PET Myocardial Perfusion using Rubidium 82

Presented by

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Presentation Outline

- What is PET
- A Little bit of History
- The Basic PET Cardiac Process
  - Patient Prep
  - Examination
  - Study Time Frame
  - Methods of Stress testing
- Basic Principle of PET
  - Rubidium 82
  - Positron Emission
  - Emission Detection

Presentation Outline

- Clinical Applications of PET
- Advantages and Disadvantages of PET
- The Generator
- SPECT vs. PET
- Images
- Viability
- Quick Note on Recall
- References

What is PET?

PET stands for Positron Emission Tomography and is an imaging technique which uses small amounts of a radioactive tracer to help in the diagnosis of heart disease. The tracer is introduced into the body, by IV injection directly from a small and portable generator, and a PET scanner is used to produce an image showing the distribution of the tracer in the heart.

A Little bit of History

"The first such 'Brain Camera' was created by Dr. Michael Phelps and his colleagues in 1973 at Washington University in St. Louis. Phelps came to UCLA in 1976 to build the world's leading PET program. He established the PET clinic for patient care at UCLA, the first of more than 800 clinics worldwide. Michael Phelps is now chair of Molecular and Medical Pharmacology at UCLA."

-Dave Greenwald

A Little bit of History

Cardiac positron emission tomography (PET) imaging has been used for more than 3 decades to study myocardial perfusion and metabolism, but for a majority of those years, confined to large academic and research centers with access to a cyclotron. With the advent of the generator-produced PET radionuclide Rubidium-82, PET myocardial perfusion imaging has become far more accessible in daily practice.

Cardiac - The Market

- Heart disease is the number one killer of American men and woman
- Some 650,000 American's will die this year in the United States
- Early detection and medical therapy can effectively treat the disease
  - Lipid control
  - Risk factor modification

Tools for risk stratification

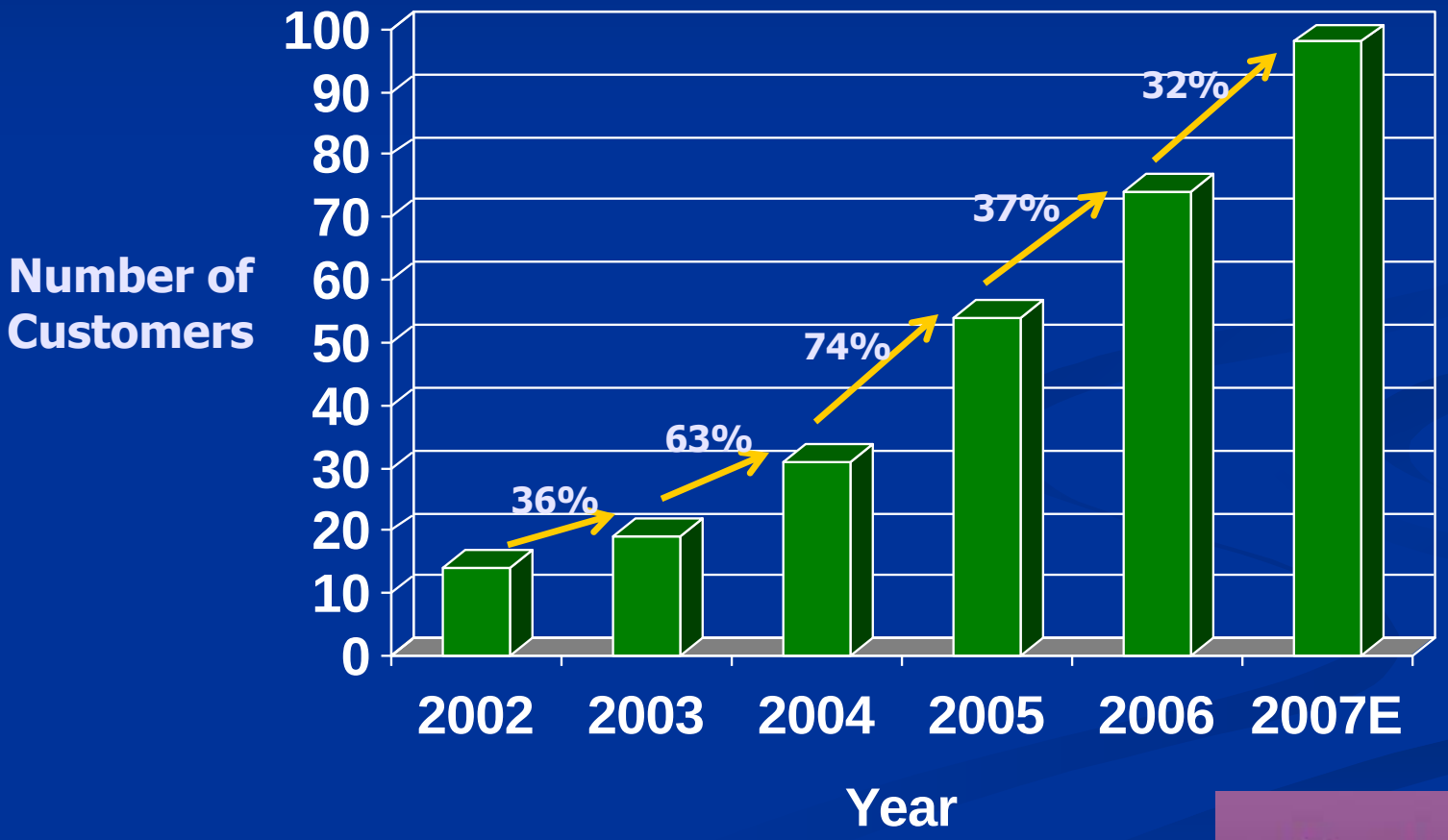
- Treadmill evaluation
  - Low sensitivity, moderate specificity
- Stress Echocardiogram
- Perfusion imaging
  - Sensitive and specific but still false positives and false negatives
  - Rb-82 higher diagnostic accuracy relative to SPECT
- Coronary calcium screening
- Viability
- Coronary angiography

The cardiac imaging market is transitioning

SPECT → PET

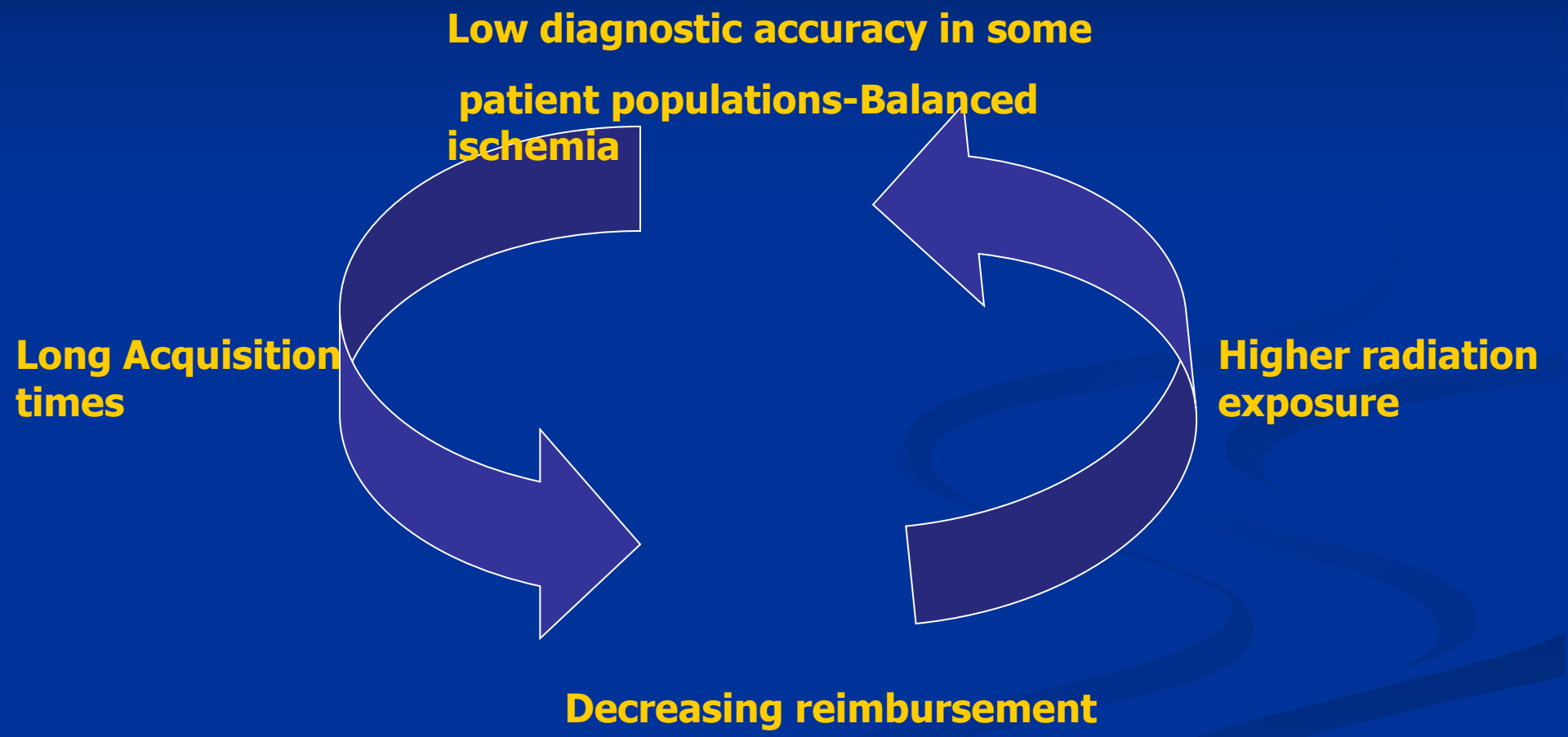
Cardiac catheterization → CT angiography

Growth of Myocardial Perfusion Imaging with Rubinium-82 PET in USA



CARDIOGEN-82®
(RUBIDIUM RB 82 GENERATOR)

SPECT perfusion imaging

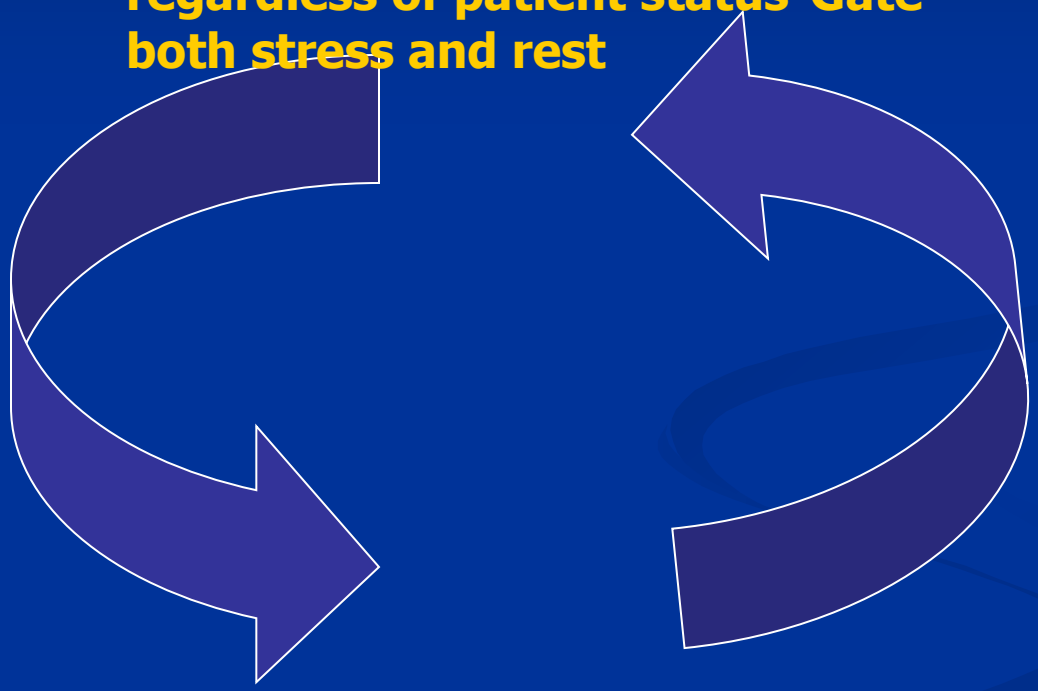


SPECT perfusion imaging

- Low energy photons
  - Thallium or Tc based
- Usually two imaging sequences (20-30 minutes each)
- Total exam time 3-4 hours
- Study of over 3000 patient with Thallium
  - Sensitivity 84% and Specificity 53%
- Attenuation/motion all impact relative accuracy
  - Equivocal studies men 10% woman 30-40%

PET perfusion imaging

High diagnostic accuracy regardless of patient status-Gate both stress and rest



Lower radiation exposure

Increasing reimbursement

Shorter acquisition times

Transitioning the perfusion market

- Why Rb-82 now?
  - Improved patient outcomes/lower false positives
  - Appointment times reduced to 30-45 minutes
  - Improved accuracy irrespective of body mass index, sex ect.
  - Lower radiation exposure
  - Improve throughput and reimbursement-favorable economic drivers
  - Equipment

Patient Preparation

Medications:

- Insulin- Take ½ of dose
- Beta Blockers- off 48 hours
- Caffeine- off 24 hours
- Nitroglycerin- 4-6 hours

NO:

- Food (4 hrs)
- Alcohol (4-6 hrs)

Patient Preparation

Clothing:

- Dress comfortably with loose shirt (arms behind head for 30 minutes)
- Dress in warm clothing, dress in layers. PET imaging rooms must stay very cool

Examination

- Verify the Patient Identity
- Verify Order
- Obtain Patient History
- Verify Patient is Prepped
- Explanation of Exam
- Answer Questions
- Consent
- Start IV (use Y connector extension, one port for chemical stress and one port for Rubidium infusion)
- Prep Chest for EKG, hook patient up to stress module and gating leads
- Place Pt Under Camera
- Hook Pt IV up to Radioactive Tracer Rubidium 82 Generator
- Acquire transmission scan and evaluate positioning

Examination

- Infuse Rubidium 82
- Once Infused set timer (generally 2 minutes)
- Begin Imaging once timer goes off
- Review Images
- Perform stress transmission scan (optional, resting transmission scan can be applied to both rest and stress images)
- Pt stays under camera while Chemical stress test is performed/infused though the IV
  - Dipyridamole vs. Regadenoson

Examination

- Pt is still hooked to the Generator and the Radioactive Tracer Rubidium is infused a second time
- Once Infused set timer (generally 2 minutes)
- Begin Imaging once timer goes off
- Reverse Dipyridamole with Aminophylline (not necessary with Regadenoson unless patient is symptomatic)
- Review Images
- Disconnect from all pumps/generators, pull IV if patient is stable, disconnect from stress module and gating leads, get patient up to leave

Study Time Frame

- From the time the patient is brought to the PET area until they leave should be about 45 minutes, however, one hour gives you wiggle room for questions, hard IV stick, repositioning, etc.
- The patient is under the camera, on their back with their arms behind their head for approximately 30 minutes

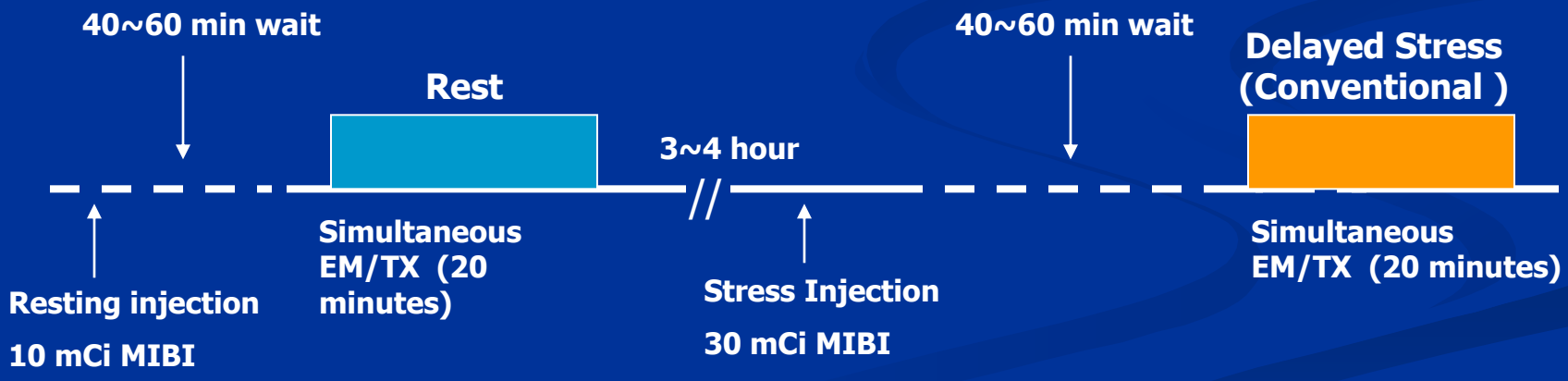
Study Time Frame

- Regadenoson vs. Dipyridamole
  - You will shave off about 7-10 minutes of your total exam time
  - Dipyridamole is infused over four minutes and the Rubidium is infused 3-5 minutes post infusion whereas Regadenoson in injected over 10 seconds and the Rubidium is infused 20 seconds later

Imaging Protocols

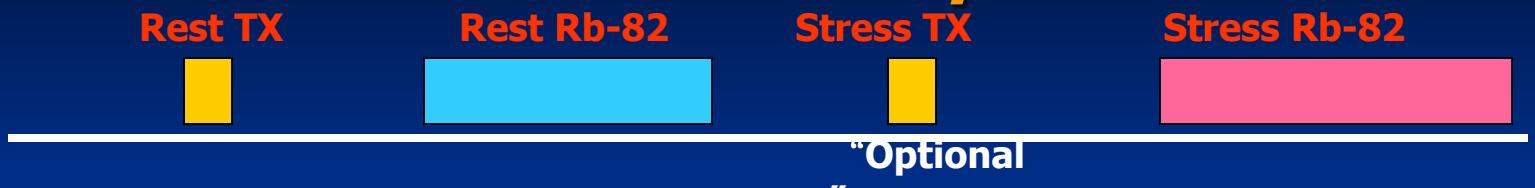
Conventional Same-day ECG-gated Tc99m-MIBI SPECT

- Image patient 30~60 minutes after peak stress
- Only provide delayed post-stress ventricular function
- Limited laboratory efficiency (6-7 pats/10 hours)

