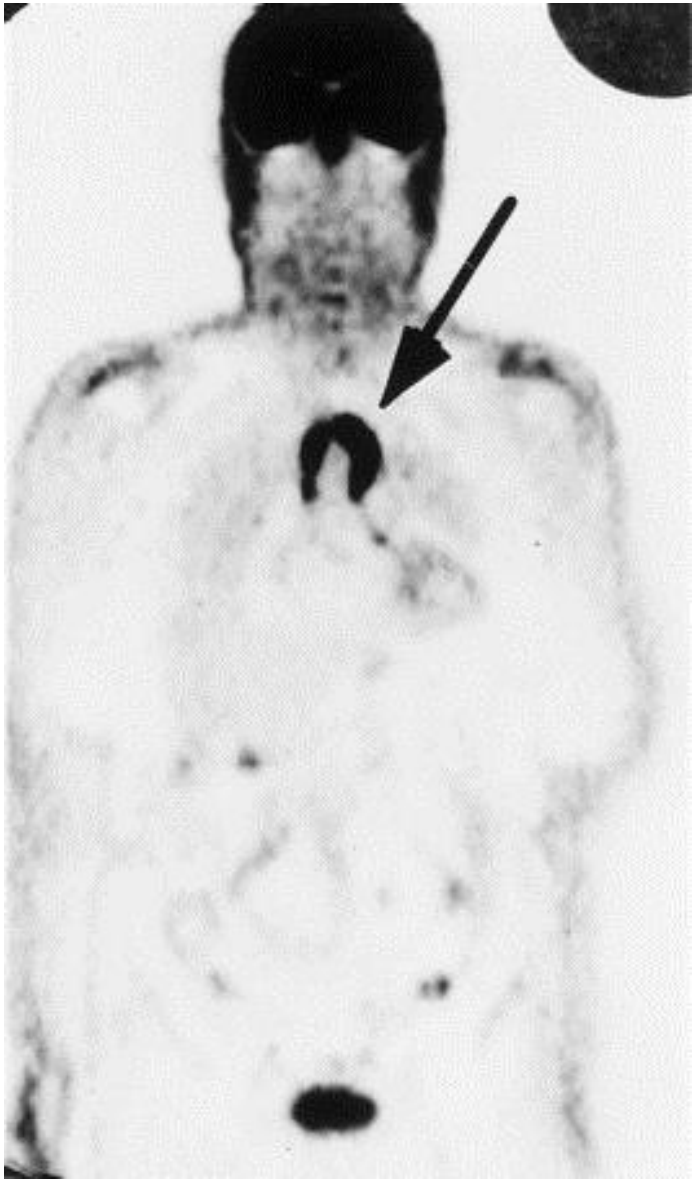
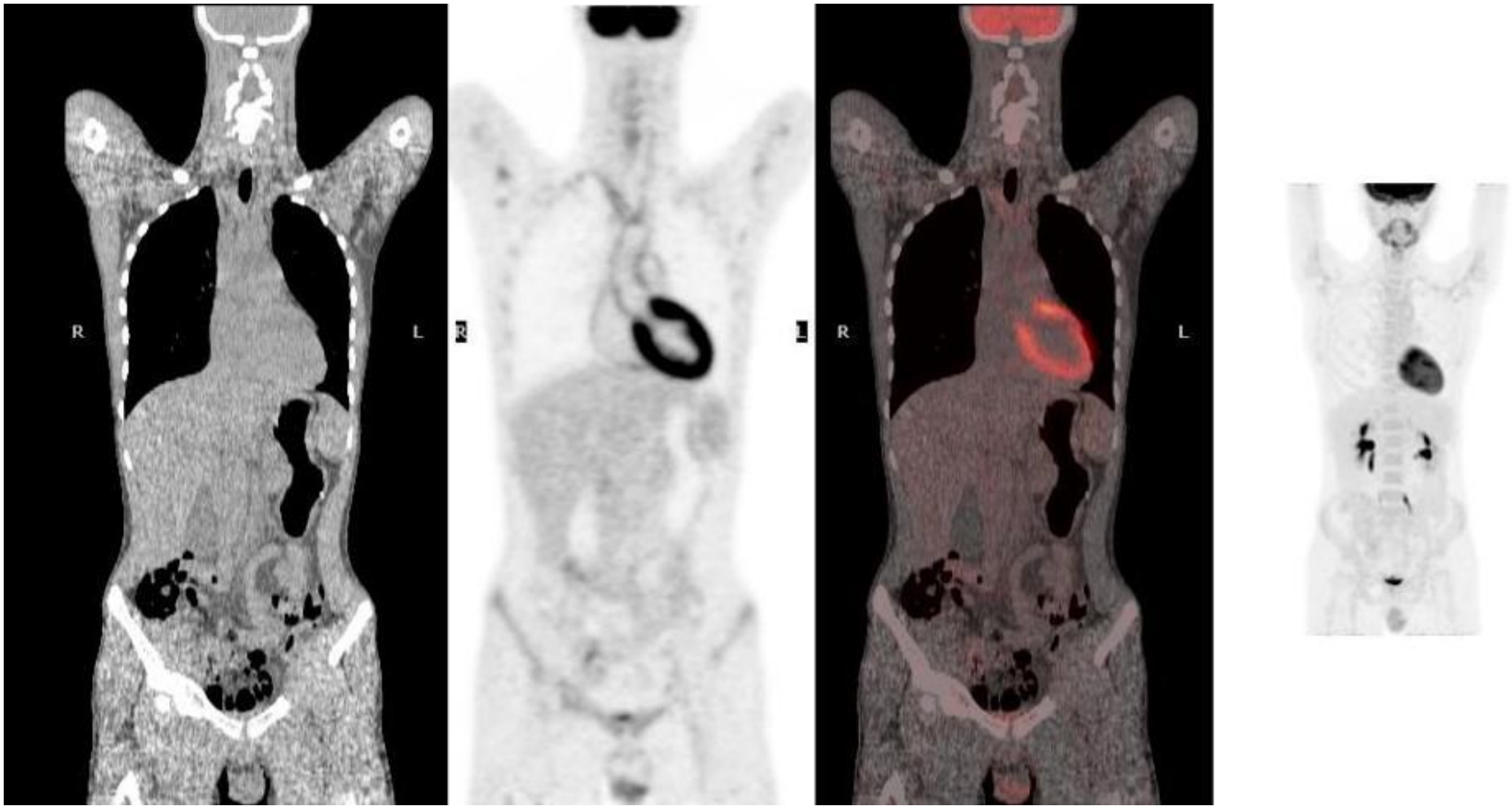