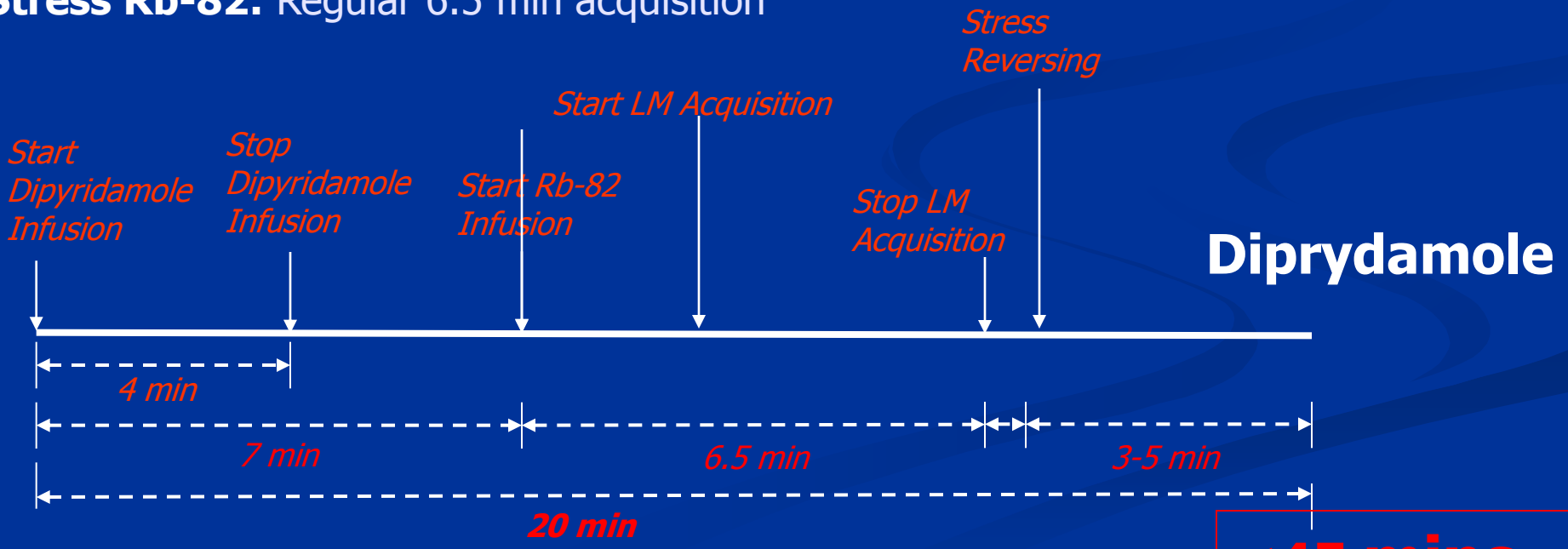


>6 hours

3D Diprydamole Peak-stress Rb-82 PET/CT



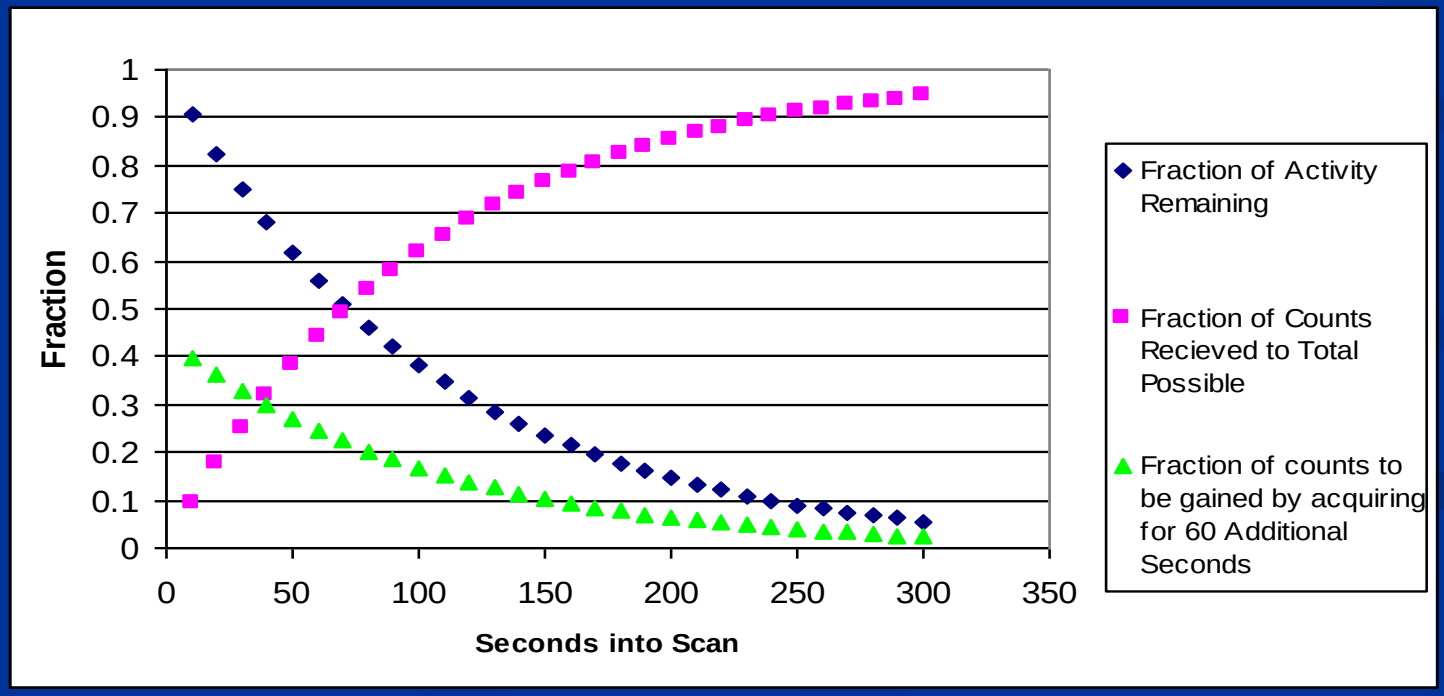
- **Rest & Stress TX scans:** 3-5 min each
- **Rest Rb-82:** Regular 6.5 min acquisition
- **Stress Rb-82:** Regular 6.5 min acquisition



<45 mins

Acquisition Times

- **Acquisition times need to recognize the fast decay time of Rb-82**
- **95% theoretical maximum of all counts will be acquired in the first five minutes**
- **Acquiring an additional 60 seconds only adds 2.4% more counts!**



Methods of Stress Testing

- 100% of patients that have PET Cardiac imaging with Rb 82 WILL have a chemical stress test with a drug called Dipyridamole or Regadenoson, there is NO Treadmill stress testing due to the 70 second half life of the Rubidiumb 82

Methods of Stress Testing

- Prior to 2010, most patients having PET Cardiac Myocardial Perfusion Imaging were stressed with the drug Dipyridamole due to insurance reimbursement lacking with the use of Regadenoson in the procedure.

Methods of Stress Testing

- Then came the Dipyridamole shortage and labs were forced to use Regadenoson, this forced the insurance companies to acknowledge the use of Regadenoson and reimbursement became much easier

Methods of Stress Testing

- Now, many labs use Regadenoson over Dipyridamole due to the shorter half life and decreased amount of symptoms, and reduced exam time
  - You might ask "Why use Dipyridamole then? Regadenoson produces less symptoms and has a shorter half life, reducing the use of Aminophylline, reducing exam time, seems altogether better, especially for the patient."

Methods of Stress Testing

- The Answer
  - Regadenoson costs significantly more. Although the is adequate reimbursement for Regadenoson, it is still more money up front going out.

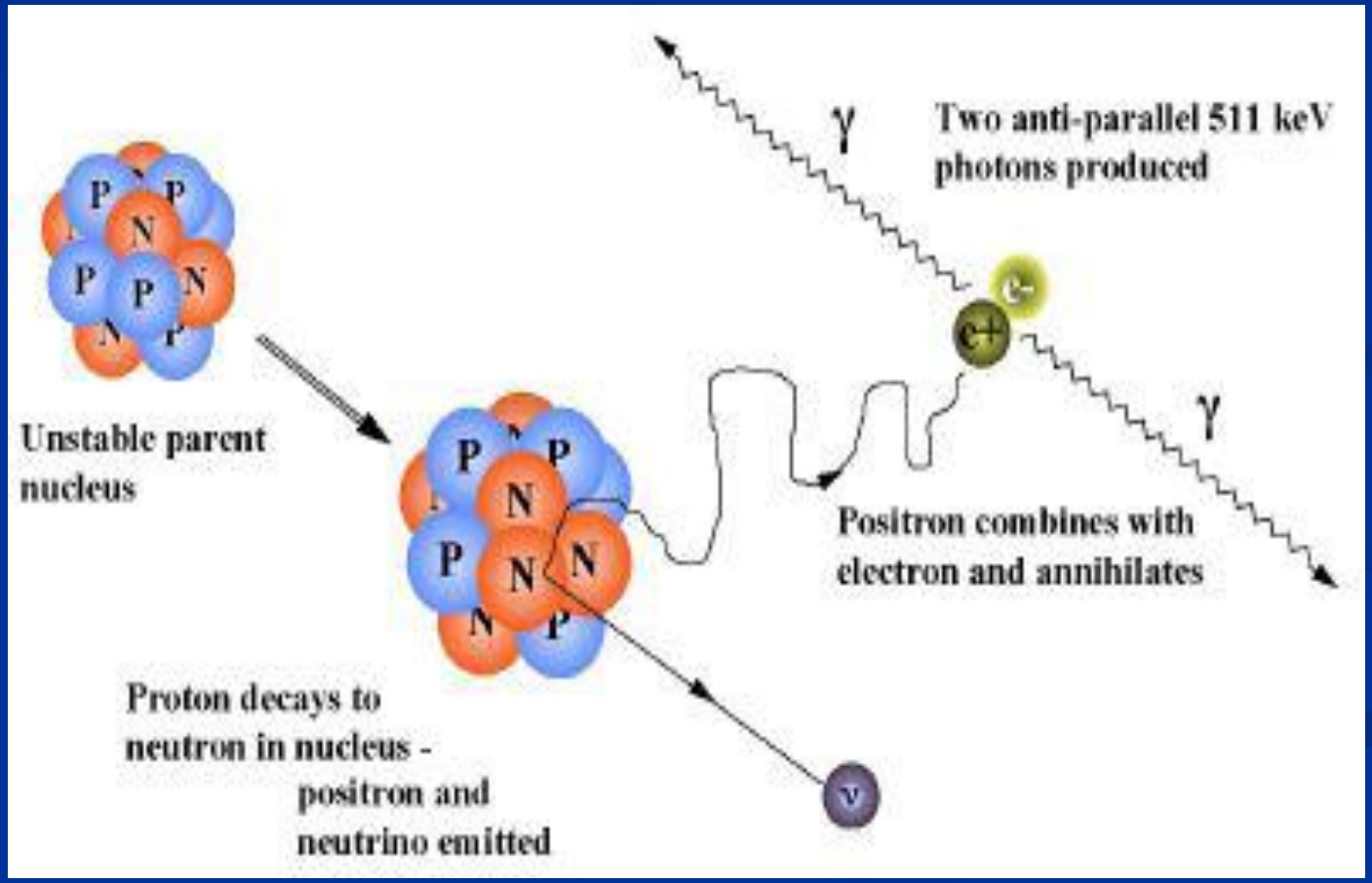
Methods of Stress Testing

- NOTE: All patients will have the Dipyridamole reversed with Aminophylline due to the prolonged half life as compared to Regadenoson.

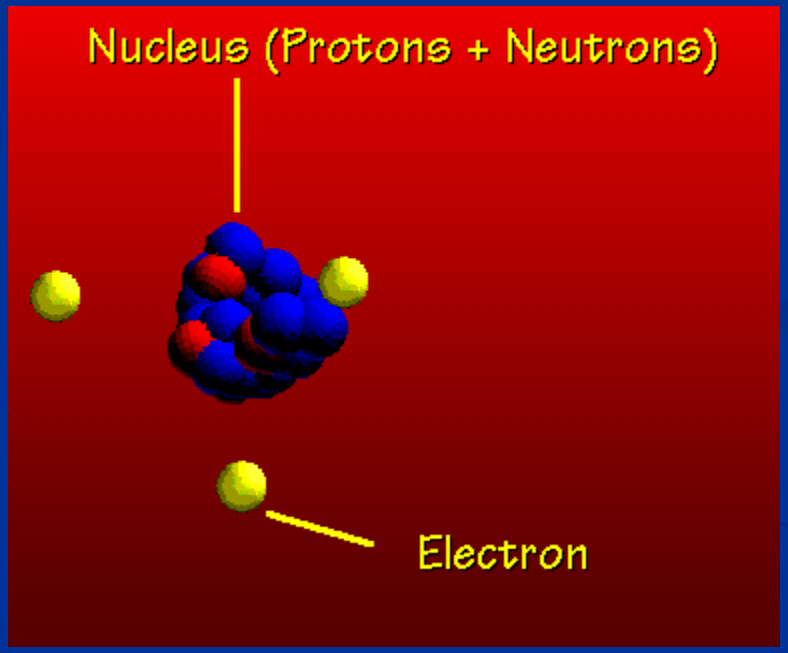
Basic Principle of PET (Positron Emission)

Positron Emission occurs when the Proton rich isotope (Unstable Parent Nucleus) decays and a Proton decays to a Neutron, a Positron and a Neutrino. After traveling a short distance (3-5mm), the positron emitted encounters an electron from the surrounding environment. The two particles combine and "annihilate" each other, resulting in the emission of two gamma rays in opposite directions of 511 keV each.

Positron Emission (continued)



Positron Emission



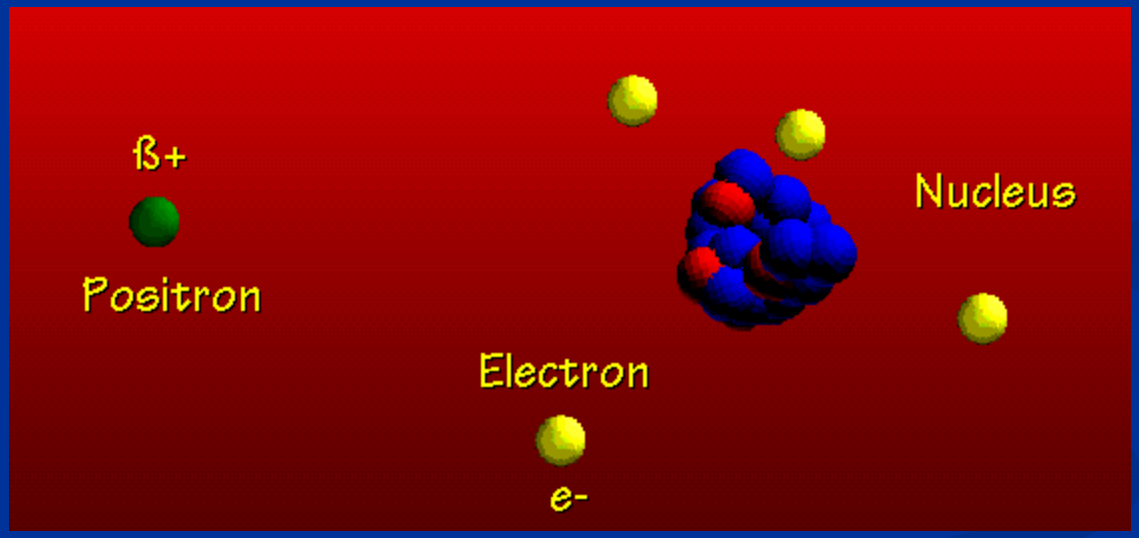
Positron Emission

The distance a positron travels depends on its energy, and varies between isotopes.

Isotope	Maximum Positron Range (mm)
F-18	2.6
C-11	3.8
Ga-68	9.0
Rb-82	16.5

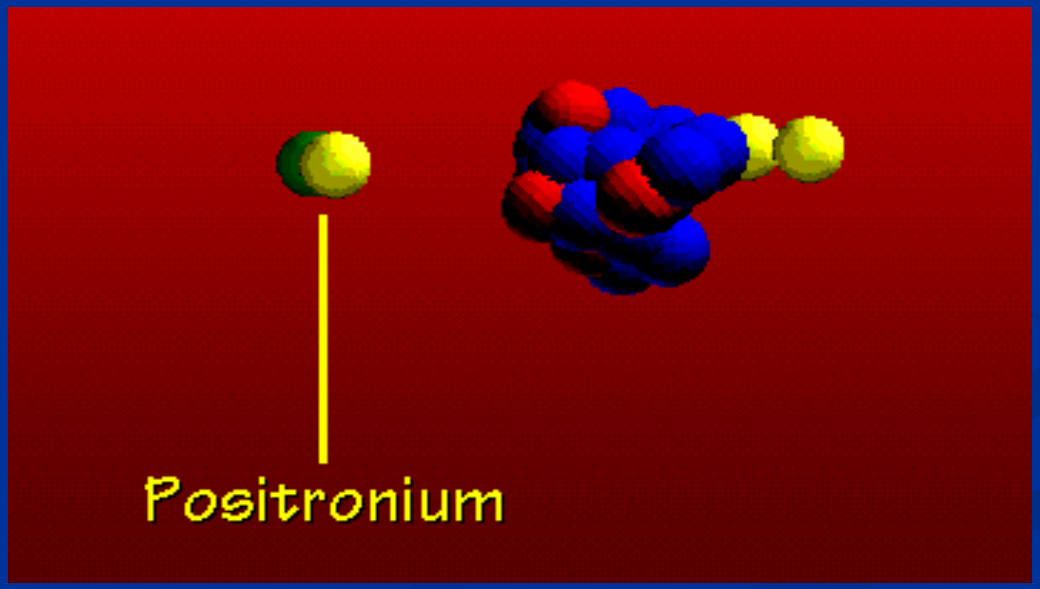
Positron Emission

Electrons and a positron traveling after being emitted from the nucleus of the radioactive element.



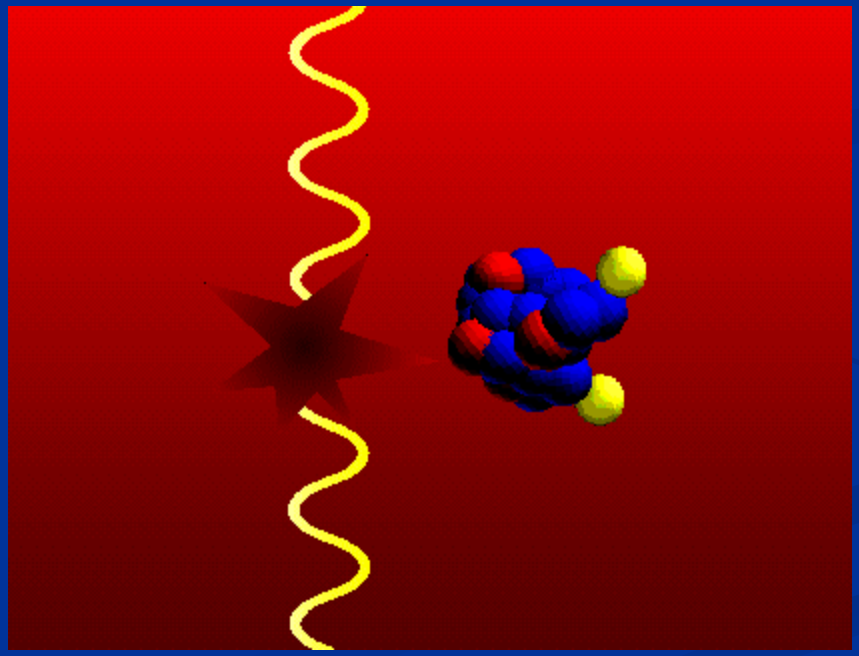
Positron Emission

The positron combines with electron forming positroniumas an intermediate.



Positron Emission

Annihilation of and electron and a positron resulting in the emission of two opposite gamma rays.



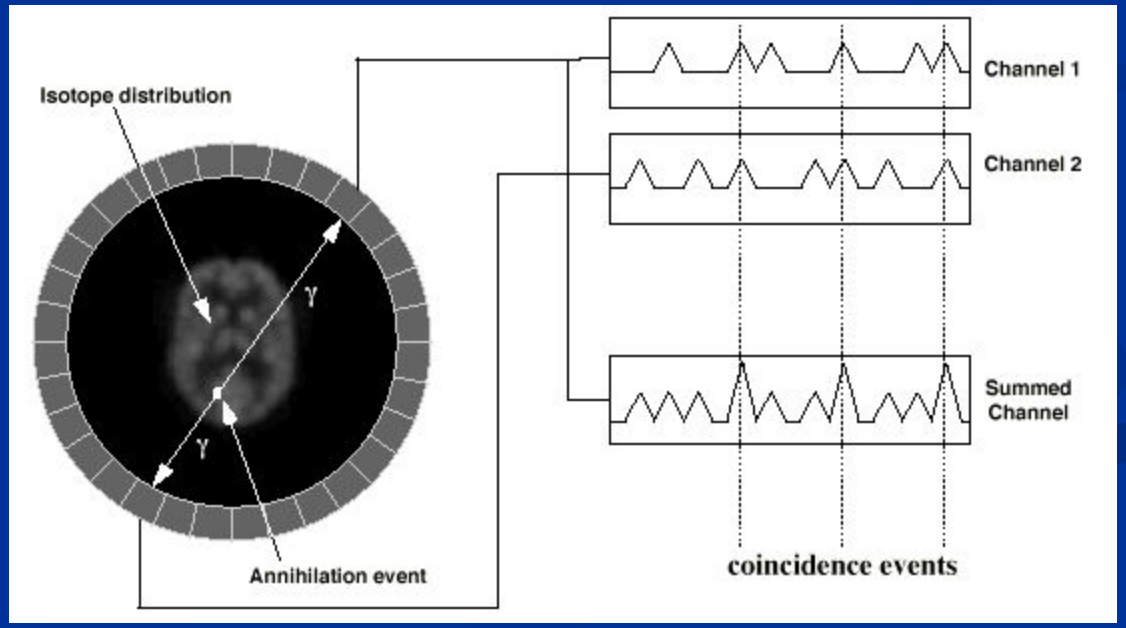
Positron Emission

The image acquisition is based on the external detection in coincidence of the emitted Gamma-rays, and a valid annihilation event requires a coincidence within 12 nanoseconds between two detectors on opposite sides of the scanner. For accepted coincidences, lines of response connecting the coincidence detectors are drawn through the object and used in the image reconstruction. Any scanner requires that the radioisotope, in the field of view, does not redistribute during the scan.

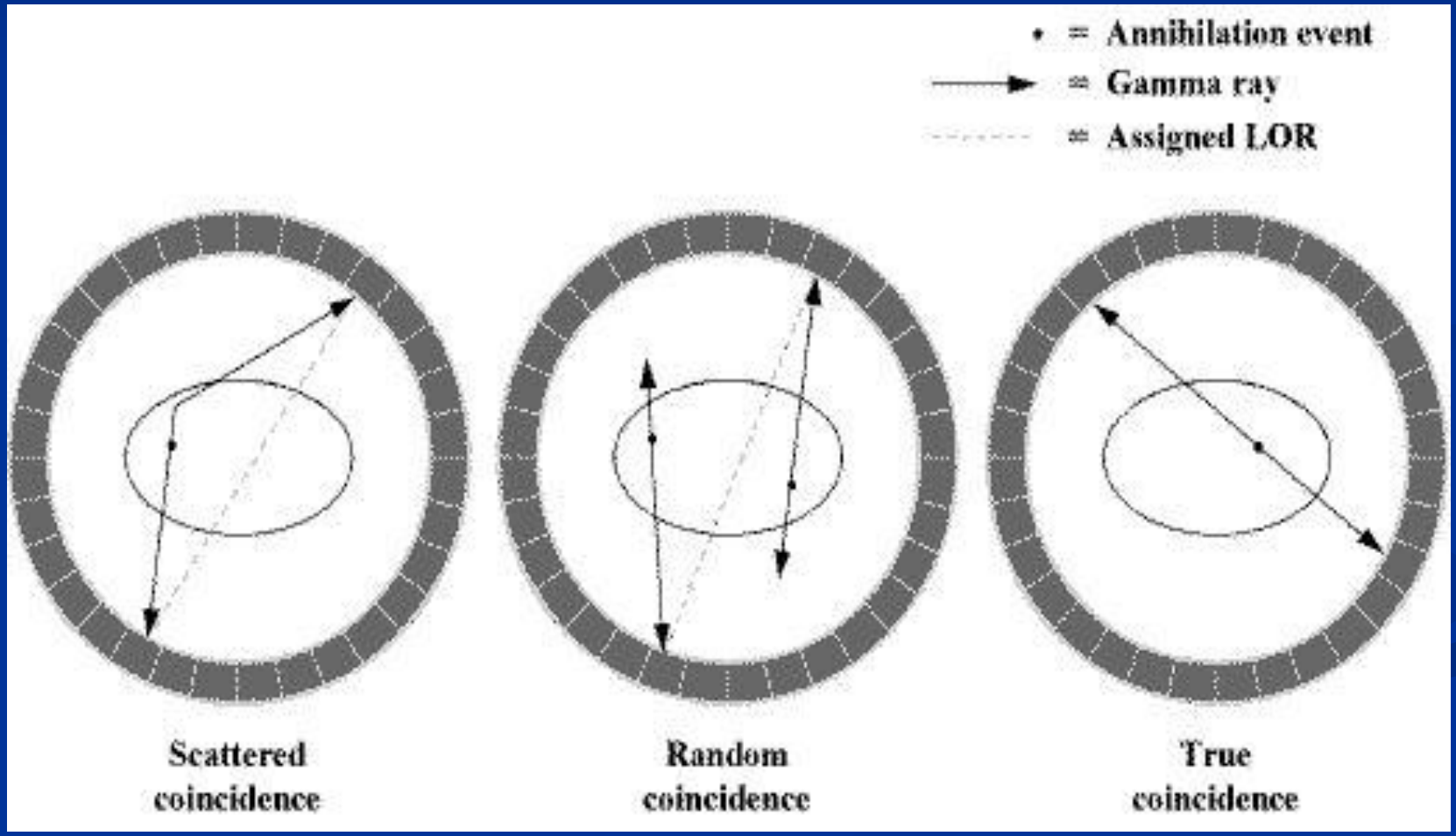
Coincidence detection in a PET camera

Each detector generates a timed pulse when it registers an incident photon. These pulses are combined in coincidence circuitry, and are deemed to be coincident if they fall within a short time-window.

Yes, this is a brain, not a heart

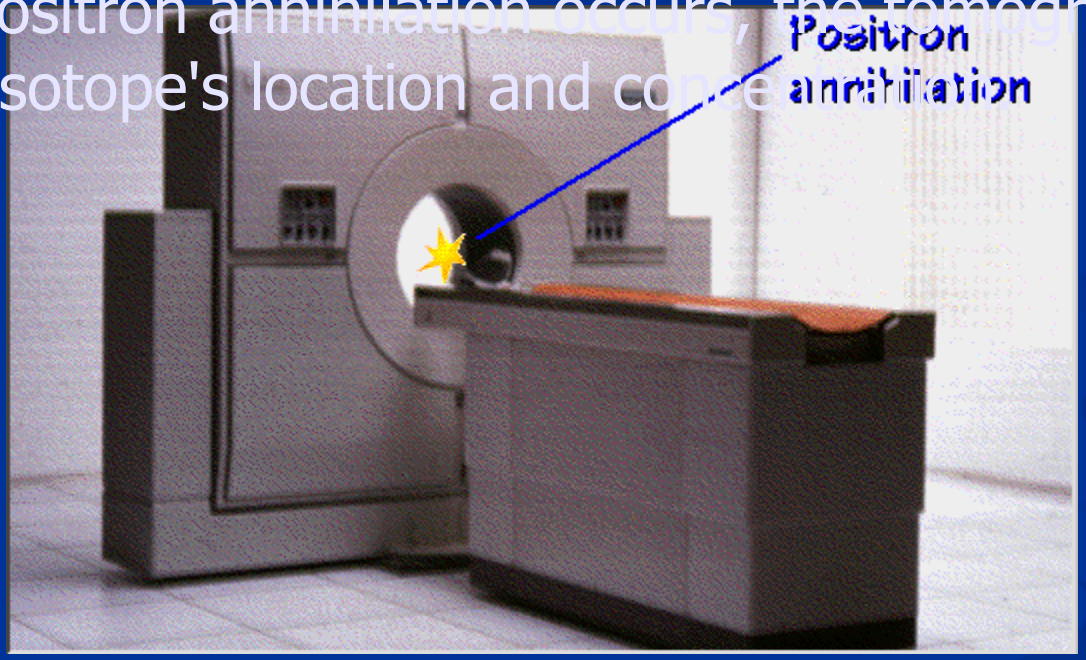


Types of Coincidences in PET



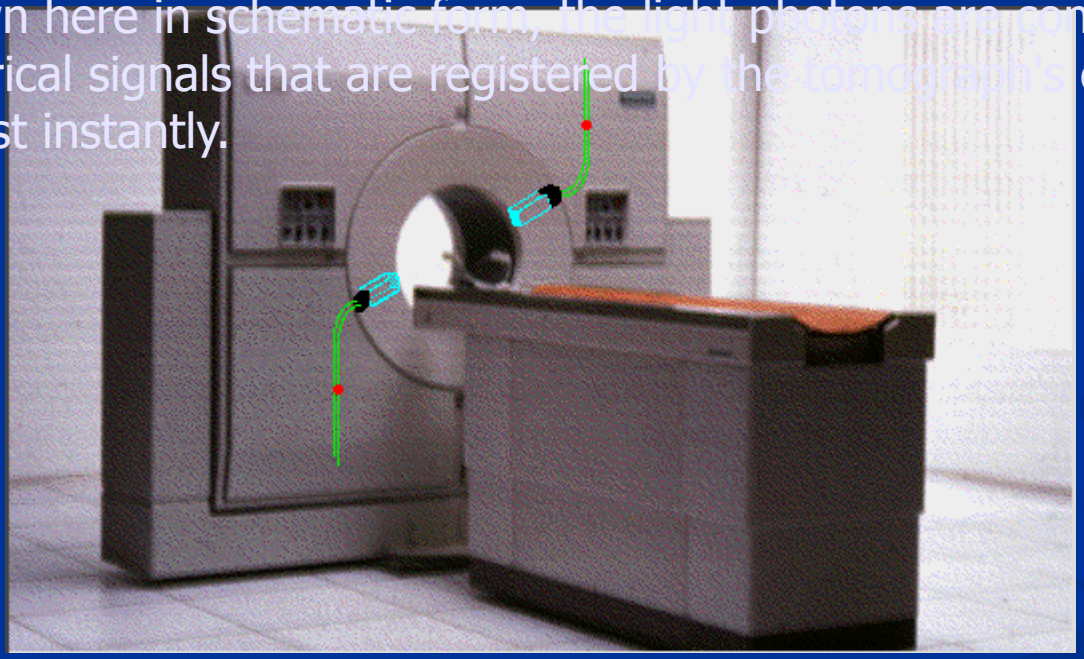
Basic Principle of PET (Emission Detection)

As positron annihilation occurs, the tomograph detects the isotope's location and conce[illegible]



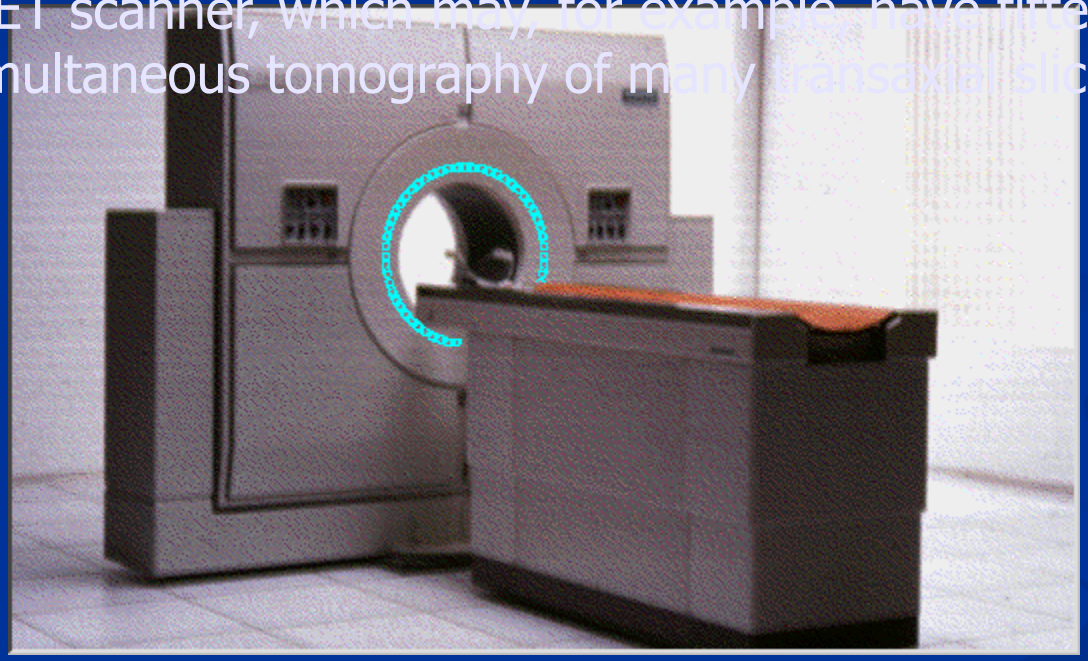
Emission Detection

Shown here in schematic form, the light photons are converted to electrical signals that are registered by the tomograph's electronics almost instantly.



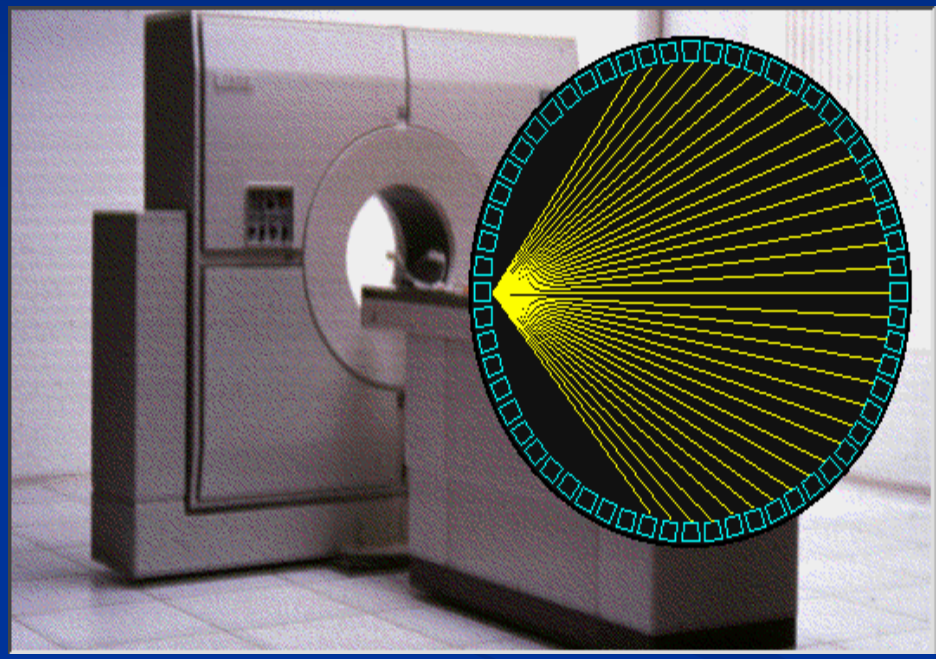
Emission Detection

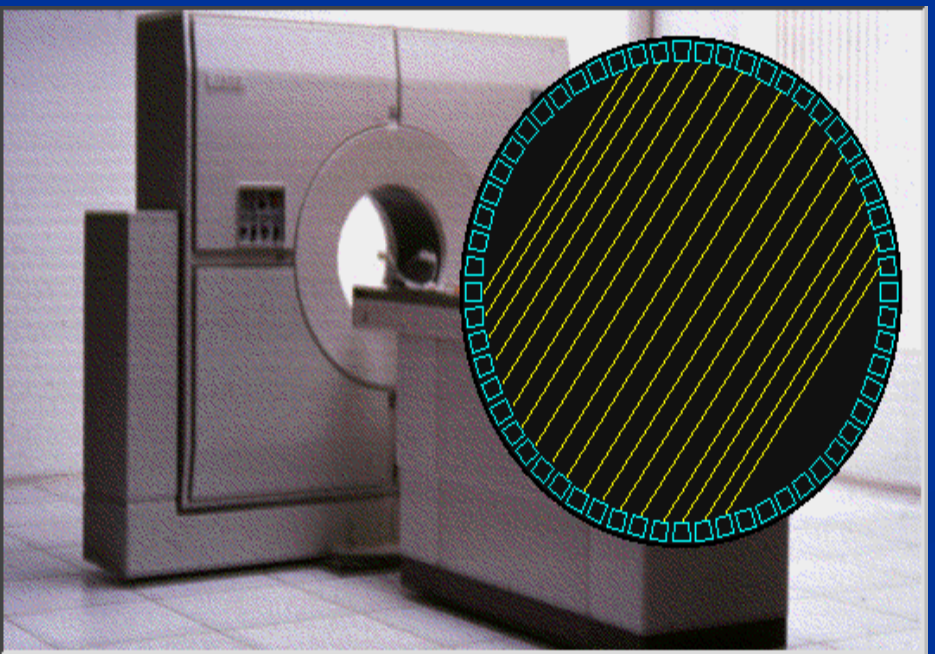
The ring of squares schematically represents one ring of detectors in a PET scanner, which may, for example, have fifteen such rings for simultaneous tomography of many transaxial slices



Emission Detection

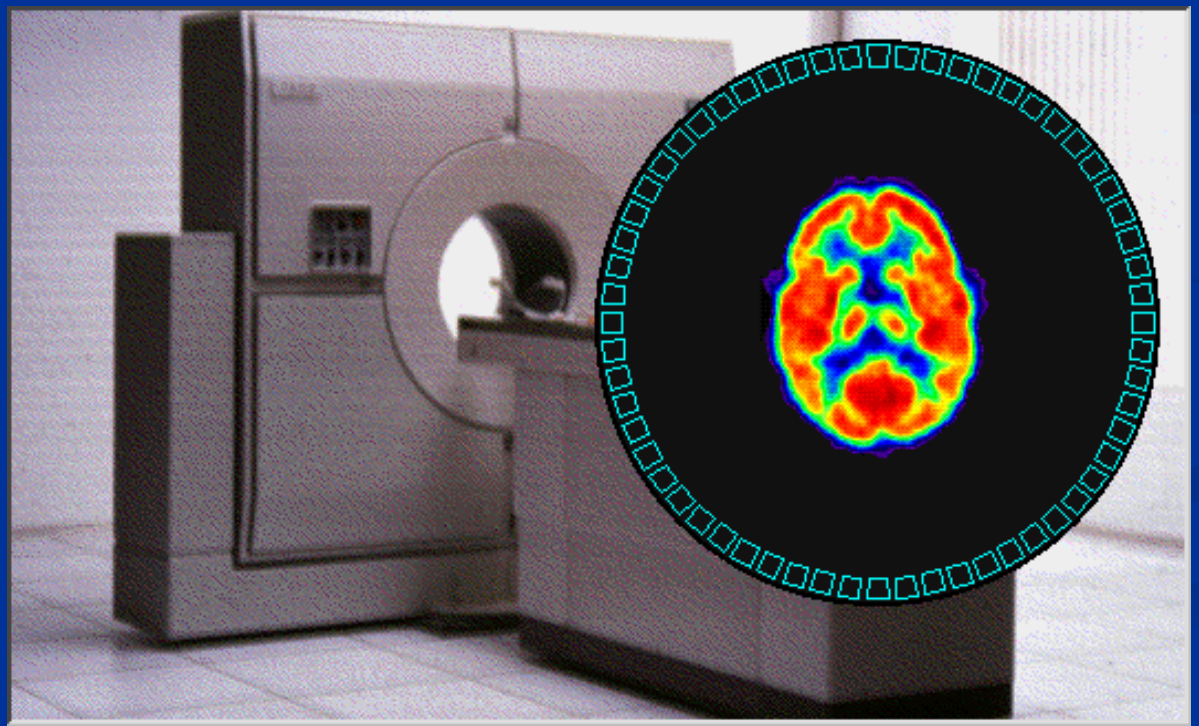
Each detector can be operated in multiple coincidence with many detectors across from it, thereby defining coincidence sampling paths over many angles.





Emission Detection

The tomograph's reconstruction software then takes the coincidence events measured at all angular and linear positions to reconstruct an image that depicts the localization and concentration of the radioisotope within a plane of the organ that was scanned.