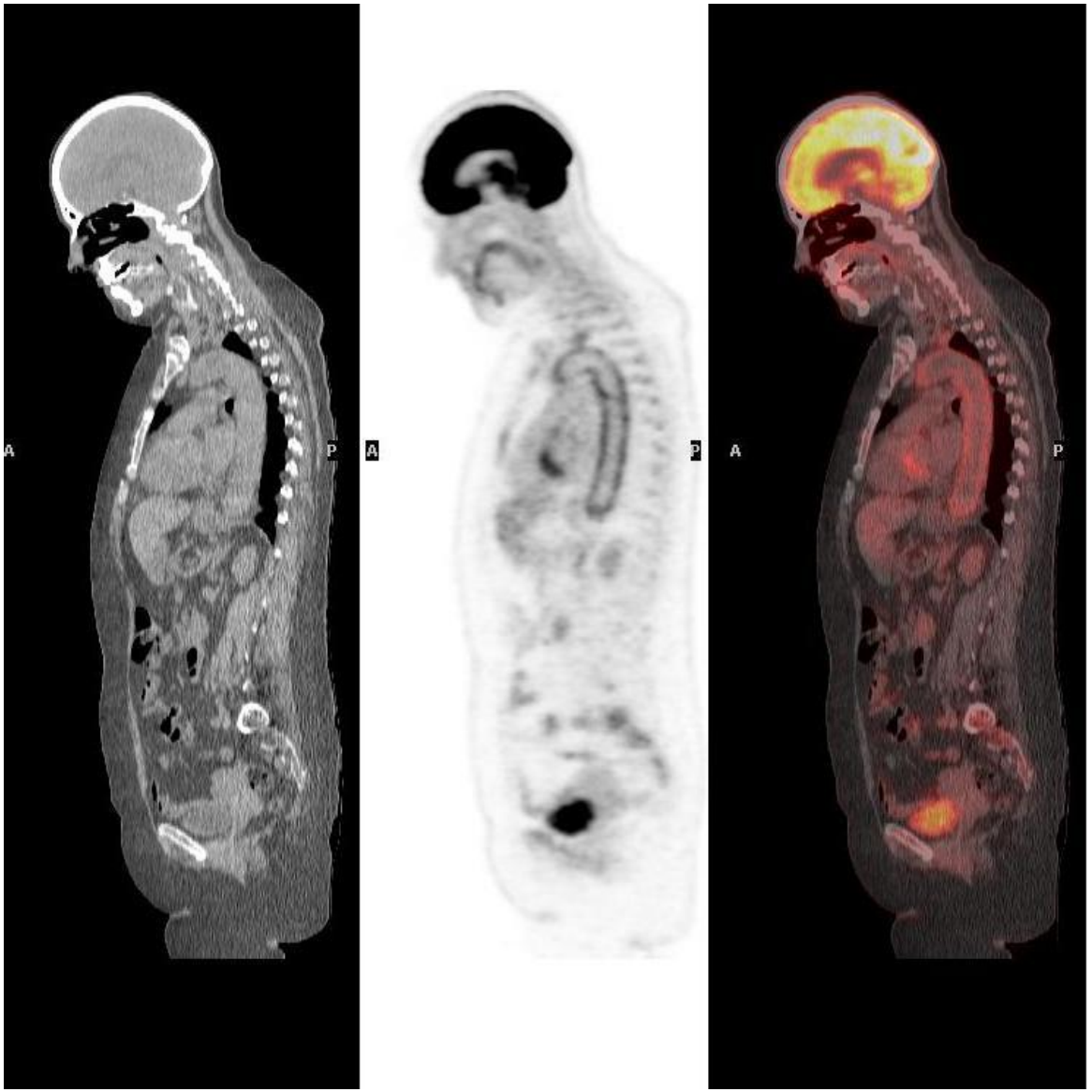
Image from Blockmans et al JNM 2002 Showing F-18 FDG uptake in infective aortitis