Yes, again that is a brain, there are not any Cardiac images out there like this, so imagine that is a heart

Resolution Effects

- Four factors determine the Resolution of a reconstructed PET image, and they are the following:
  - Positron Range
  - Annihilation non-co-linearity
  - Detector Size
  - Block Effect ~2mm

Examples of Radiotracers and their Applications

Isotope	Tracer Compound	Physiological process or function	Typical application (Cardiac)
13N	Ammonia	Blood Perfusion	Myocardial Perfusion
18F	Fluoro-deoxy-glucose	Glucose metabolism	Cardiac Viability
82Rb	Rubidium	Blood Perfusion	Myocardial Perfusion

N_{13}-Ammonia

- Half-life 10 minutes
- Requires near-by cyclotron
- Excellent myocardial uptake & retention
- Bolus (20 - 60 mCi)
- Applicable to exercise or pharmacologic stress
- High start-up costs (cyclotron) but then costs relatively fixed
- Half-life long: may lower through-put efficiency
- In some pts, increased lung retention; frequent liver uptake
- Lower counts in lateral wall

Rubidium-82

- Half-life 70 seconds
- Strontium-82 generator renewed every 28 days
- Radionuclide always available (facilitates add-ons)
- Can re-image in minutes if technical problems (should almost never have a poor quality study, poor gate will)
- Tl-201 – like kinetics: high extraction at high flows (enhances detection of mod-severity CAD)
- Short half-life (technically challenging; pharm stress only; less useful for very obese)
- High on-going costs (30K mo)

The Radioactive Tracer

- The radioactive tracer (isotope), Rubidium, is primarily the tracer of choice for PET Myocardial Perfusion Imaging
- Rubidium is what is absorbed by the heart muscle and it is this that allows us to see the blood flow to the heart at rest and at stress
- There is no Rubidium shortage. You will have your own Generator and will be able to do add ons; however, most patients will require preauthorization (not medicare)
- The patients radiation exposure with Rubidium is minimal with a half life of 70 seconds compared to Thallium's half life of 3 days or even Tc99m of 6 hrs

Note: The Rb Generator is currently recalled

Patient Radiation Dosimetry

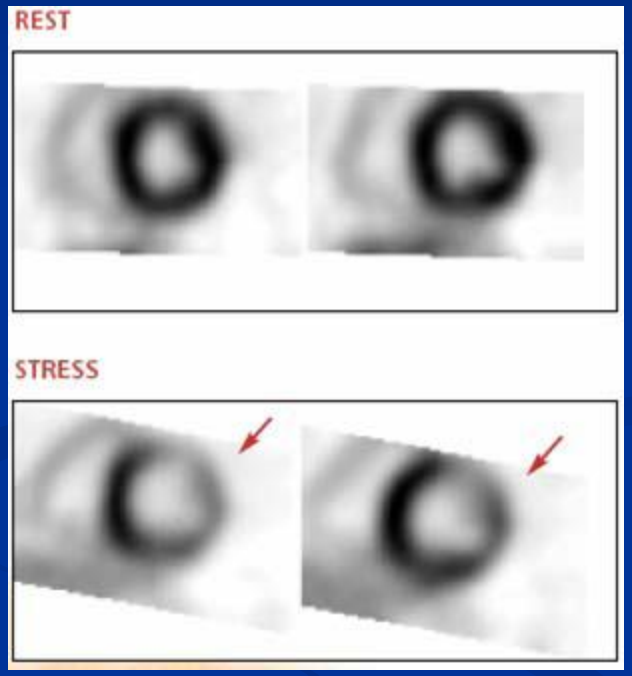
Isotope	Effective Dose Equivalent	Per study	Total
Rb-82	1.6 mrem/mCi	50 mCi	80 mrem
Tc-99m mibi	51 mrem/mCi	30 mCi	1500 mrem
Th-201	850 mrem/mCi	4 mCi	3200 mrem
CT mu-map	440 mR	1 scan	440 mrem

Clinical Applications of Cardiac PET Rubidium 82

- Heart Disease:
  - Coronary Artery Disease

Heart Diseases

PET is the most accurate test to reveal coronary artery disease or rule out its presence. The PET images show inadequate blood flow to the heart during stress undetected by other non-invasive cardiac tests.



Short Video Clip
Advantages of PET

Advantages and Disadvantages of Cardiac PET using Rubidium 82

- Advantage:
  - increased sensitivity and accurate attenuation correction provided by the PET imaging modality
  - Decreased Cardiac Cath
  - PET testing minimizes equivocal or non- diagnostic results
  - There are fewer questions about the results

Advantages and Disadvantages of Cardiac PET using Rubidium 82

- Advantage:
  - This is a much shorter test of 45 minutes compared to 1.5-3 hrs
  - You never have a tracer shortage (unless the generator is recalled!!)
  - Minimal Exposure due to the 70 second half life

Advantages of PET

- Faster study
- More accurate
- Attenuation correction
- Health care cost savings

PET perfusion imaging

Value for the patient

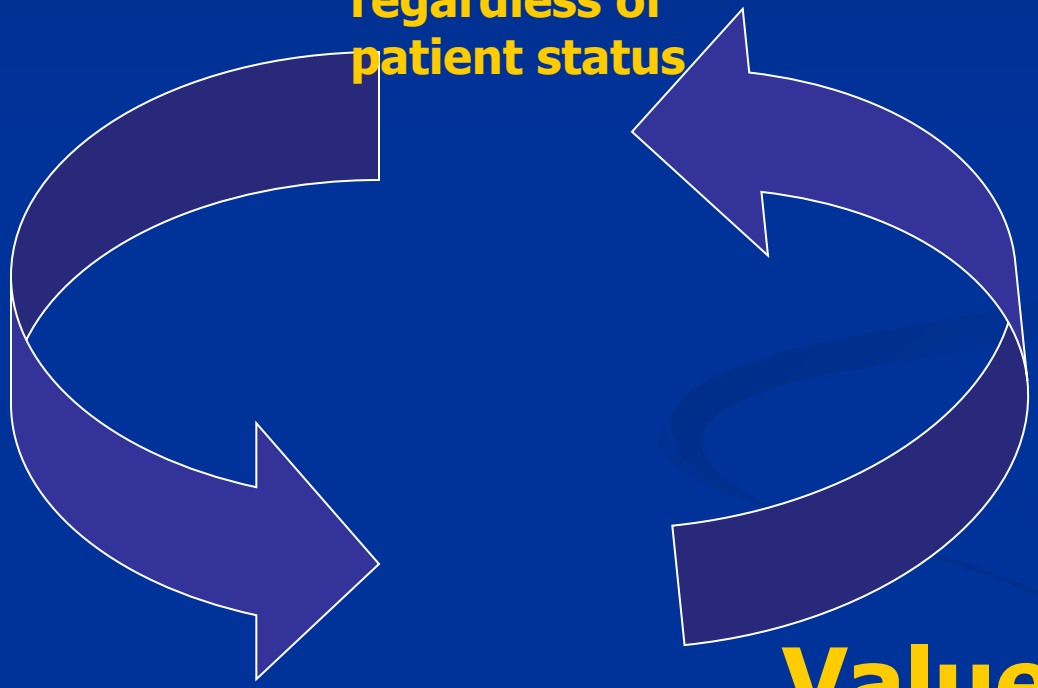
High diagnostic accuracy regardless of patient status

Lower radiation exposure

Value for the practice

Higher insurance reimbursement

Shorter acquisition times



Diagnostic Accuracy

- PET image quality excellent 78% and 79% for rest and stress
- SPECT image quality excellent 62% and 62% for rest and stress
- Intepretations
  - Definitely normal/abnormal
  - PET 96%
  - SPECT 81%

Diagnostic Accuracy

- Diagnostic accuracy

	PET	SPECT
Stenosis (70%)	89%	79%
Stenosis (50%)	87%	71%
Men vs Women	+	-
Obese vs. nonobese	+	-

Transmission Quality Control

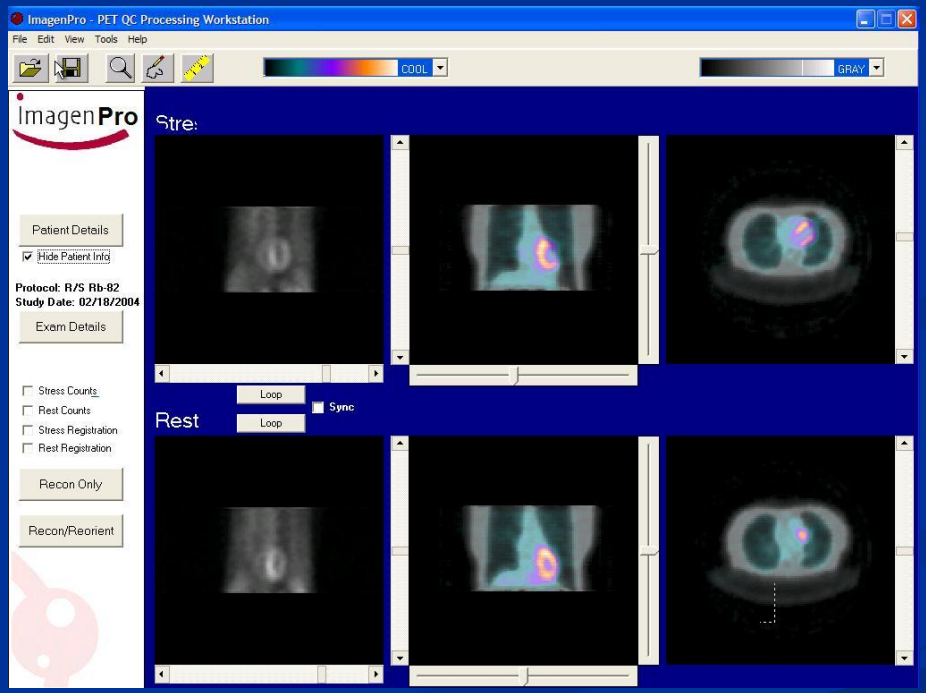
Counts, Truncation and Registration

Good transmission counts, no truncation, but stress misregistration

MISREGISTRATION OF TRANSMISSION AND EMISSION DATA IS THE #1 SOURCE OF DIAGNOSTIC ARTIFACTS

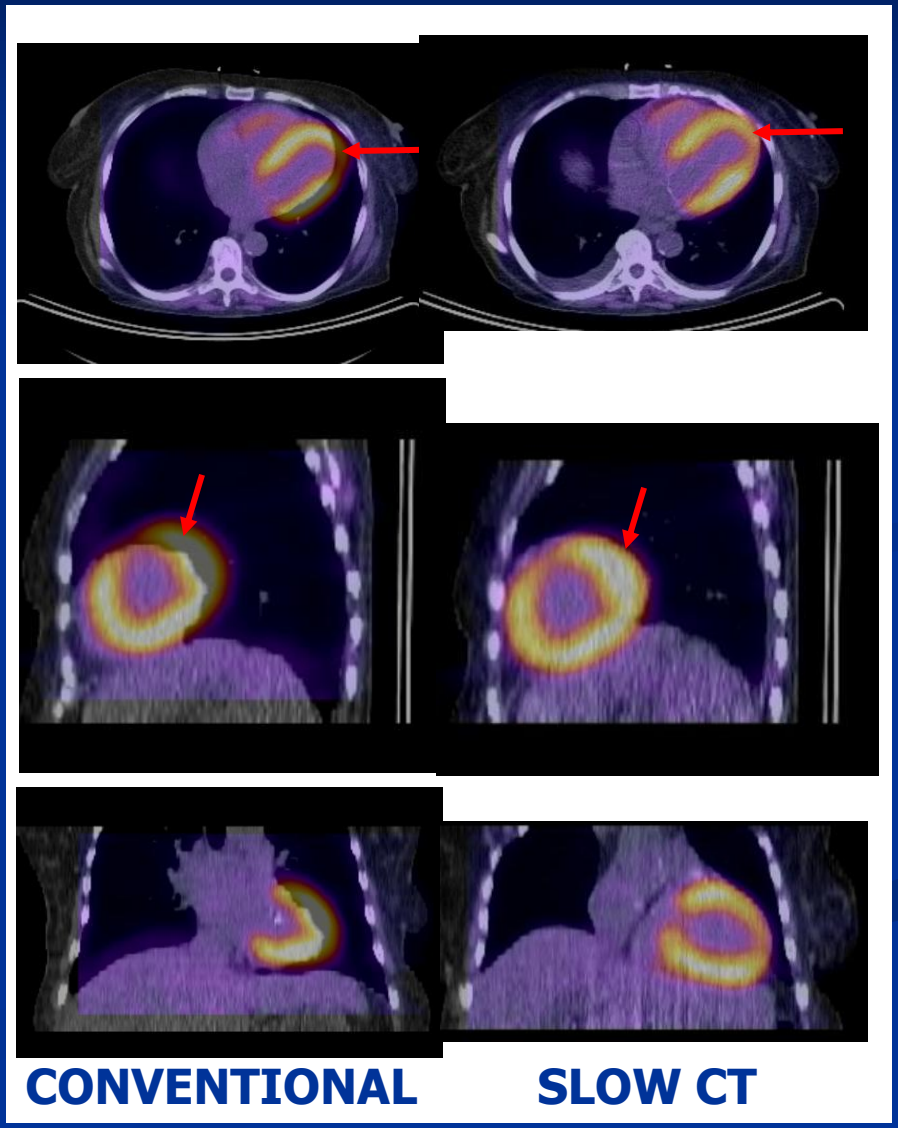
Must always correct this artifact

Misregistration appear as LCx or left main disease

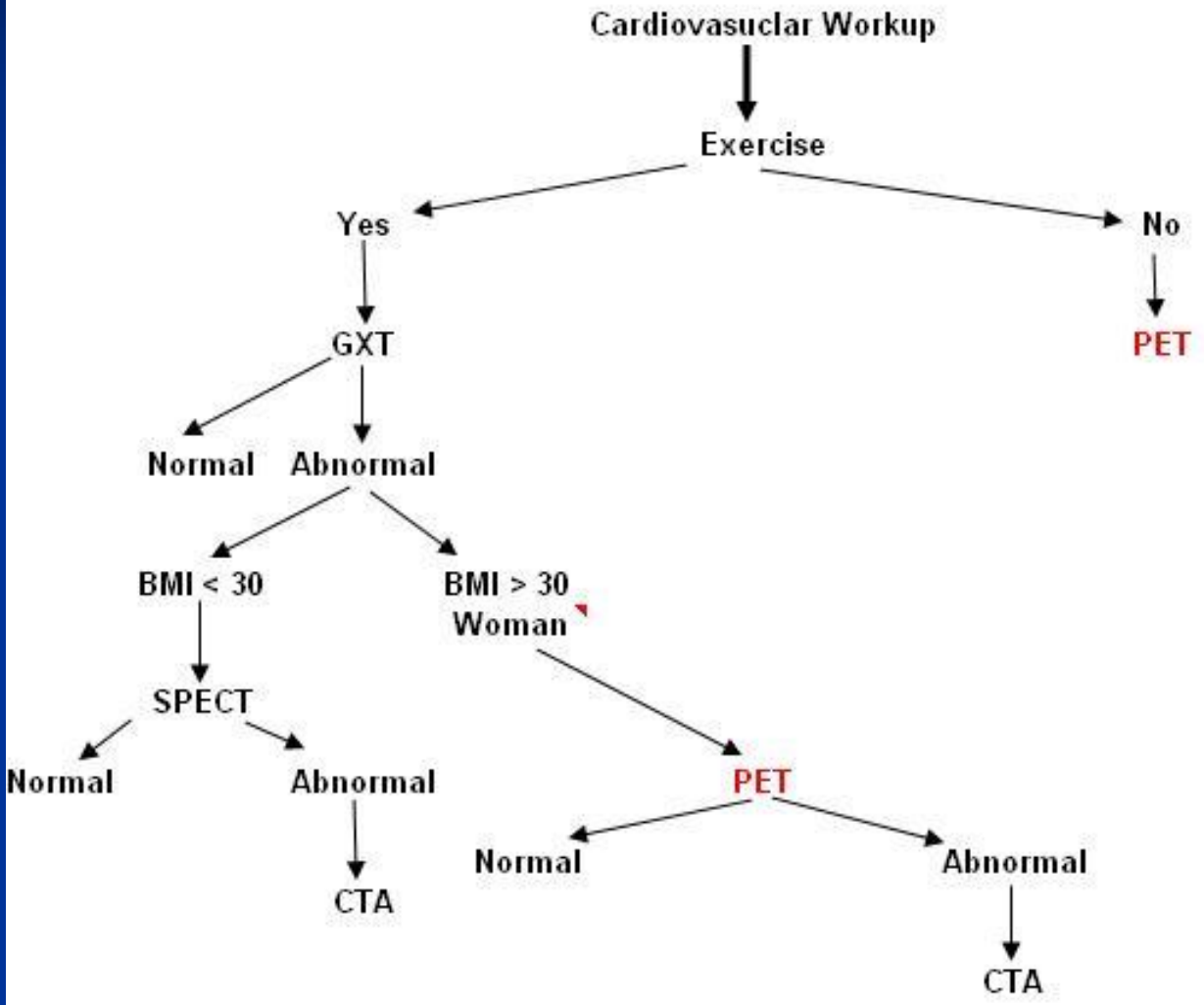


Mismatch artifact

- Slow CT designed to match transmission and emission data sets
- Minimize artifacts



Clinical Pathway for Cardiac PET Practice



Advantages and Disadvantages of Cardiac PET using Rubidium 82

- Disadvantages:
  - If the Generator is recalled or shipment delayed, you can't do any patients
  - Cost: the Generator costs slightly of $30,000.00 per month. You make that up, but it's a substantial amount going out up front each month

The Generator

- **What is CardioGen-82?**

  CardioGen-82 is a radionuclide generator that produces and administers the radioisotope rubidium-82 for positron emission tomography (PET) myocardial perfusion imaging (MPI) in a controlled fashion through the use of an infusion device, the CardioGen-82 Infusion System. In simpler terms, it is a system for infusing a radioactive nuclear medicine agent, rubidium-82, for the purpose of imaging the heart to determine if the heart's blood supply is normal or not.

The Generator

- **How does it work?**

  The CardioGen-82 generator is used with an infusion system. The generator and the infusion system produce the desired radioisotope (rubidium-82) from its precursor (strontium-82) and control its administration into a patient for the purpose of imaging of the heart. The generator also contains some natural, very low and acceptable levels of strontium-85, which is produced during the manufacturing of strontium-82, and cannot be separated from it.

The Generator

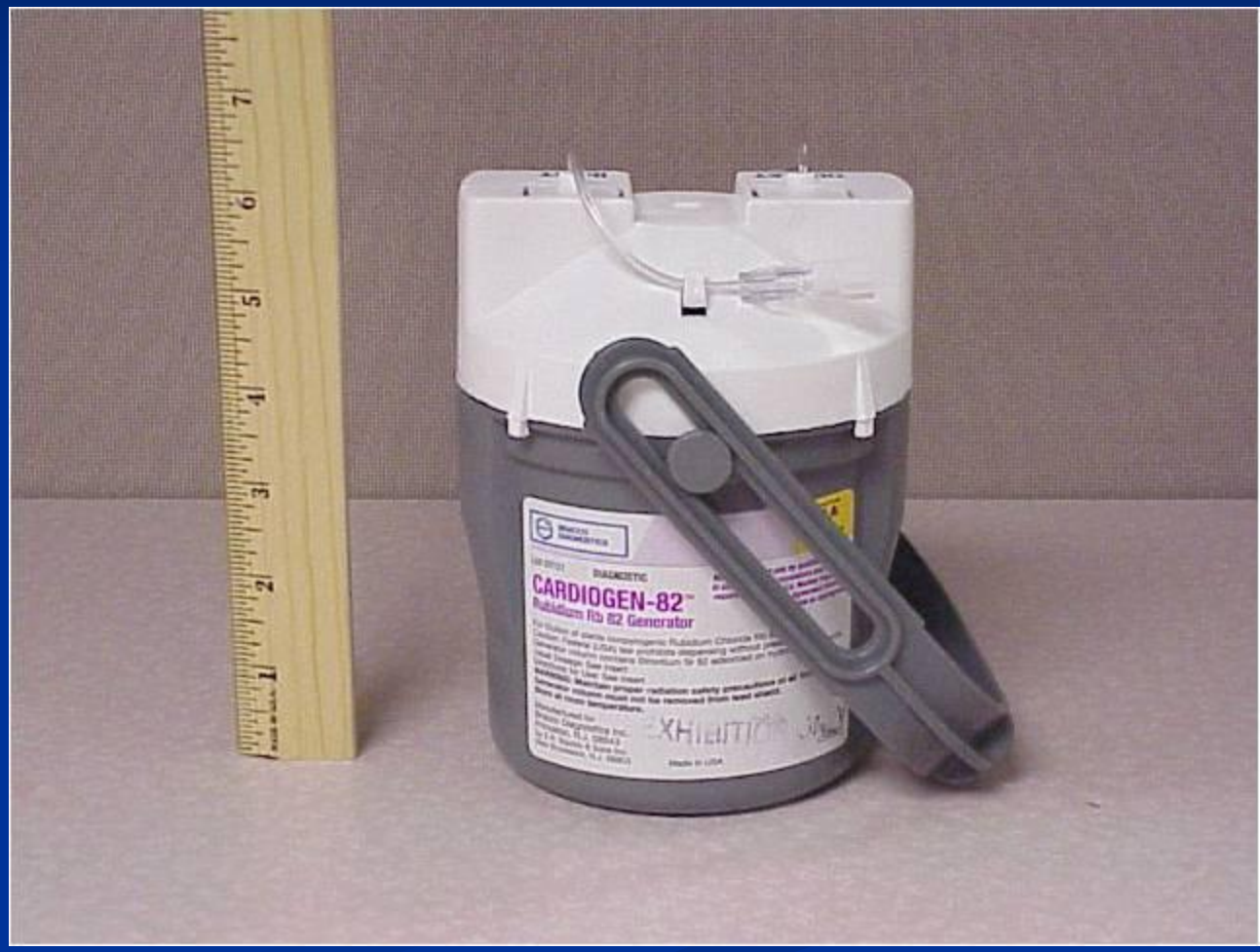
- **How long has the CardioGen-82 been on the market?**
  22 years

The Generator

This is the generator cart, the actual Rb generator is housed underneath in lead shielding

The Generator

This is the generator, as you can see it is very compact



CardioGen-82® (Rubidium Rb 82 Generator)

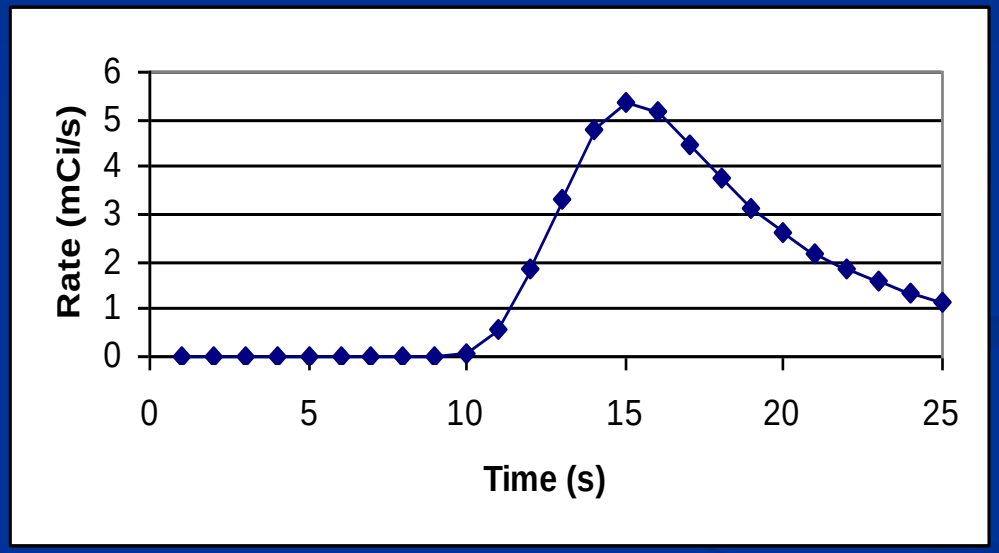
- Rubidium-82 (Rb-82) is produced by decay of Strontium-82 (Sr-82)
- 75 second T½
- Kinetics:
  - Potassium analog
  - High extraction fraction at high flow rates
- Defects visualized 2-7 minutes after injection
- Same sized dose at stress & rest due to short T½
- New generator every 28 days
- Fixed price, not unit dose
- Dose available 24 hours per day, 7 days per week
- Pharmacologic stress studies

CardioGen-82®
(Rubidium Rb 82 Generator)

- Generator replaced every 28 days
- Rb-82 dose is provided within 10 minutes
- Infusion System is automated for the infusion and patient dose
- Permits accurate dosing with minimal operator interface, thus decreasing radiation exposure
- Contains shielding vault for CardioGen-82® Generator and waste container

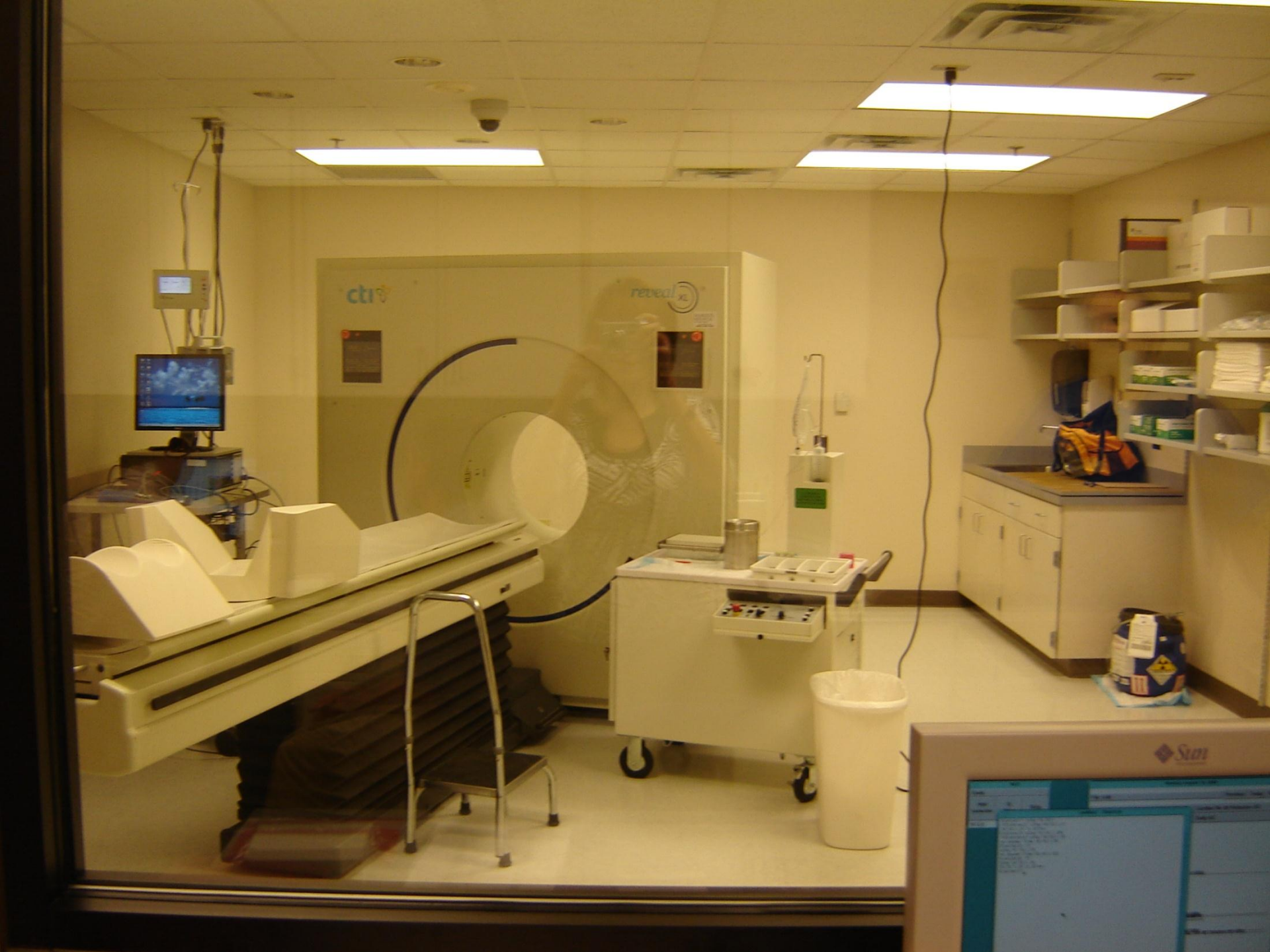
Dose delivery by Infusion System

As generator decays, amount of dose delivered may drop. Consistent bolus delivery can improve count statistics near the end of generator life.



Infusion pump set to deliver 60 mCi or operate for 25 sec, whichever is reached first. Maximizes bolus of Rb-82.


reveal XL


cti
reveal
Sun

Overview of Generator QC

PET MYOCARDIAL BRACCO RUBIDIUM GENERATOR QC

WASH: place empty vial in lead pig labeled W. Place patient line with needle into the vial. Place one vent needle into the vial. Wash settings: 50 ML's, 99 mCi. Hit the infuse button. When orange light goes out, start timer. At 5 minutes measure activity. At 10 minutes start the break through.

BREAK THROUGH: place empty vial in lead pig labeled B. Place patient line with needle into the vial. Place one vent needle into the vial. Break through settings: 50 ML's, 99 mCi. Hit the infuse button. When orange light goes out, start timer. At 5 minutes measure activity. Record the activity on the break through worksheet. At 10 minutes start the calibration. At 30 minutes, recheck the activity and record the activity on the break through worksheet.

CALIBRATION: place empty vial in lead pig labeled C. Place patient line with needle into the vial. Place one vent needle into the vial. Calibration settings: 50 ML's, 60 mCi. Hit the infuse button. When orange light goes out, start timer. At 5 minutes measure activity. Record the activity on the calibration worksheet.

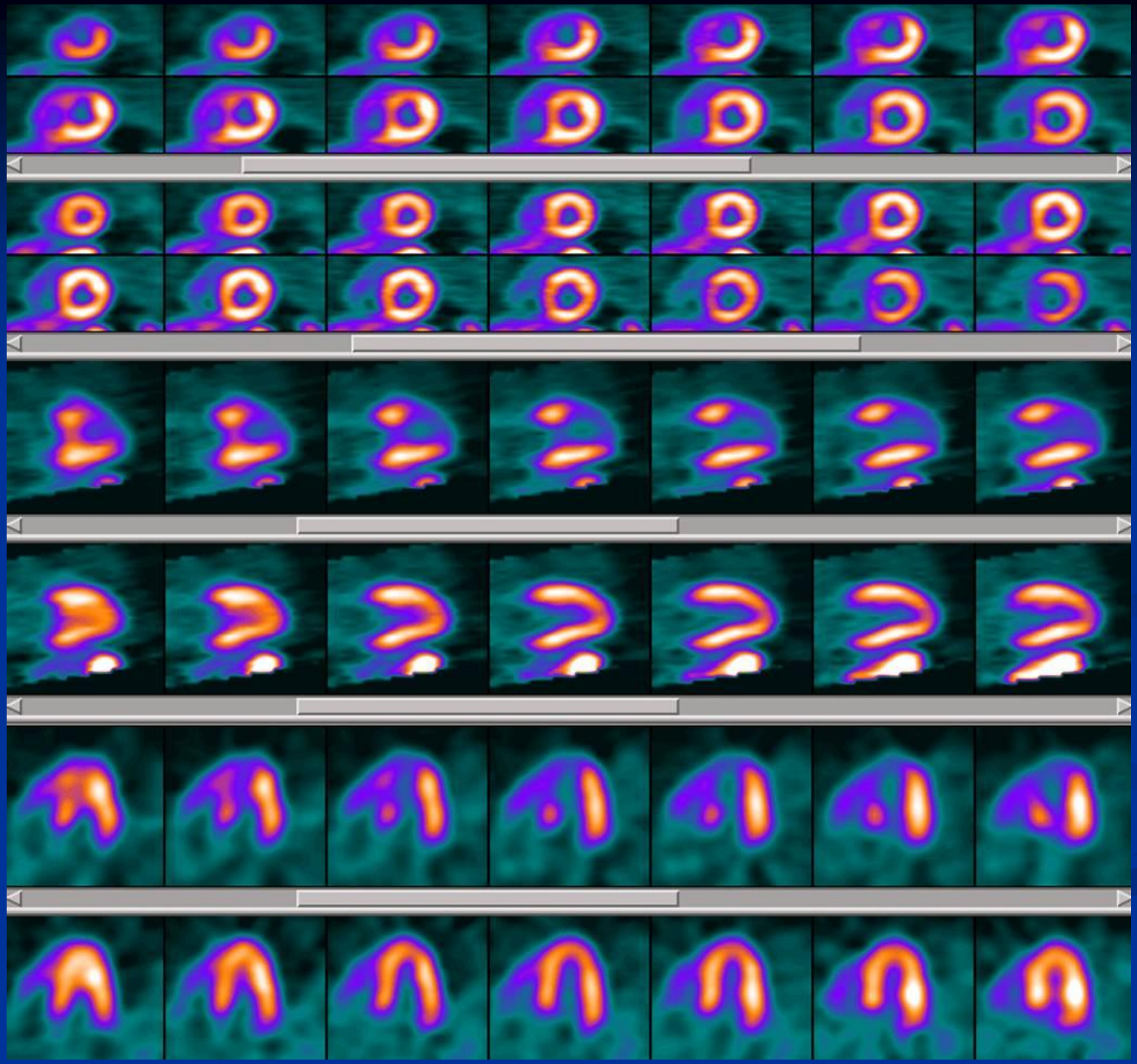
Reset the setting to: 35 ML's, 60 mCi

Images of PET MPI using Rb 82

The following images are of PET MPI with RB 82

Patient 1

- 65yo male 280 lbs
- Chest pain syndrome
- Cannot exercise due to knee arthritis

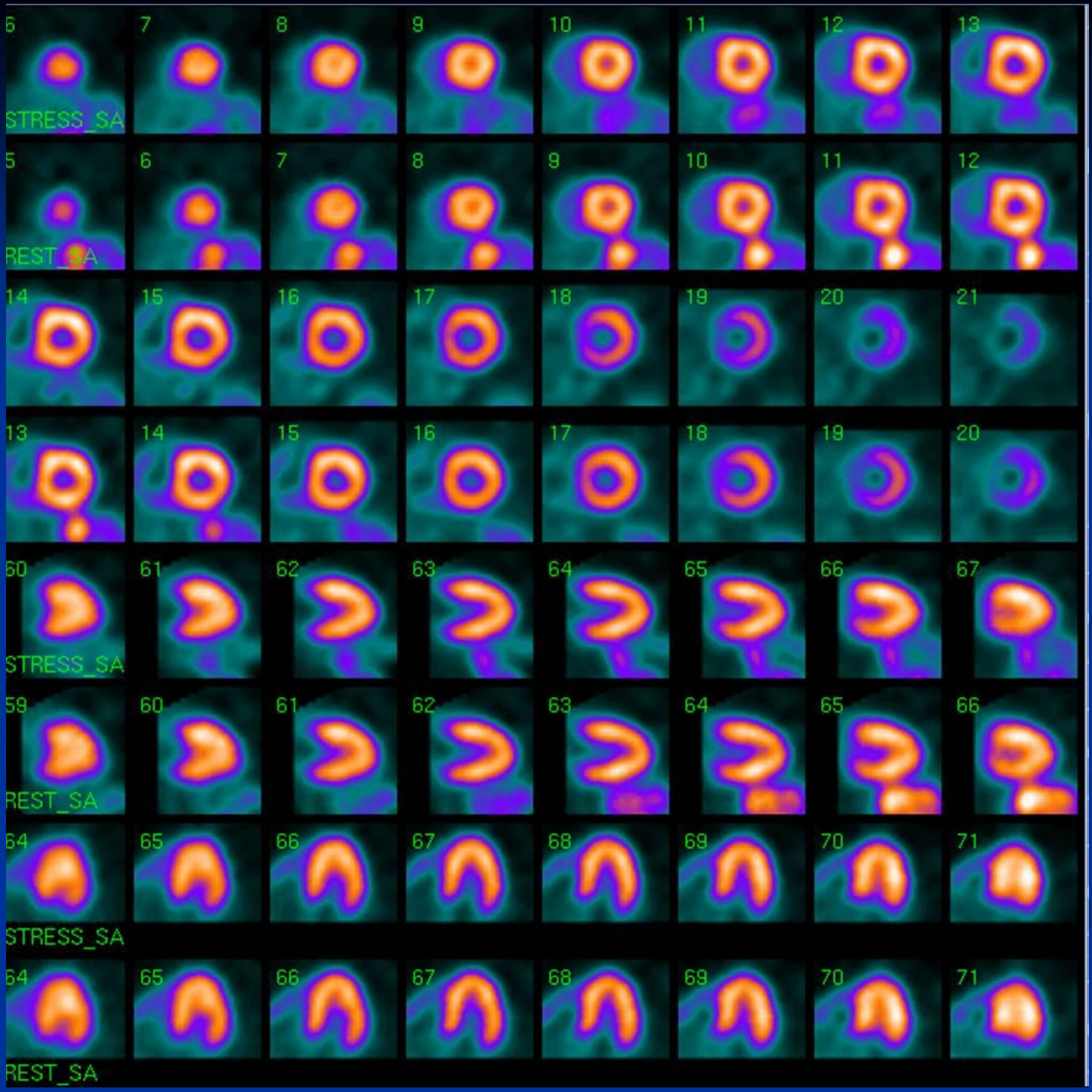


The Power of PET

- Perfusion images reveal reversible perfusion defects involving the anterior/ anterior septal and septal walls consistent with LAD obstruction
- Coronary catherization revealed 85% proximal stenosis of the LAD

Patient 2

- 45 yo female with abnormal non diagnostic GXT
- Perfusion study ordered

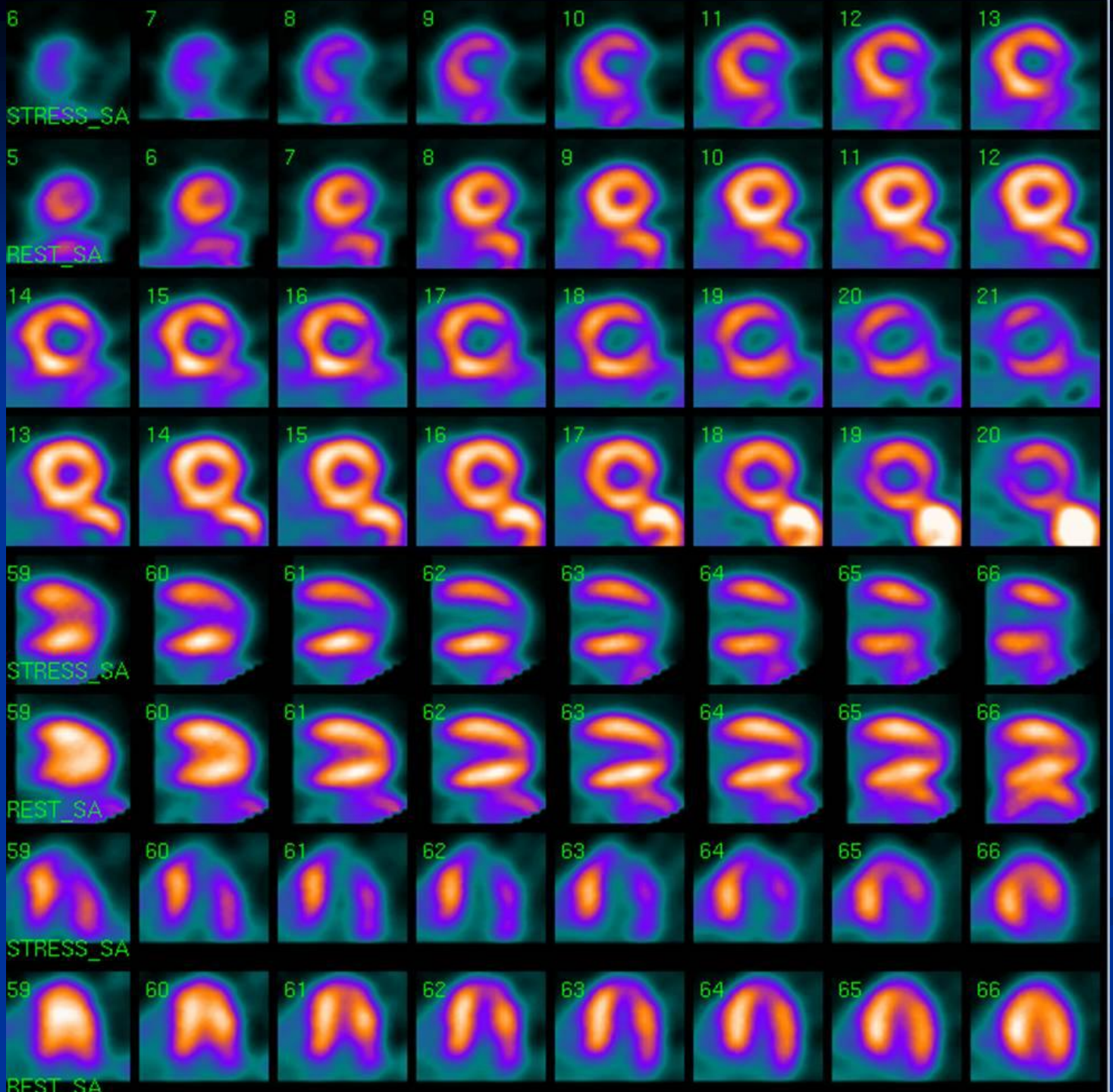

6 7 8 9 10 11 12 13
STRESS_SA
5 6 7 8 9 10 11 12
REST_SA
14 15 16 17 18 19 20 21
13 14 15 16 17 18 19 20
60 61 62 63 64 65 66 67
STRESS_SA
59 60 61 62 63 64 65 66
REST_SA
64 65 66 67 68 69 70 71
STRESS_SA
64 65 66 67 68 69 70 71
REST_SA