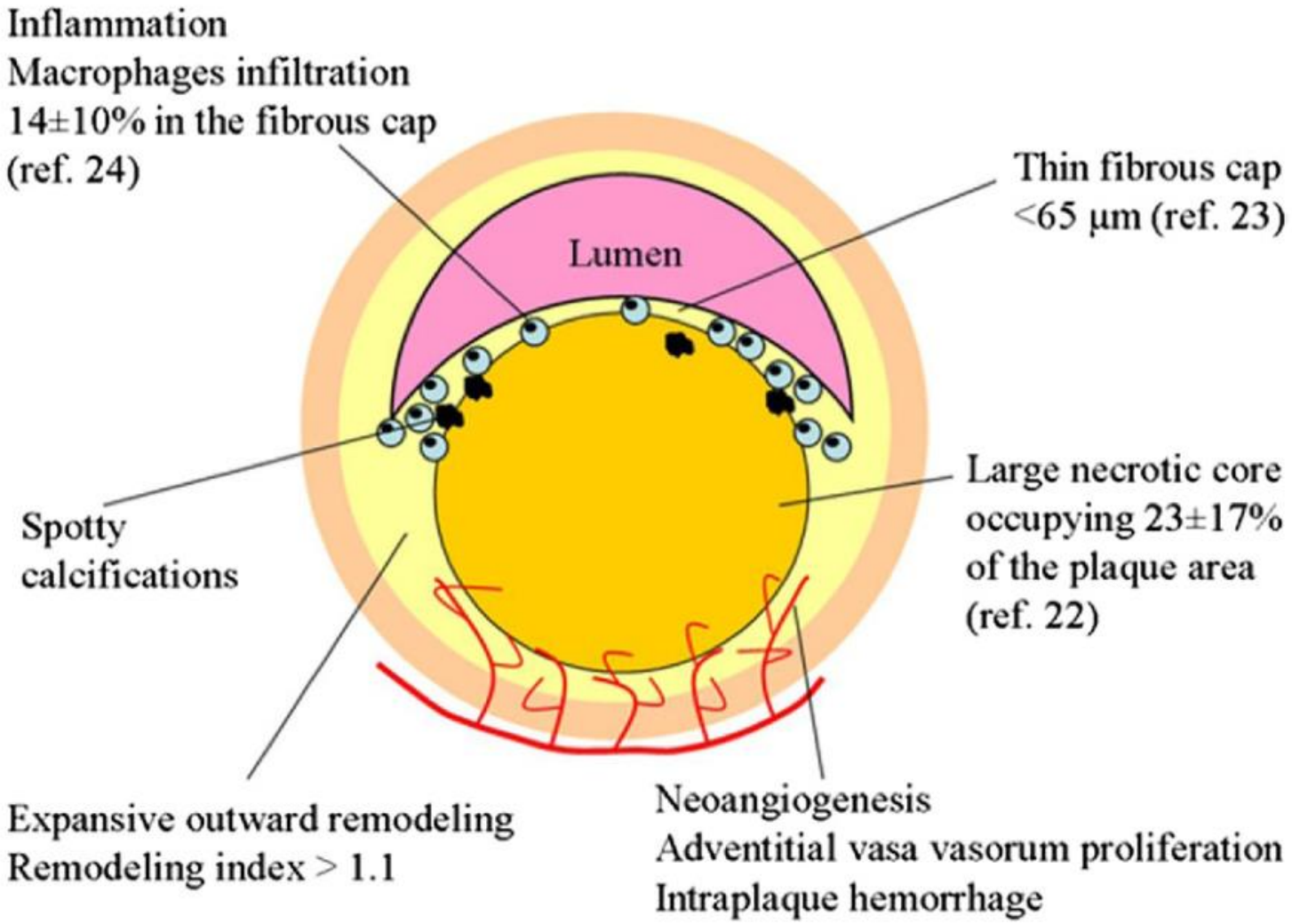
Giant cell arteritis



Aortitis

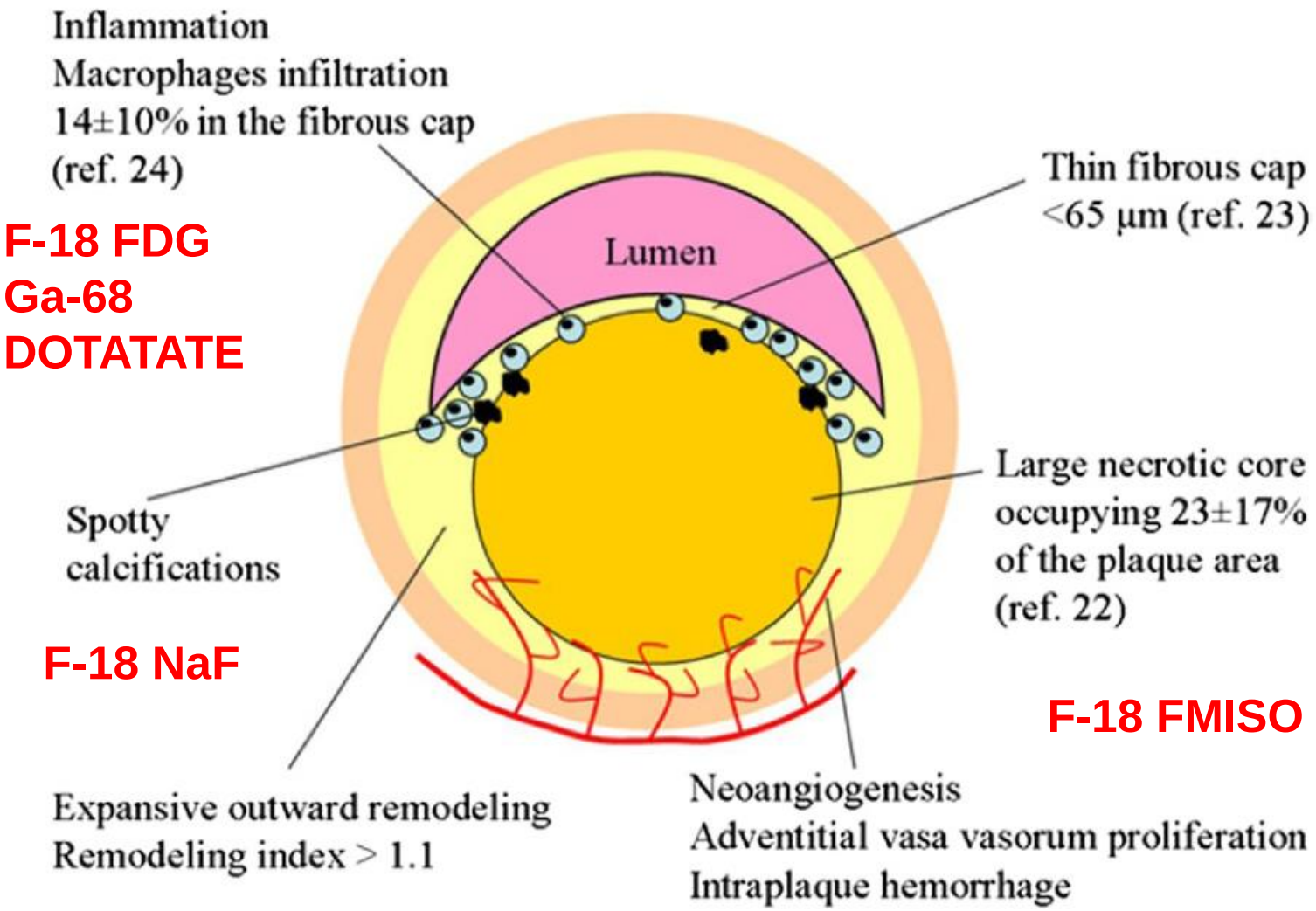