The Power of PET

- Normal perfusion pattern
- Prognosis good

Patient 3

- 75yo female with history of PTCA of left circumflex artery
- Now presents with recurrent atypical chest pain syndrome and fatigue


6
7
8
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10
11
12
13
STRESS_SA
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6
7
8
9
10
11
12
REST_SA
14
15
16
17
18
19
20
21
13
14
15
16
17
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19
20
59
60
61
62
63
64
65
66
STRESS_SA
59
60
61
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66
REST_SA
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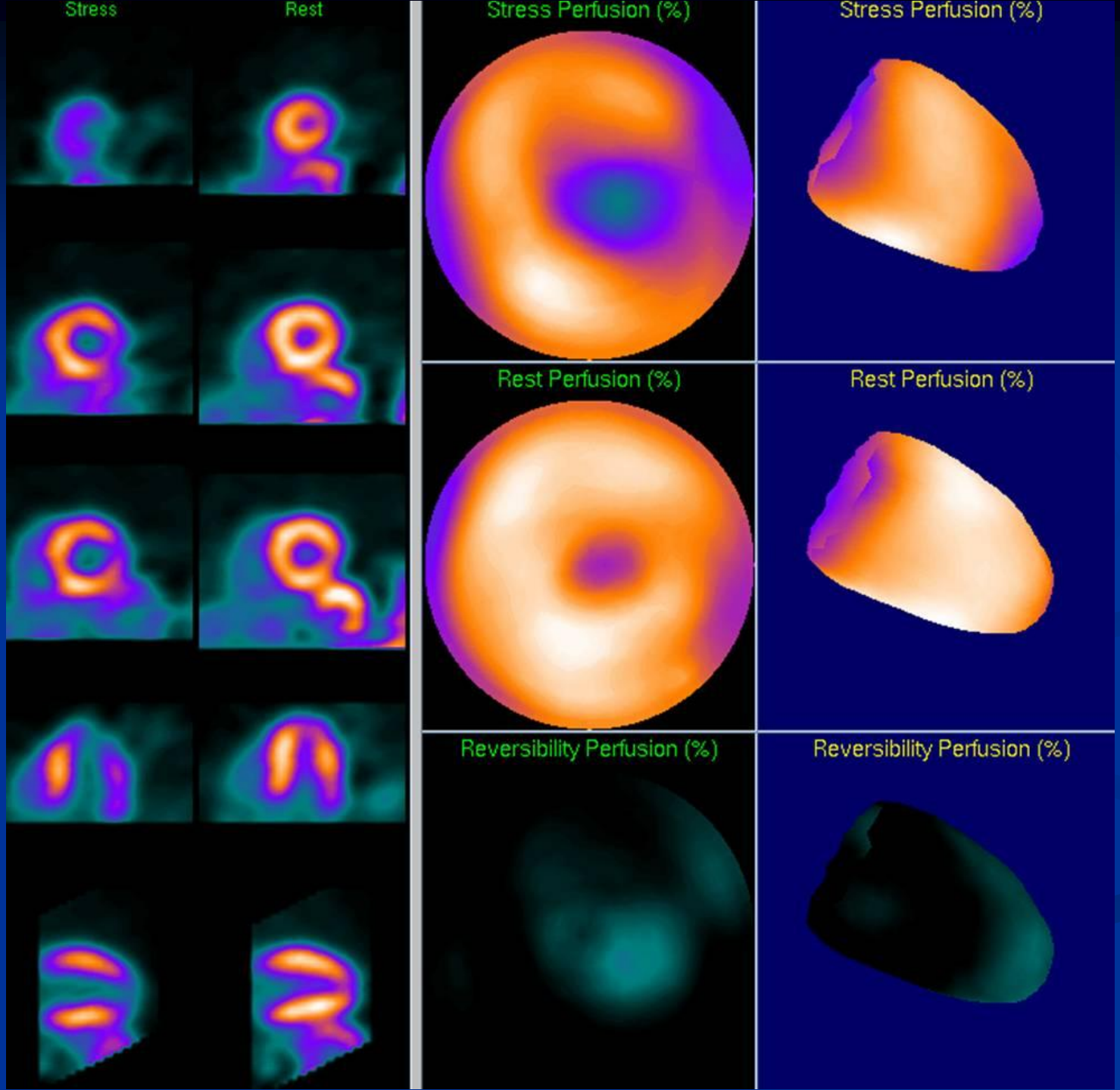
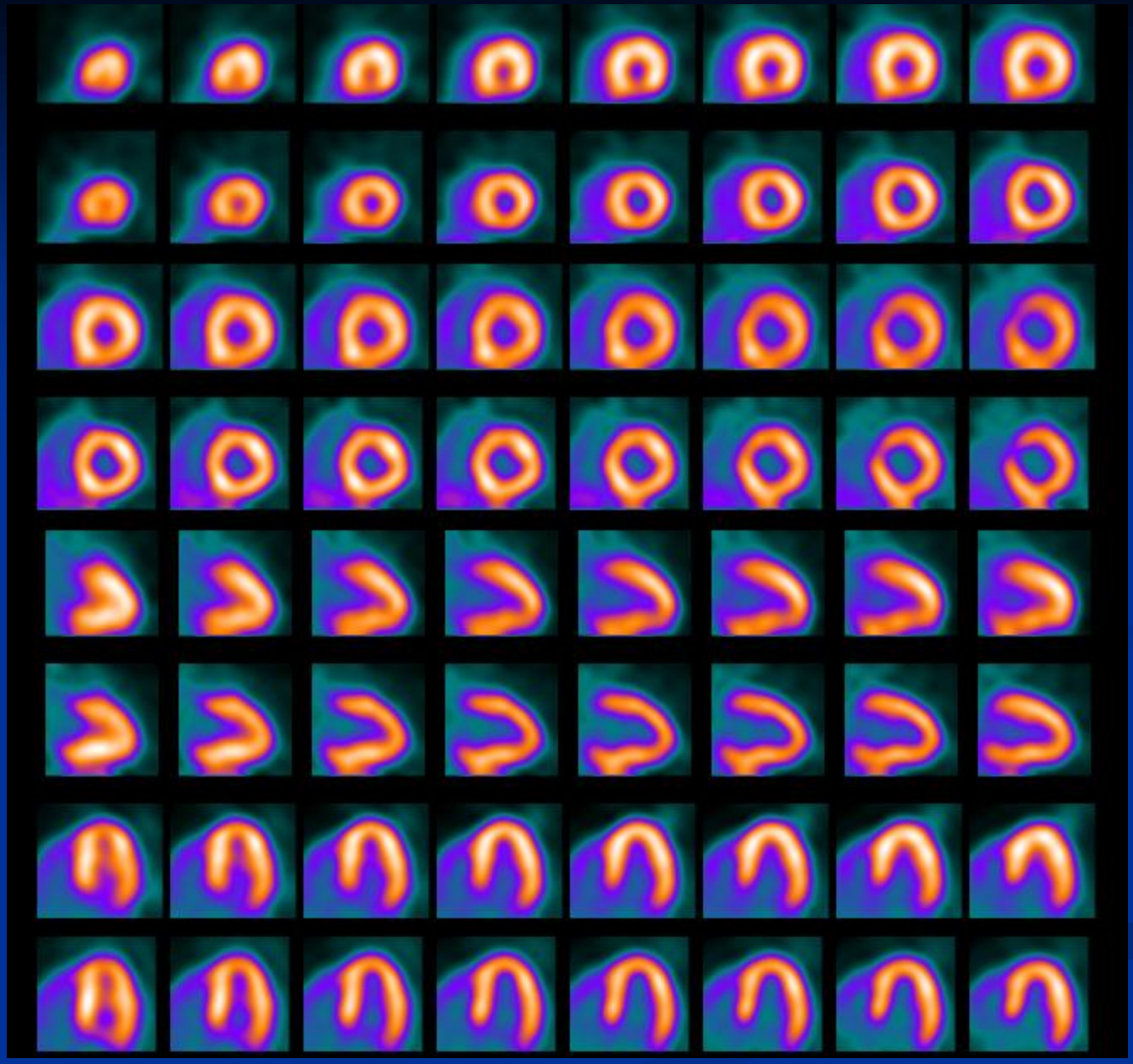
59
60
61
62
63
64
65
66
REST_SA


Stress
Rest
Stress Perfusion (%)
Stress Perfusion (%)
Rest Perfusion (%)
Rest Perfusion (%)
Reversibility Perfusion (%)
Reversibility Perfusion (%)

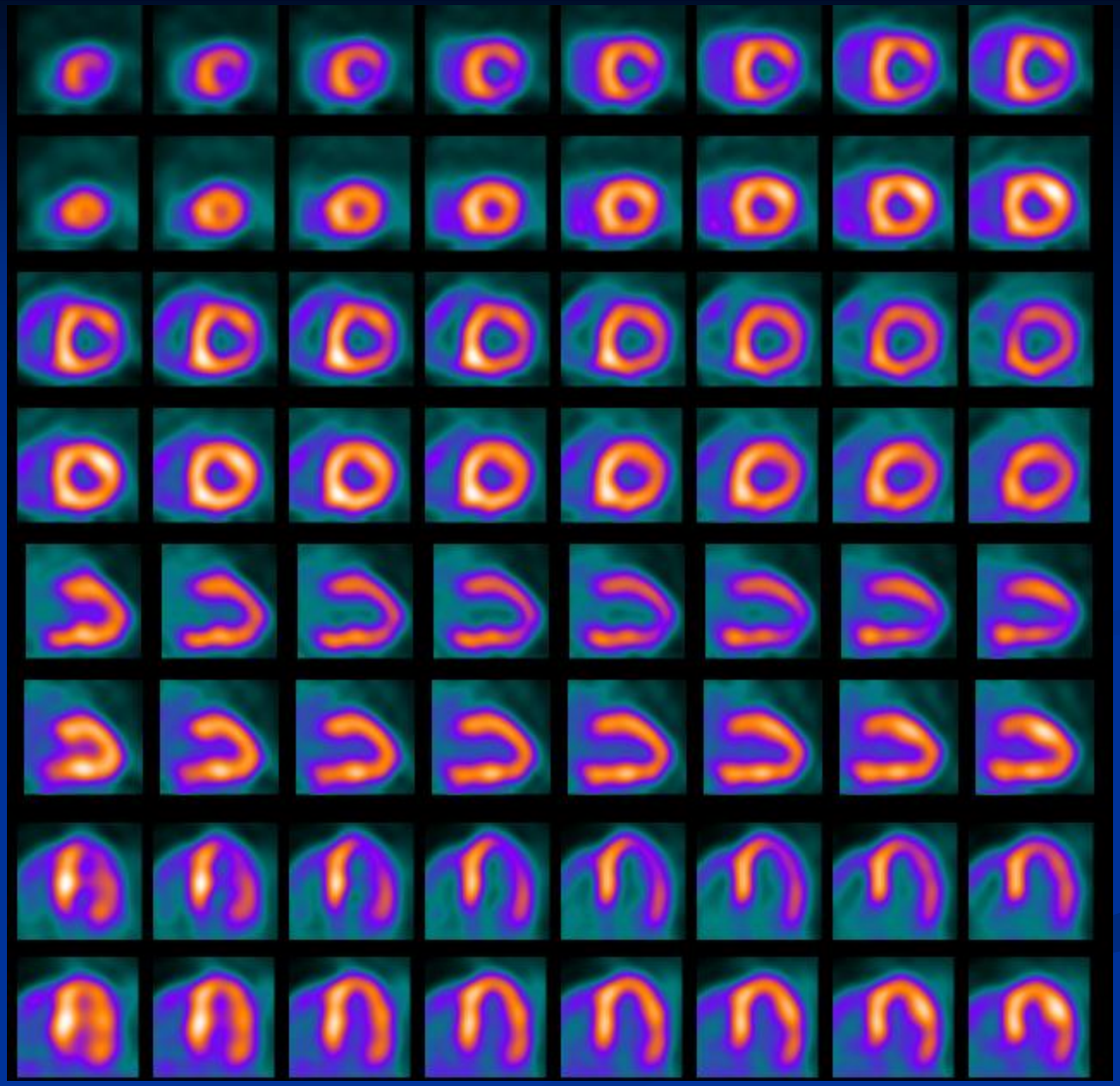
The Power of PET

- Rb-82 PET revealed a reversible perfusion pattern in the distribution of the left circumflex artery consistent with re stenosis of the artery

Normal Study



Abnormal Study



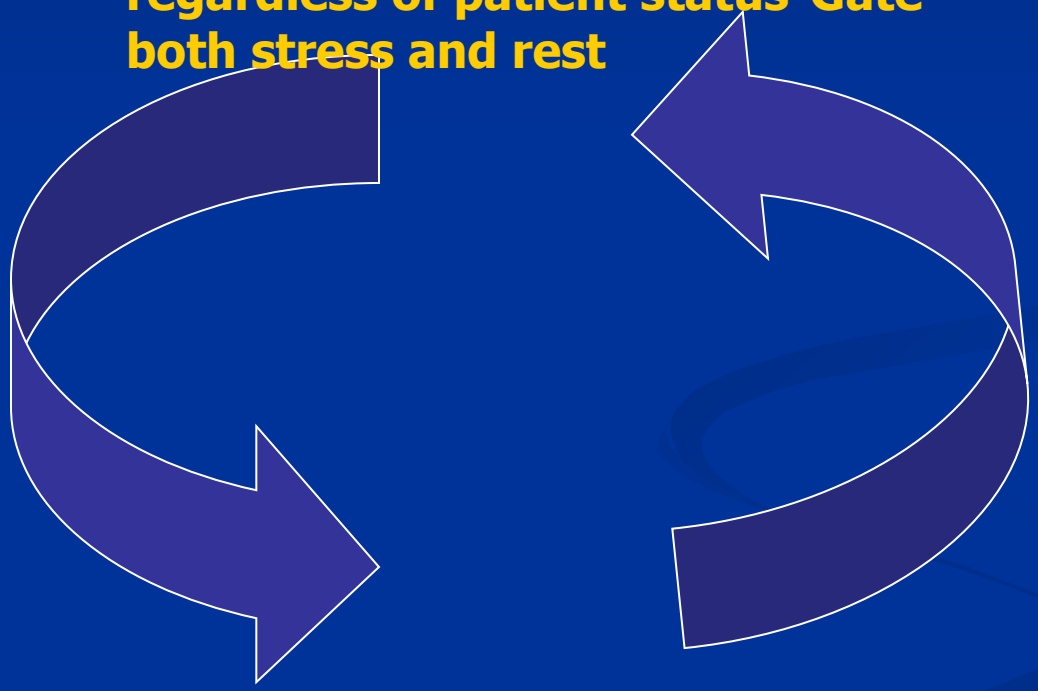
SPECT vs. PET

SPECT perfusion imaging

- Low energy photons
  - Thallium or Tc based
- Usually two imaging sequences (20-30 minutes each)
- Total exam time 3-4 hours
- Study of over 3000 patient with Thallium
  - Sensitivity 84% and Specificity 53%
- Attenuation/motion all impact relative accuracy
  - Equivocal studies men 10% woman 30-40%

PET perfusion imaging

High diagnostic accuracy regardless of patient status-Gate both stress and rest



Lower radiation exposure

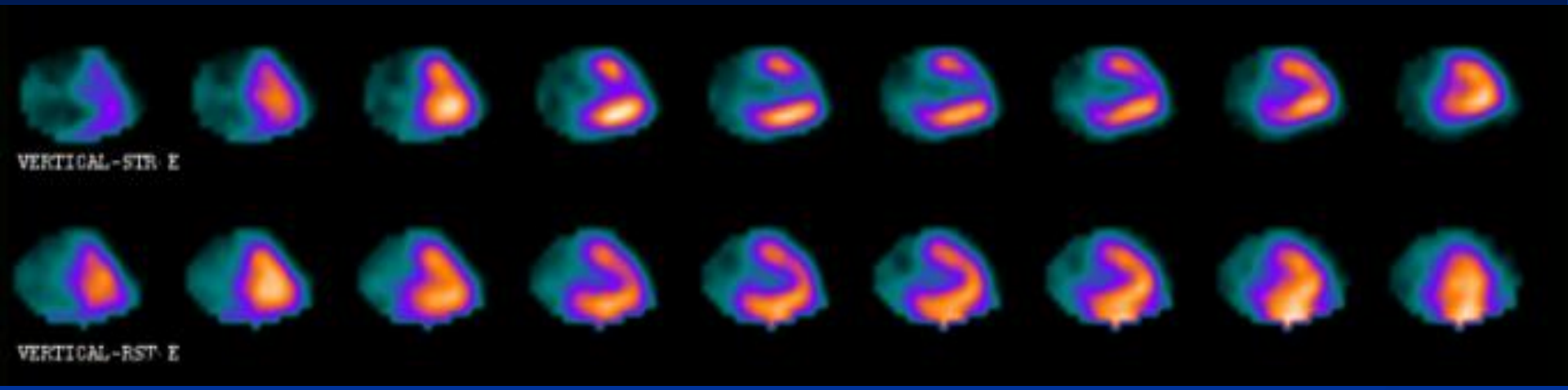
Increasing reimbursement

Shorter acquisition times

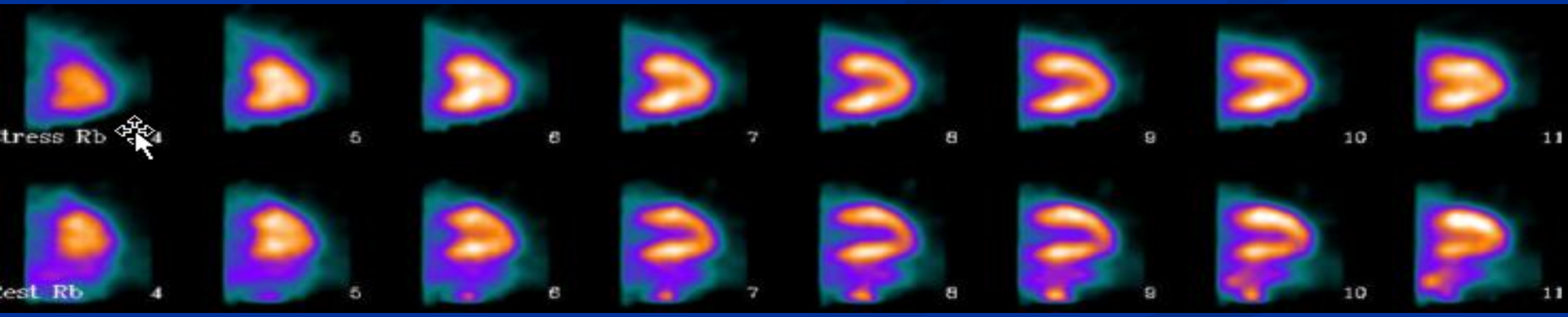
Case study

- 50yo female patient with breast implants
- MPS ordered for evaluation of chest pain syndrome with equivocal GXT
- Patient underwent MPS with Tc-99m Sestamibi
- Patient then underwent Rb-82 PET perfusion

SPECT


VERTICAL-STR E
VERTICAL-RST E

PET


tress Rb
5
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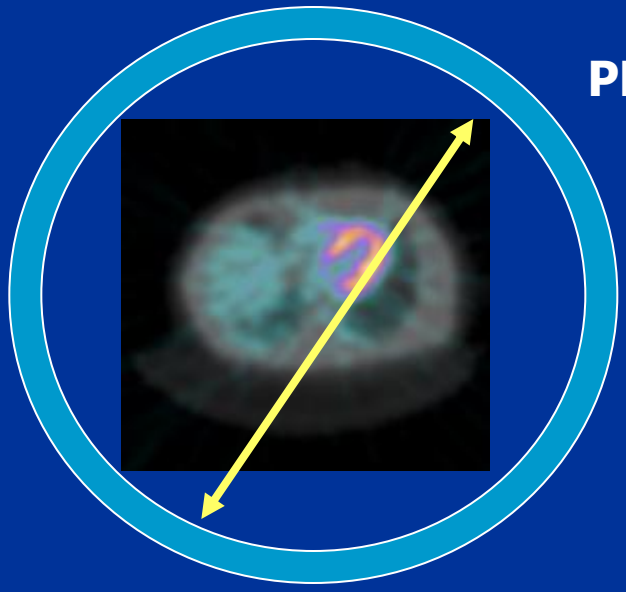
11
est Rb
4
5
6
7
8
9
10
11