What is a high-risk plaque?



Vancraeynest et al, JACC 2011

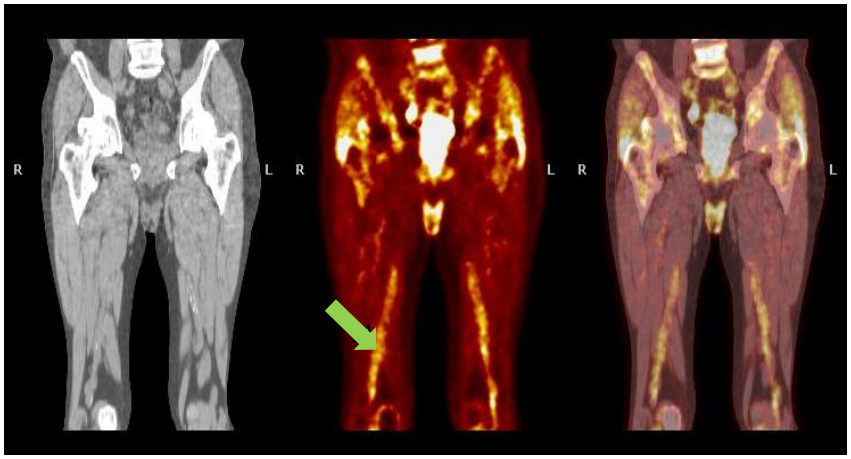
What is a high-risk plaque?



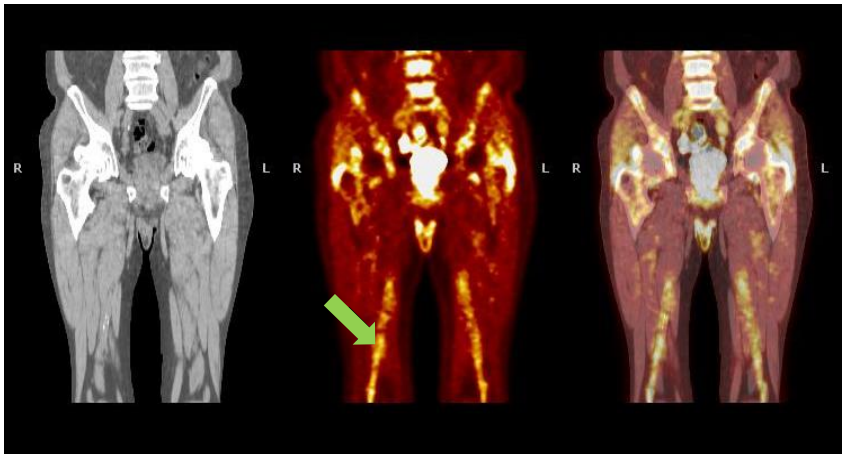
Vancraeynest et al, JACC 2011

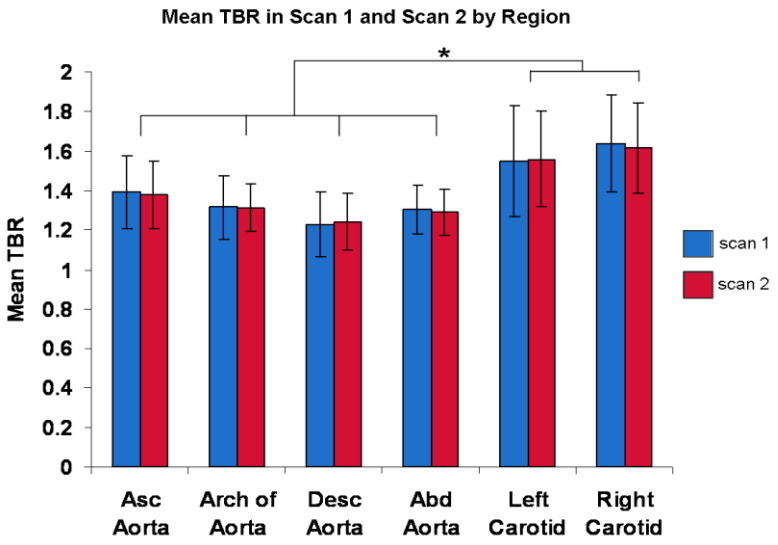
Arterial FDG Signal Is Reproducible

Day 1



Day 14





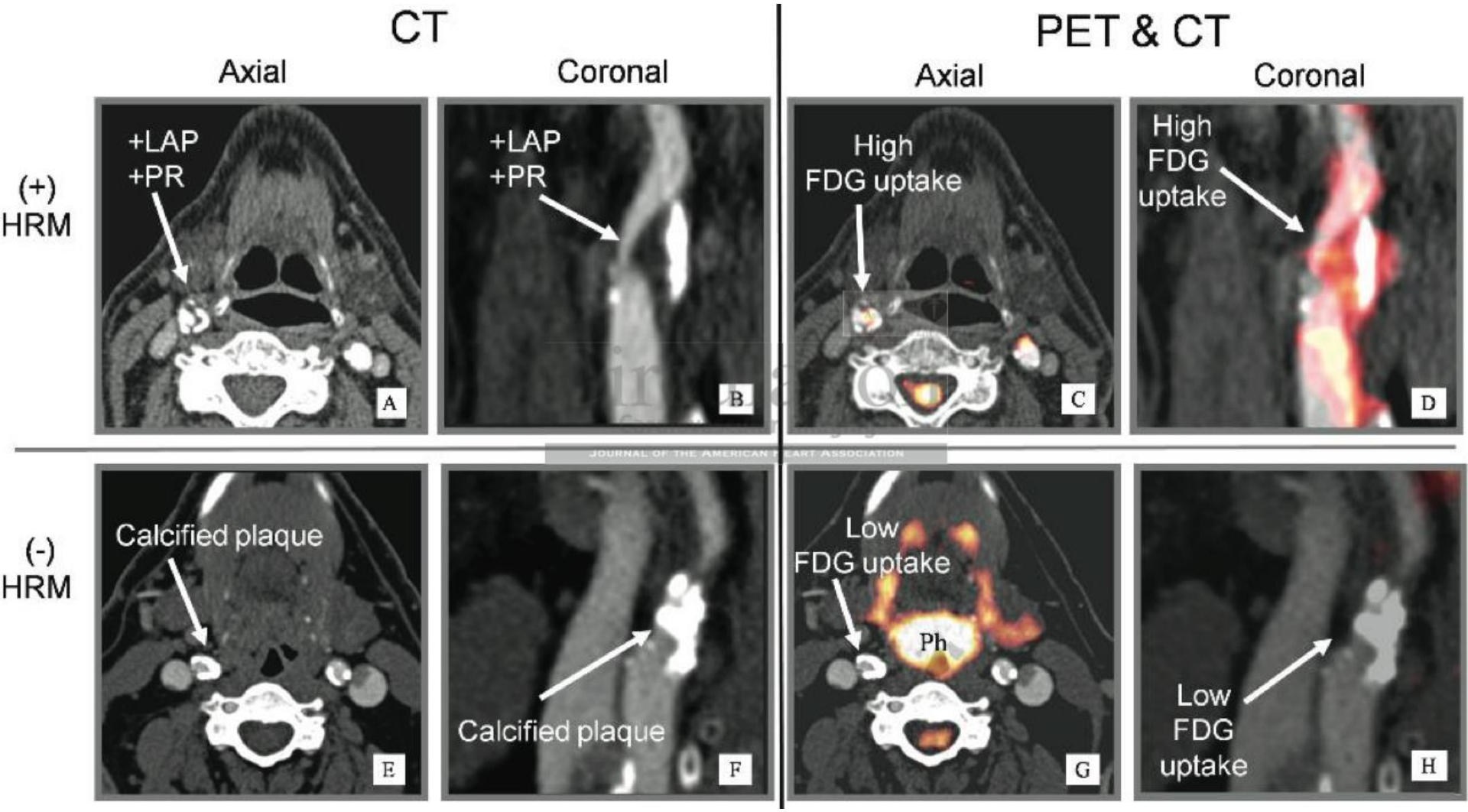
Rudd JHF et al JACC 2007
Rudd JHF et al JNM 2008

Rudd et al Circ CV Imag 2009

- Looked at 41 patients with known cardiovascular disease or multiple risk factors
- F-18 FDG imaging compared to intra-vascular contrast
- Found there was a clear correlation between F-18 FDG uptake patients with atherosclerosis
- Noted inflammation and calcification rarely overlapped.