Case Study

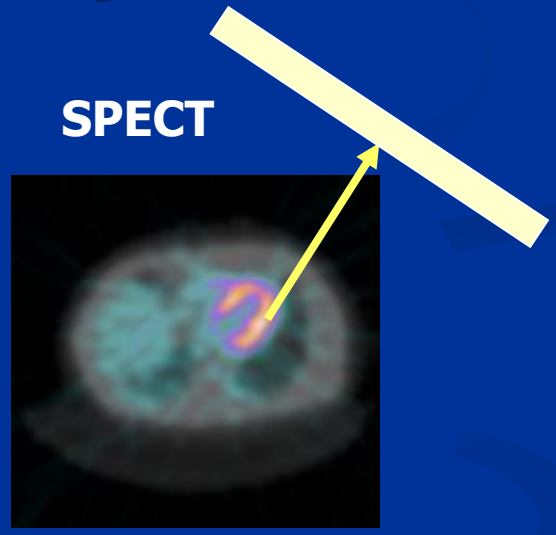
- Comparison between SPECT and PET
- Normal scan with Rb-82 PET
- Abnormal with SPECT
- False positive SPECT, patient risk stratified away from invasive evaluation
- No cardiac events in follow up

SPECT vs. PET
PET Fundamentals

- Higher system sensitivity than SPECT
- Higher resolution than SPECT (3-4 mm vs >8 mm)
- **Attenuation compensation is very straight forward and accurate.**

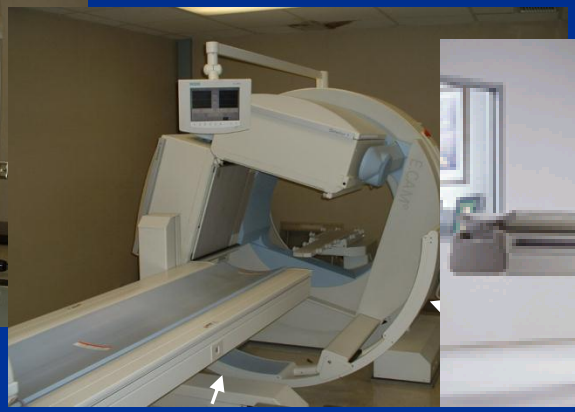


Attenuation independent of depth



Attenuation dependent of depth

Myocardial Perfusion Imaging: SPECT vs. PET

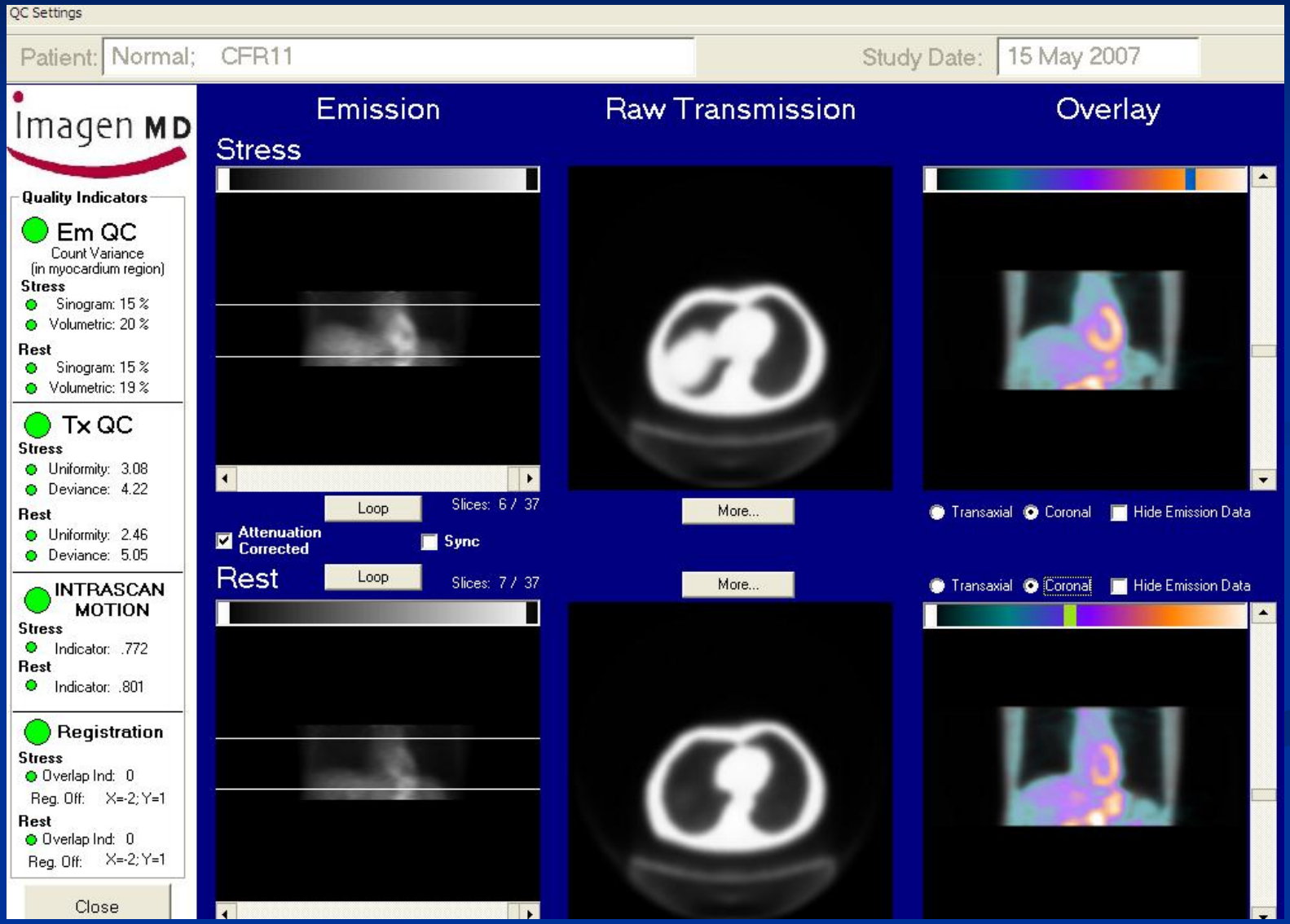



SPECT: Tl-201, Tc99m-based

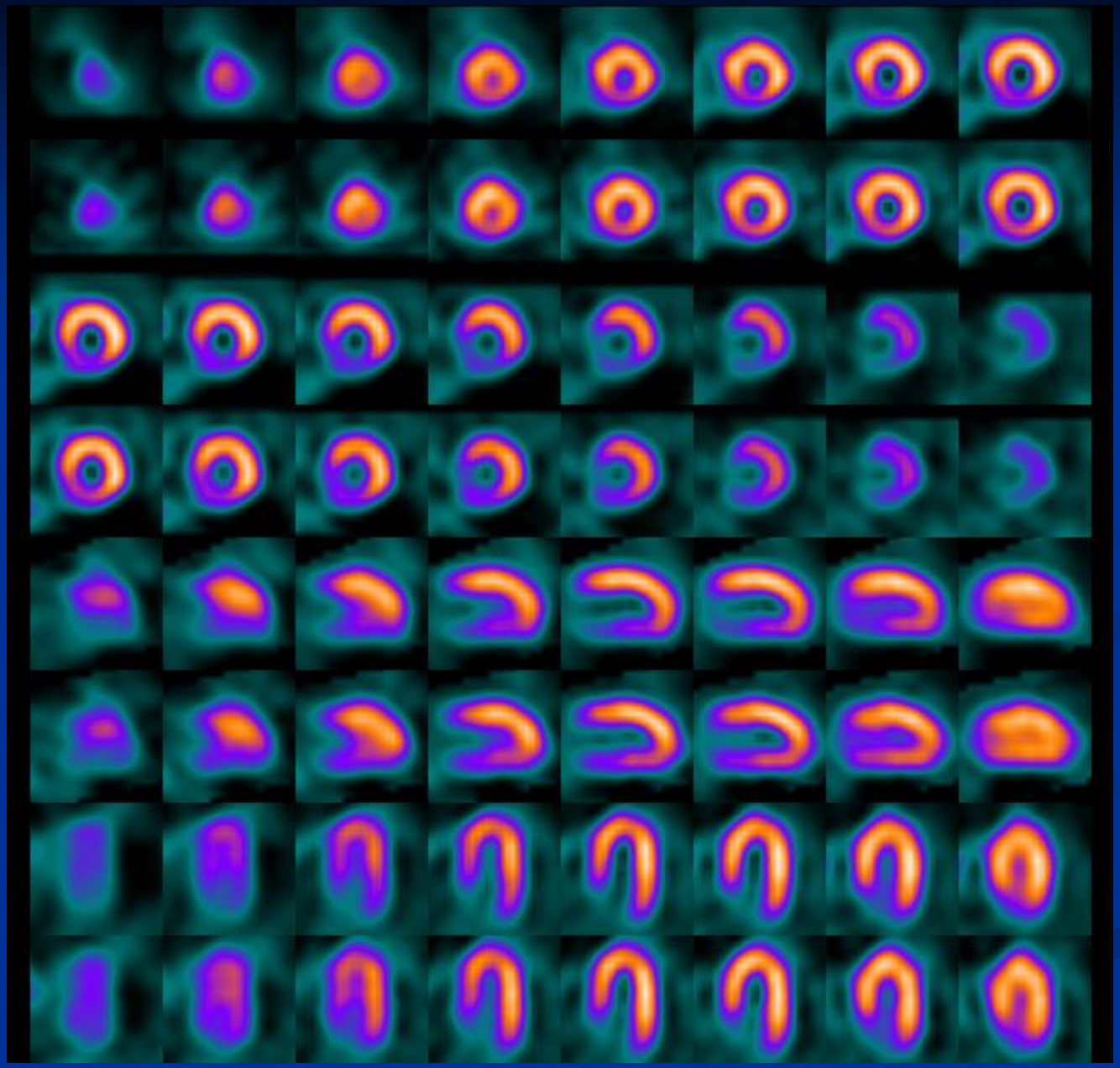
PET: Rubidium-82, N^{13}-Ammonia

	SPECT	PET
Spatial Resolution	X	~ 2X
Contrast Resolution	X	~ 2X
Count Density/unit time	X	~ 4X
Attenuation Correction	Not usual	Always
Scatter compensation	X	~ 5X