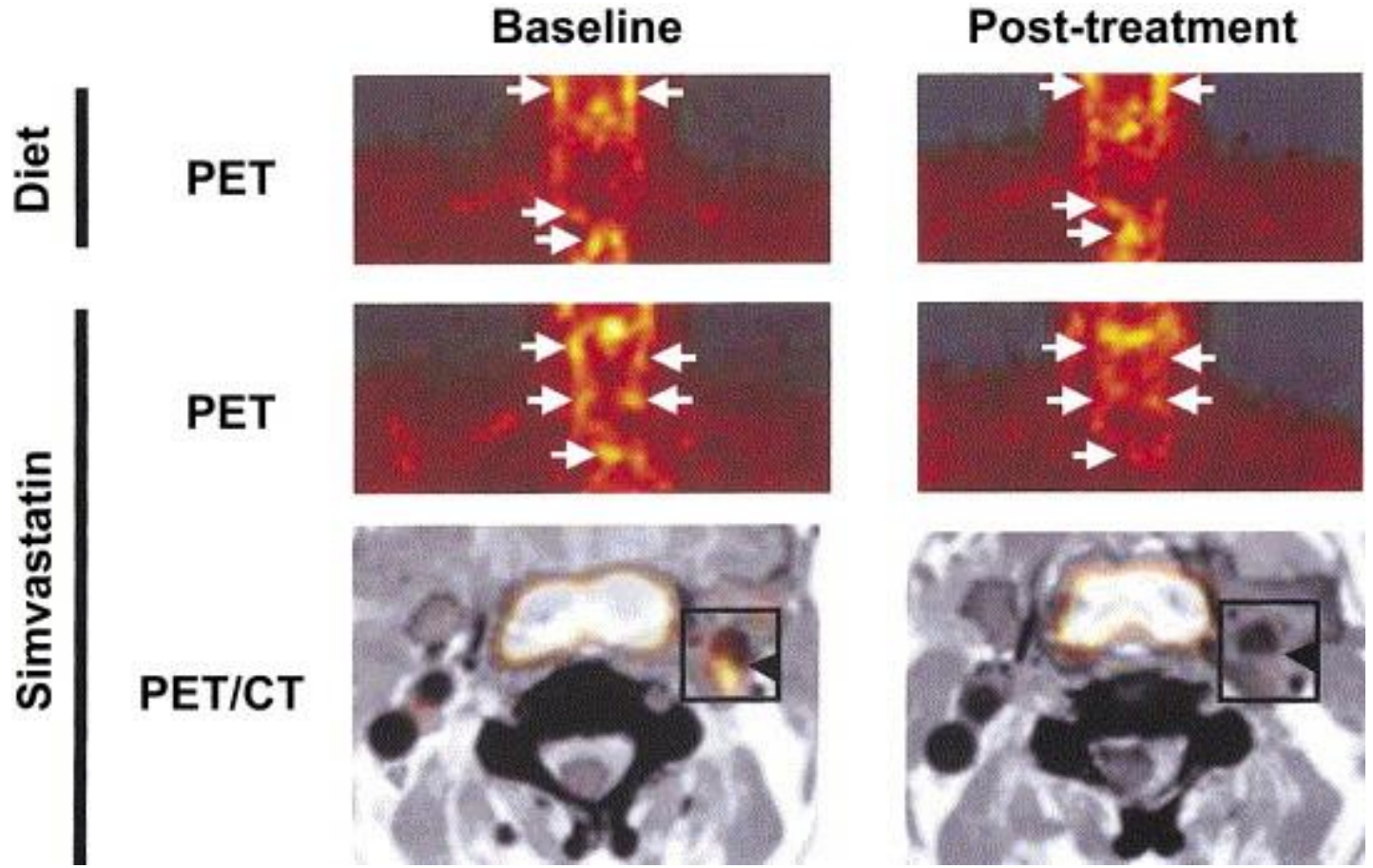
Bucerius et al JACC 2011

- F-18 FDG images in 82 patients with established CAD
- 67% patients had TBR>1.7, 23% had TBR>2.4
- Reverse analysis found correlation of FDG uptake and the following;
  - High BMI
  - Smoking
  - Hypertension



Figuerola et al Circ Imaging 2011

Response To Therapy: Simvastatin Treatment Study

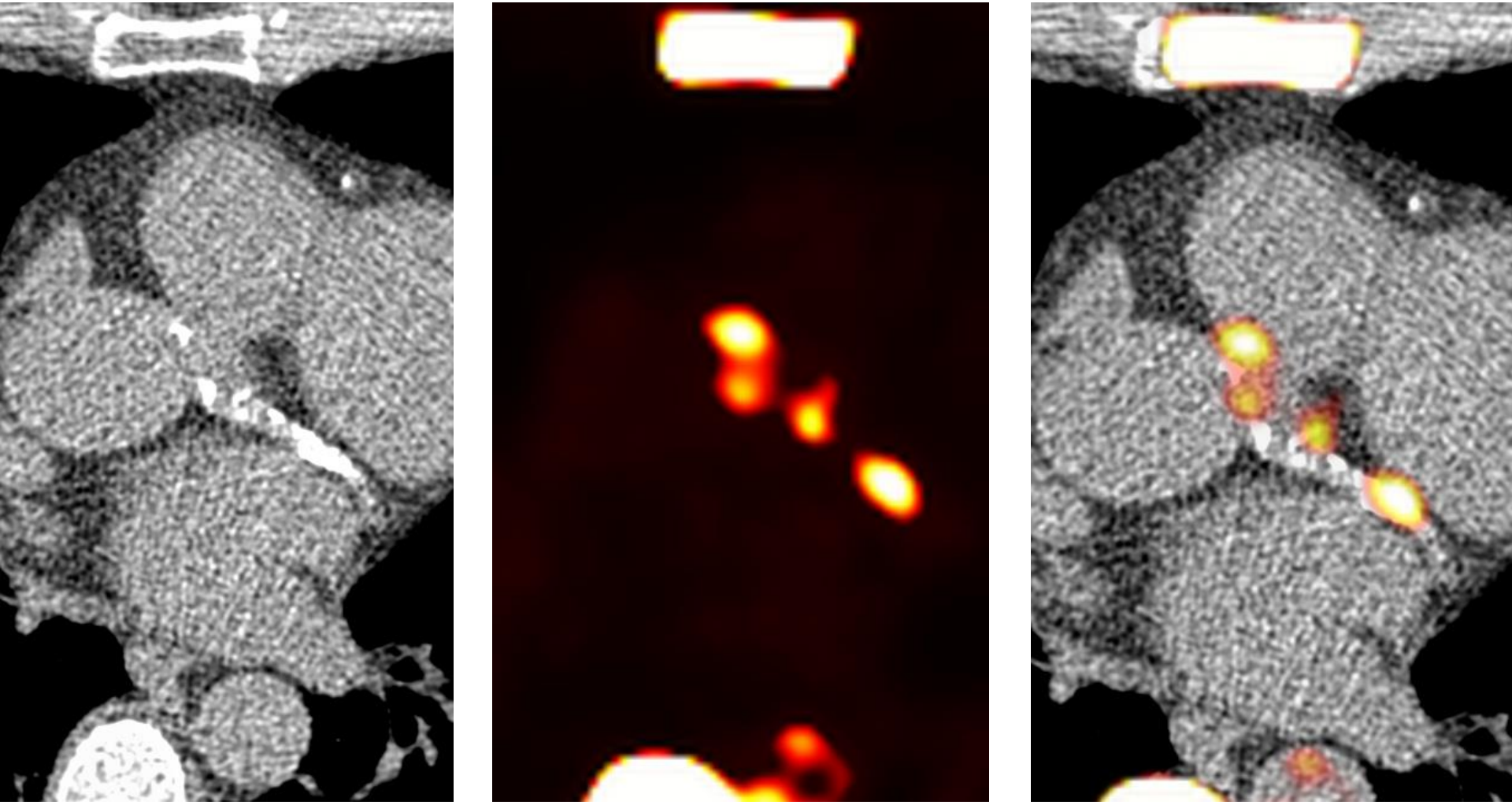


Tahara N et al JACC 2006, Japan

What about the heart

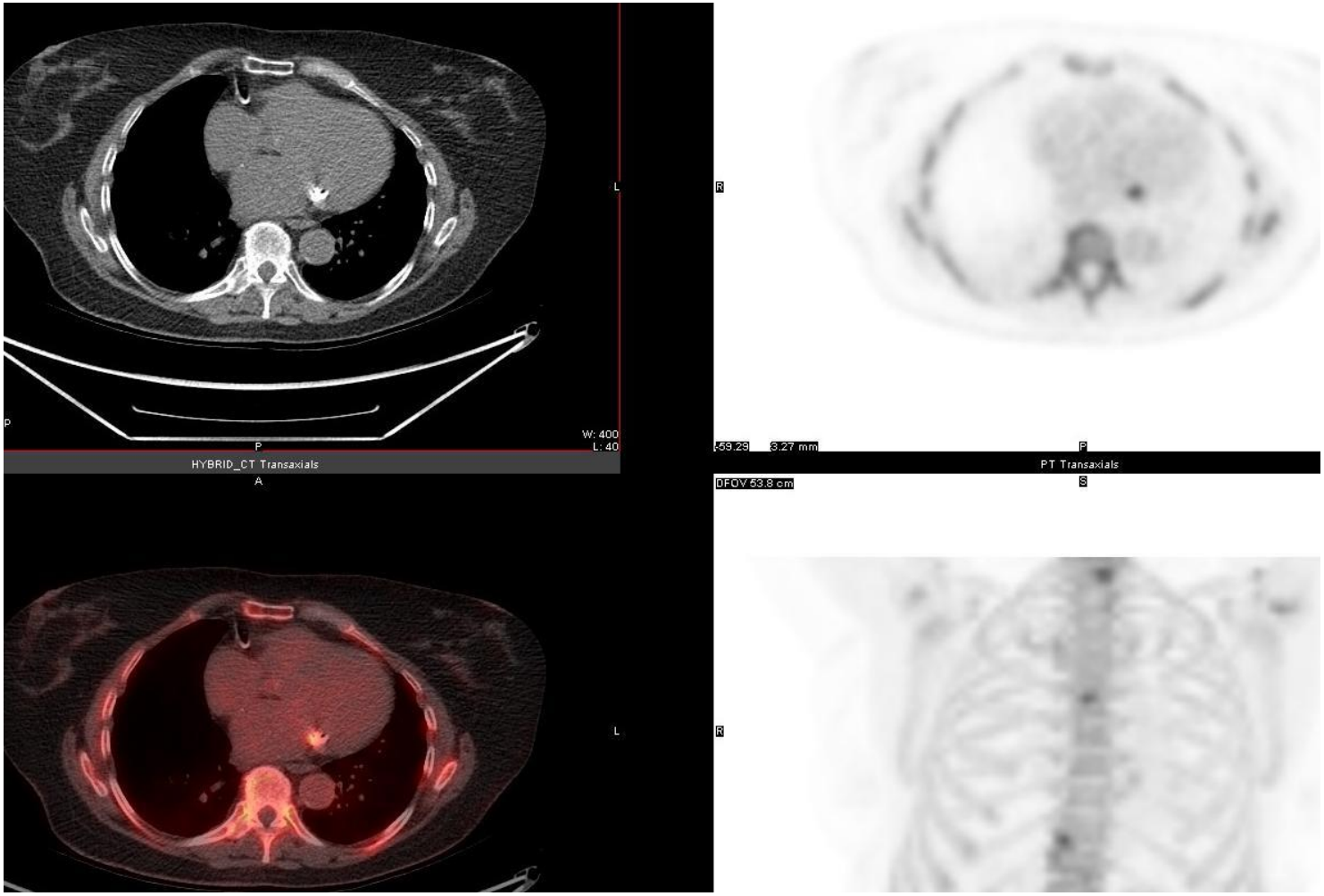
- Tracers such as F-18 FDG have uptake in normal myocardium making imaging of the myocardiunm easy but coronary arteries difficult
- Recent innovation include:
  - "Time of flight" improves sensitivities near centre of field of view
  - Gating reduces blurring due to heart movement
  - Sharp IR helps to reduce blurring due to scatter
  - Non FDG tracers look at other aspects of atheroma

NaF Uptake in Coronary Atheroma looks at active calcification

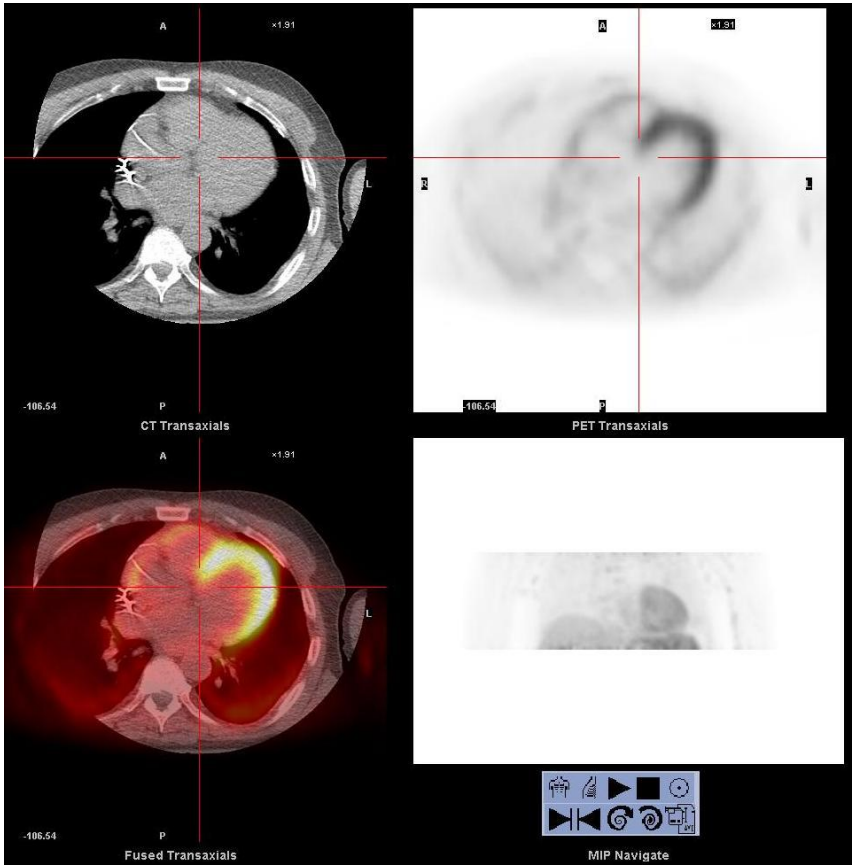


Dweck, Rudd, Newby et al, JACC 2012

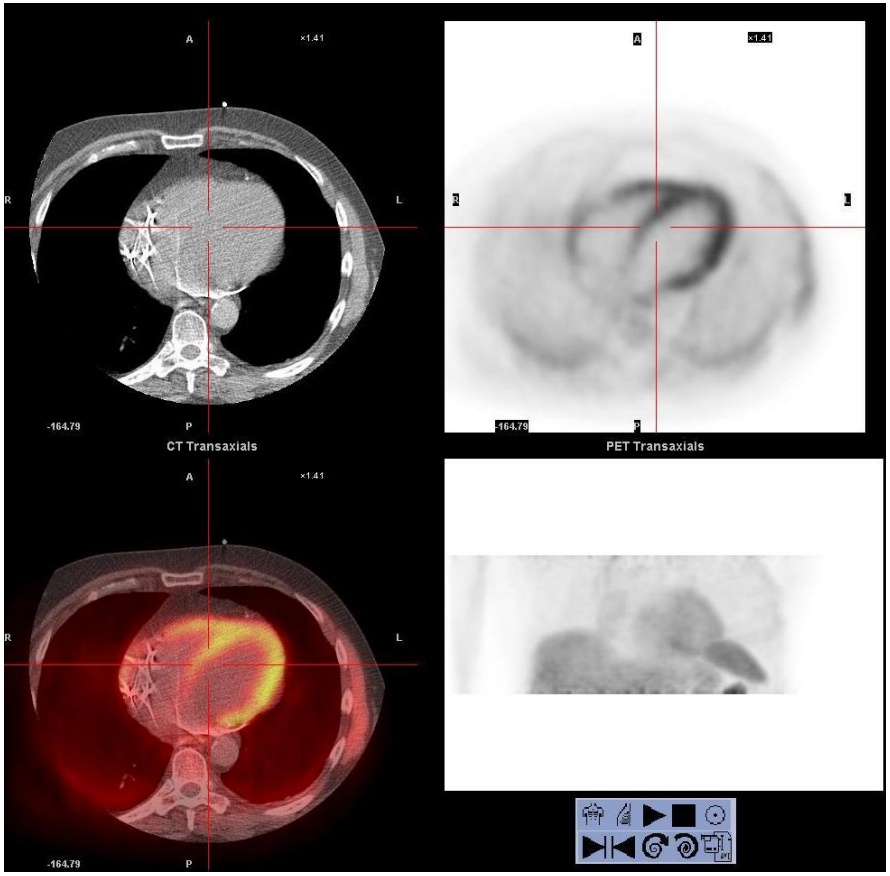
F-18 NaF in new coronary atheroma



Cardiac metabolism



F-18 FDG measures glucose uptake



C-11 acetate measures fatty acid uptake