Interpretation on PET Study Is Much Easier and Accurate

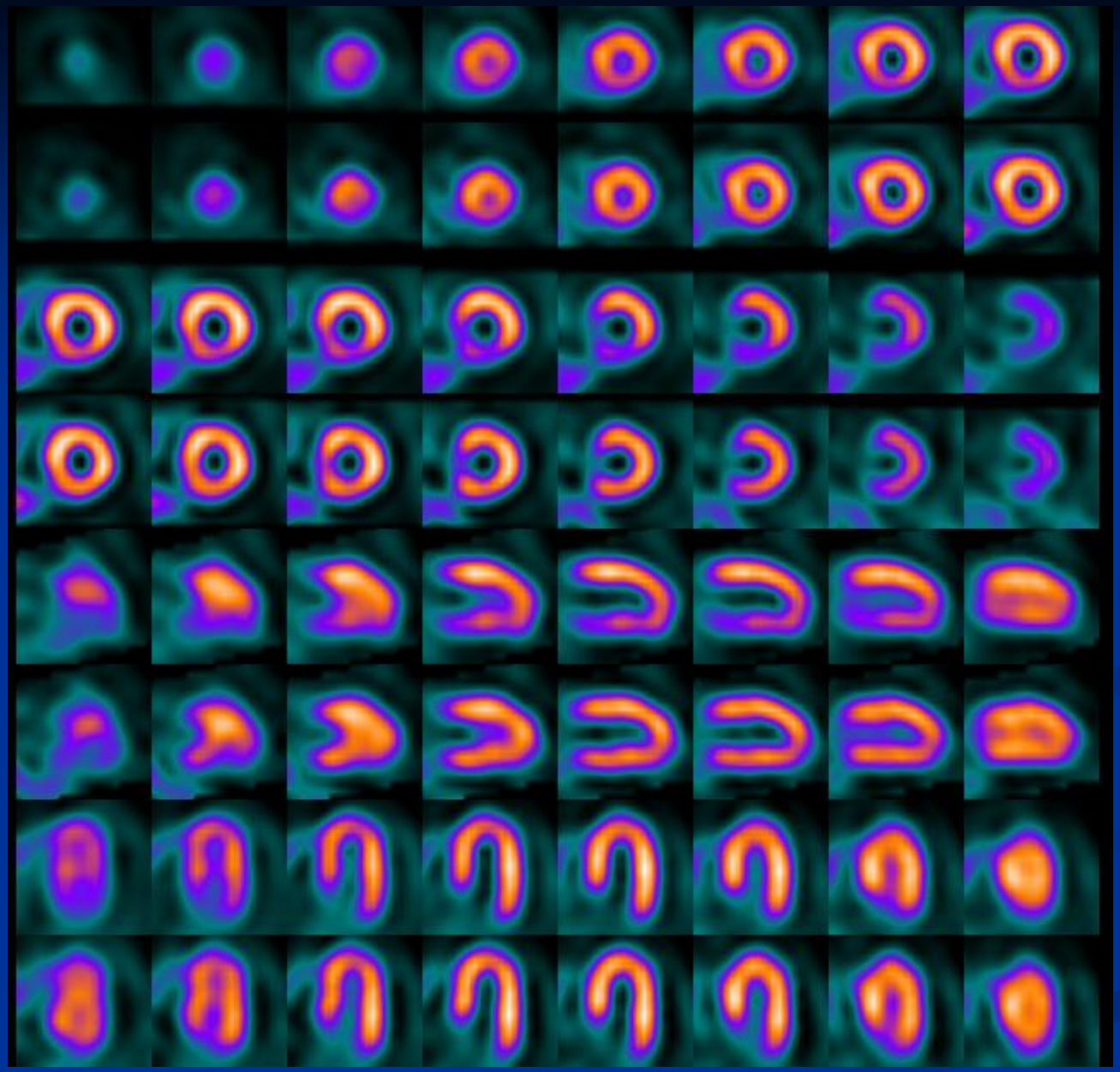


Pat03



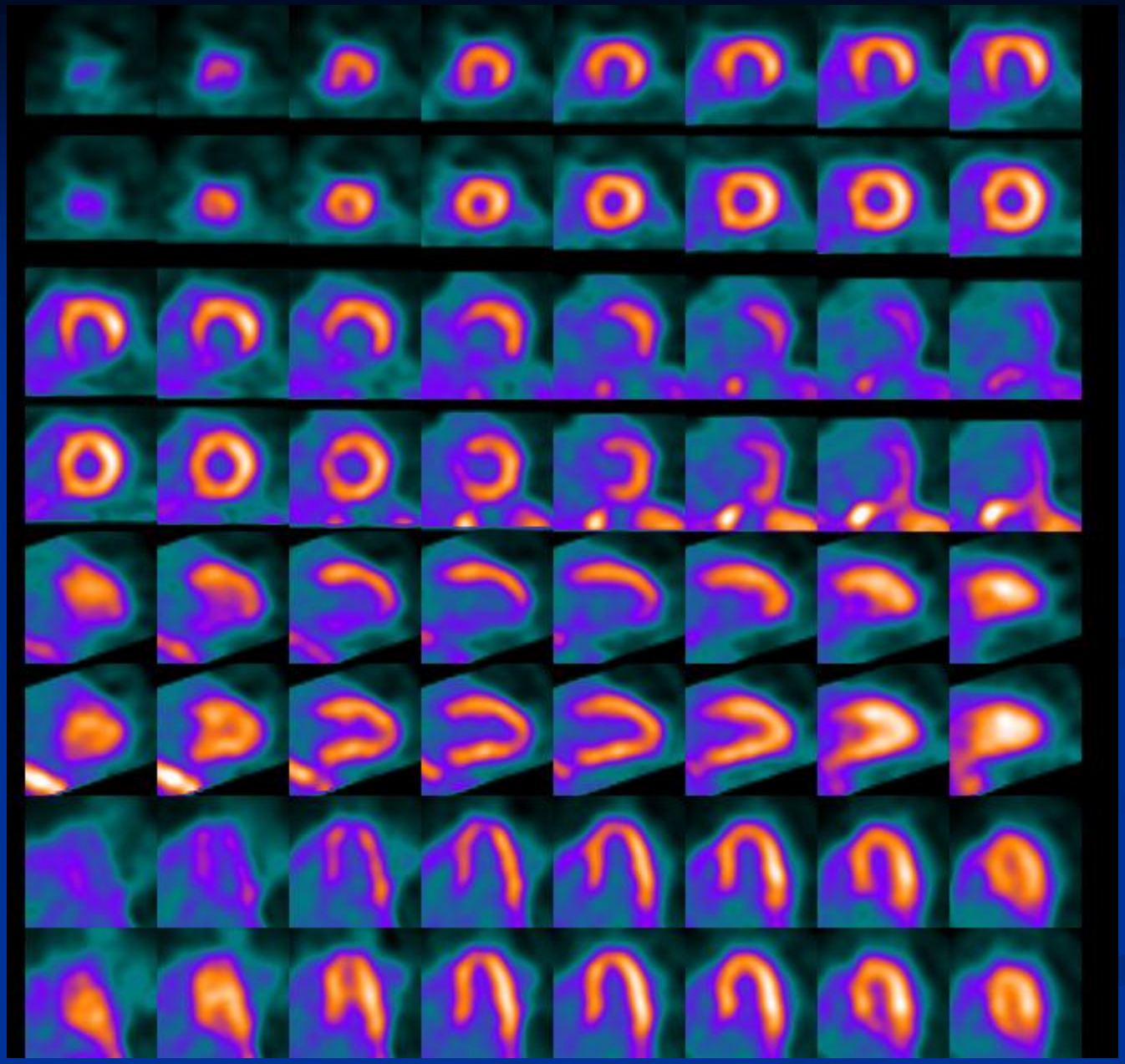
SPECT

Pat03

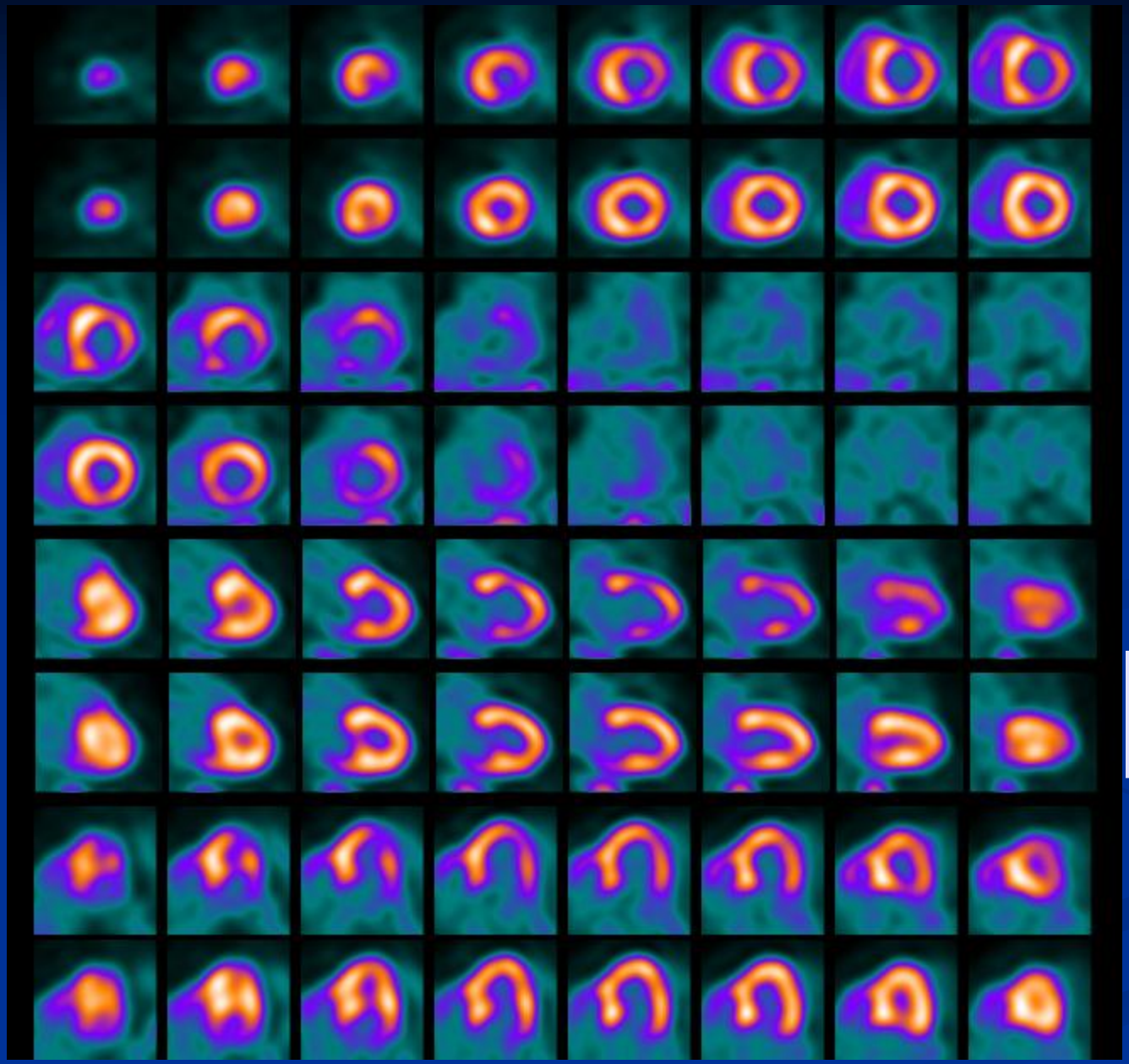


AC SPECT

Pat03



PET



Pat04

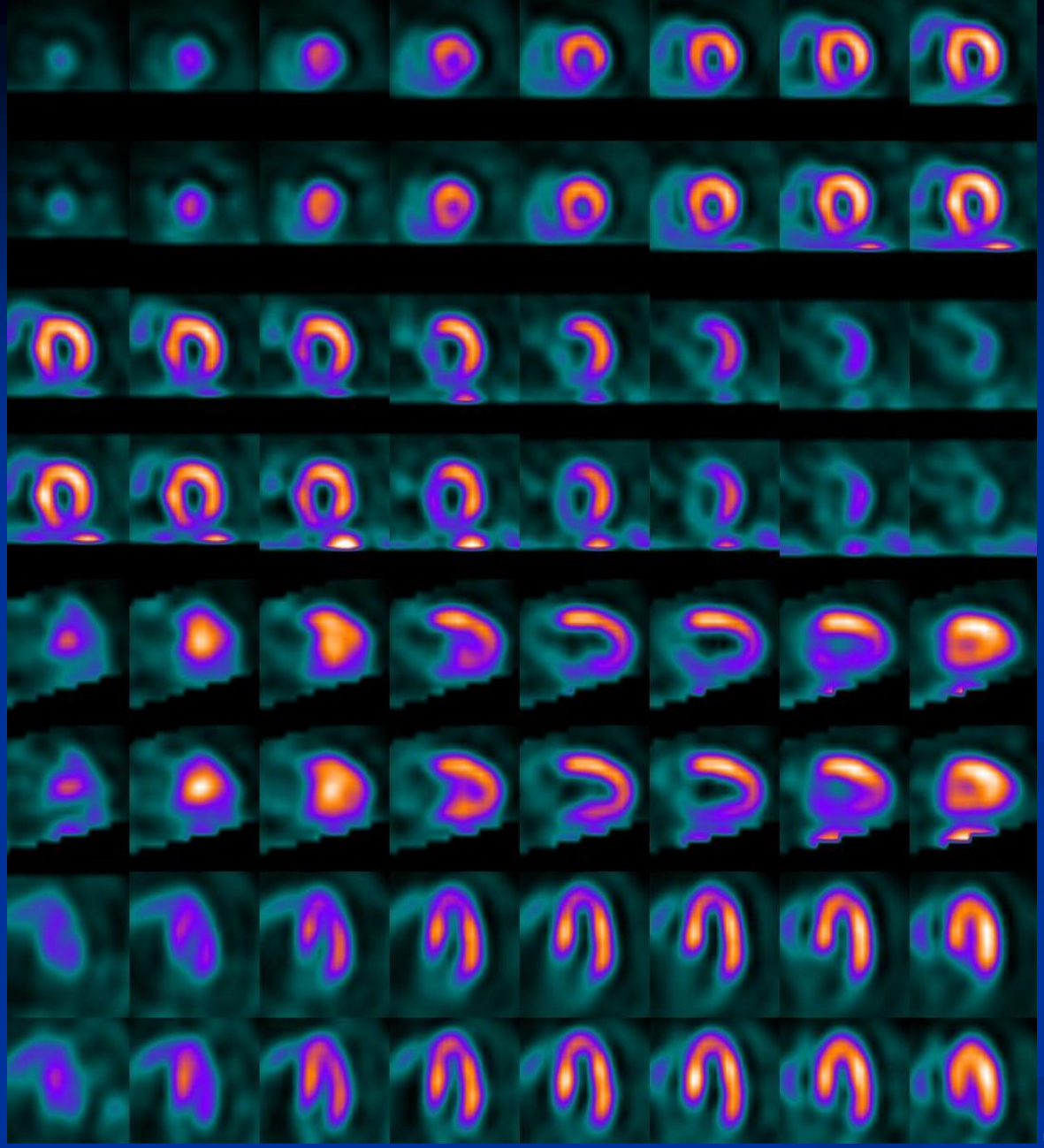
PET

Peak-stress
Gated Images

LVEF=38% (Str)

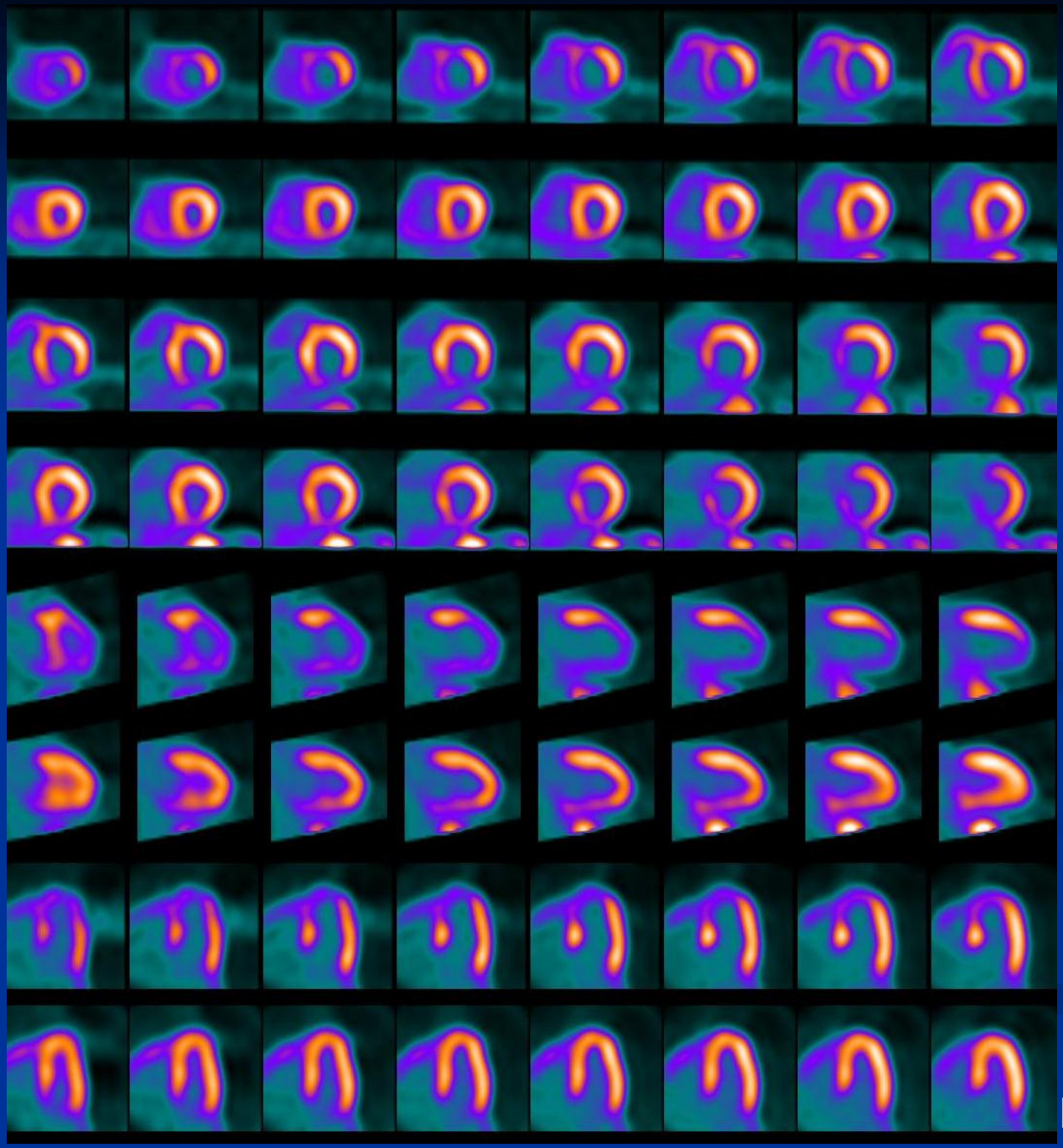
LVEF=60% (Rt)

Pat05



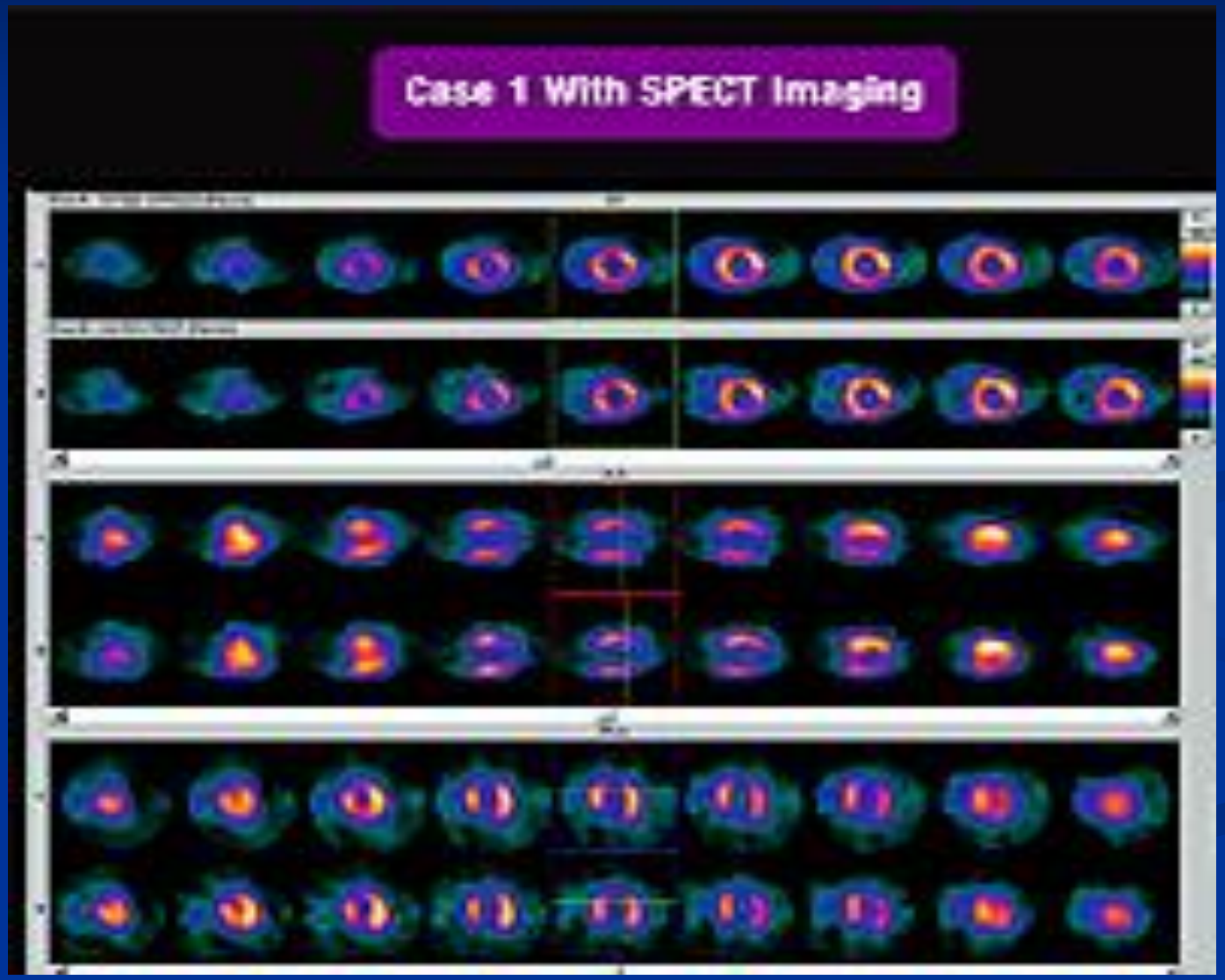
SPECT

Pat05

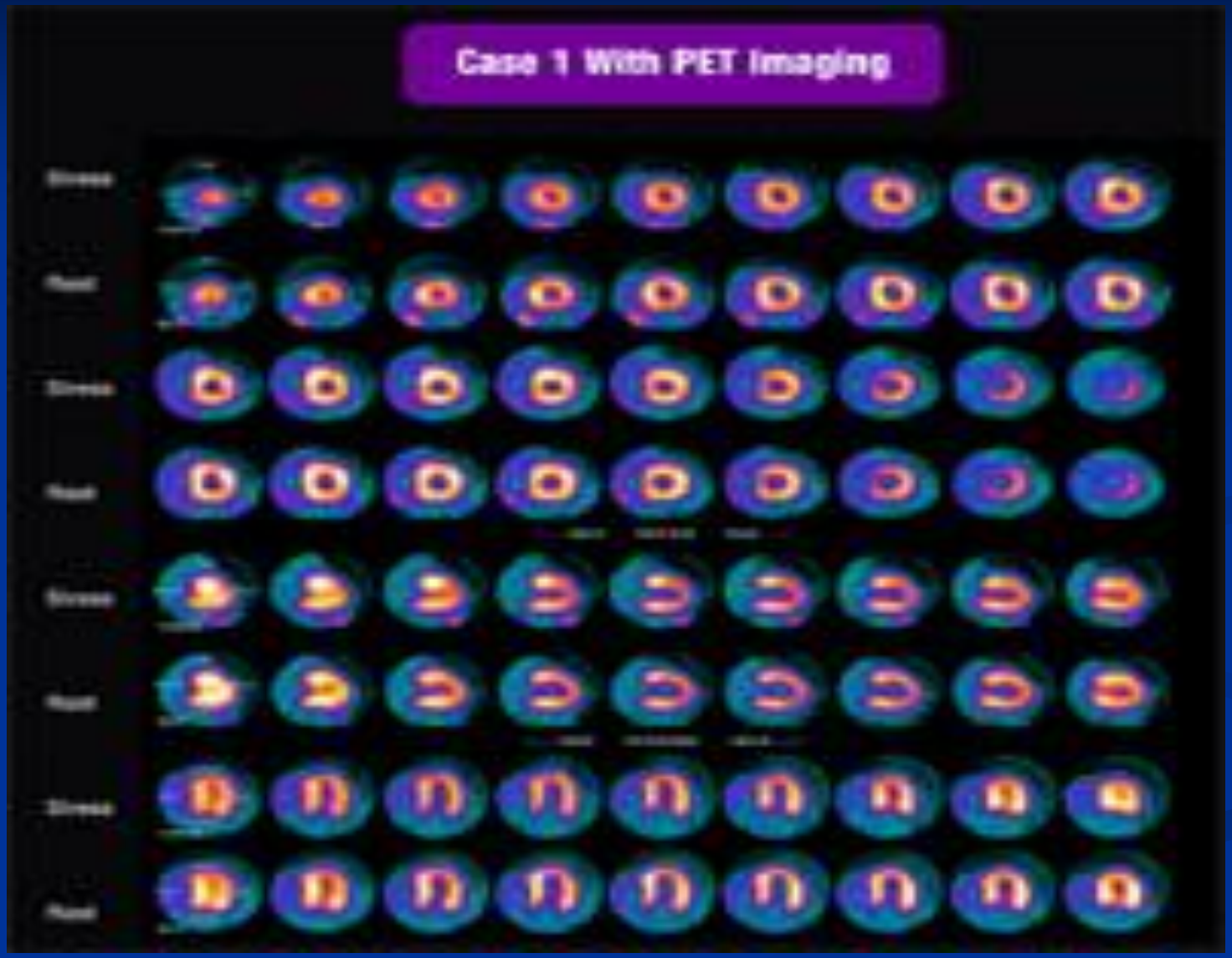


PET

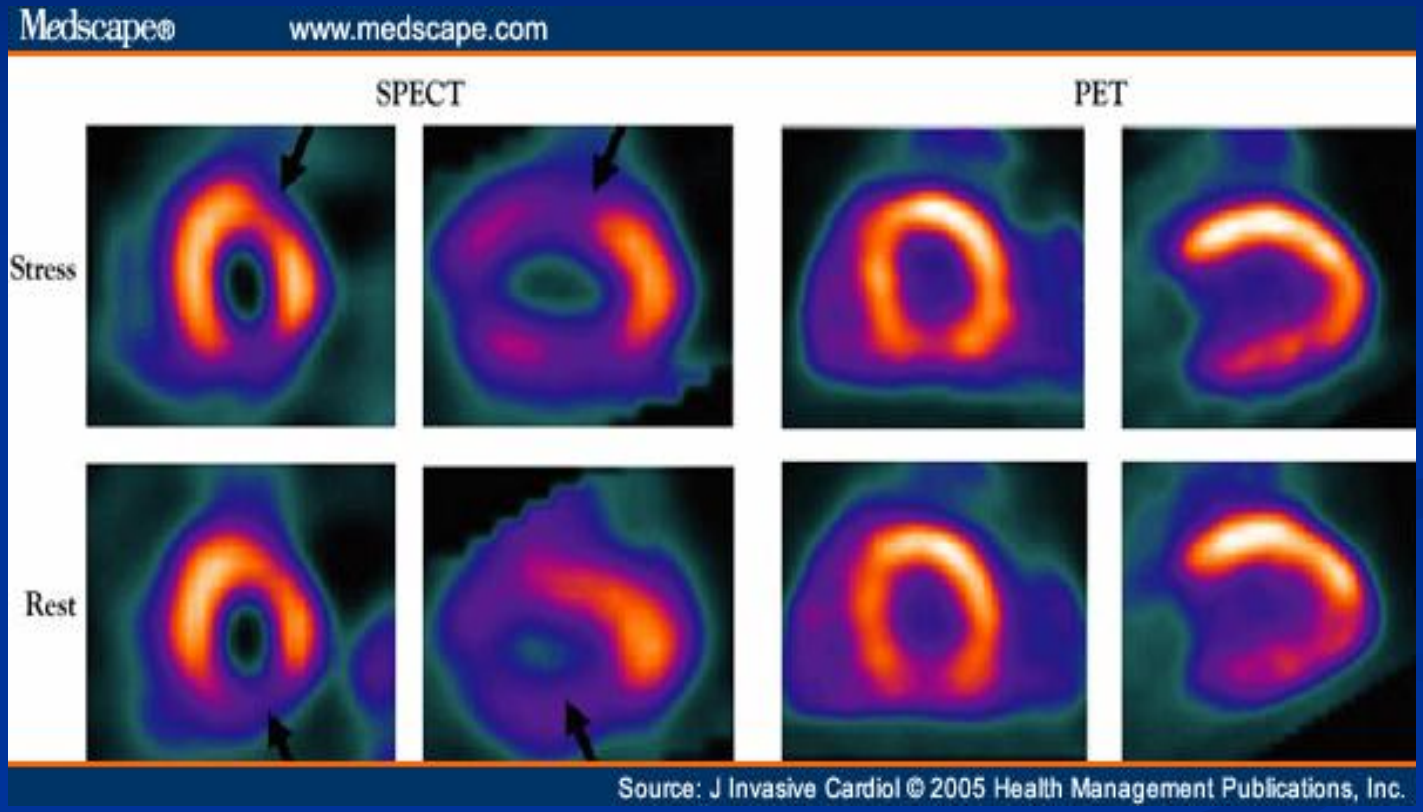
SPECT



PET



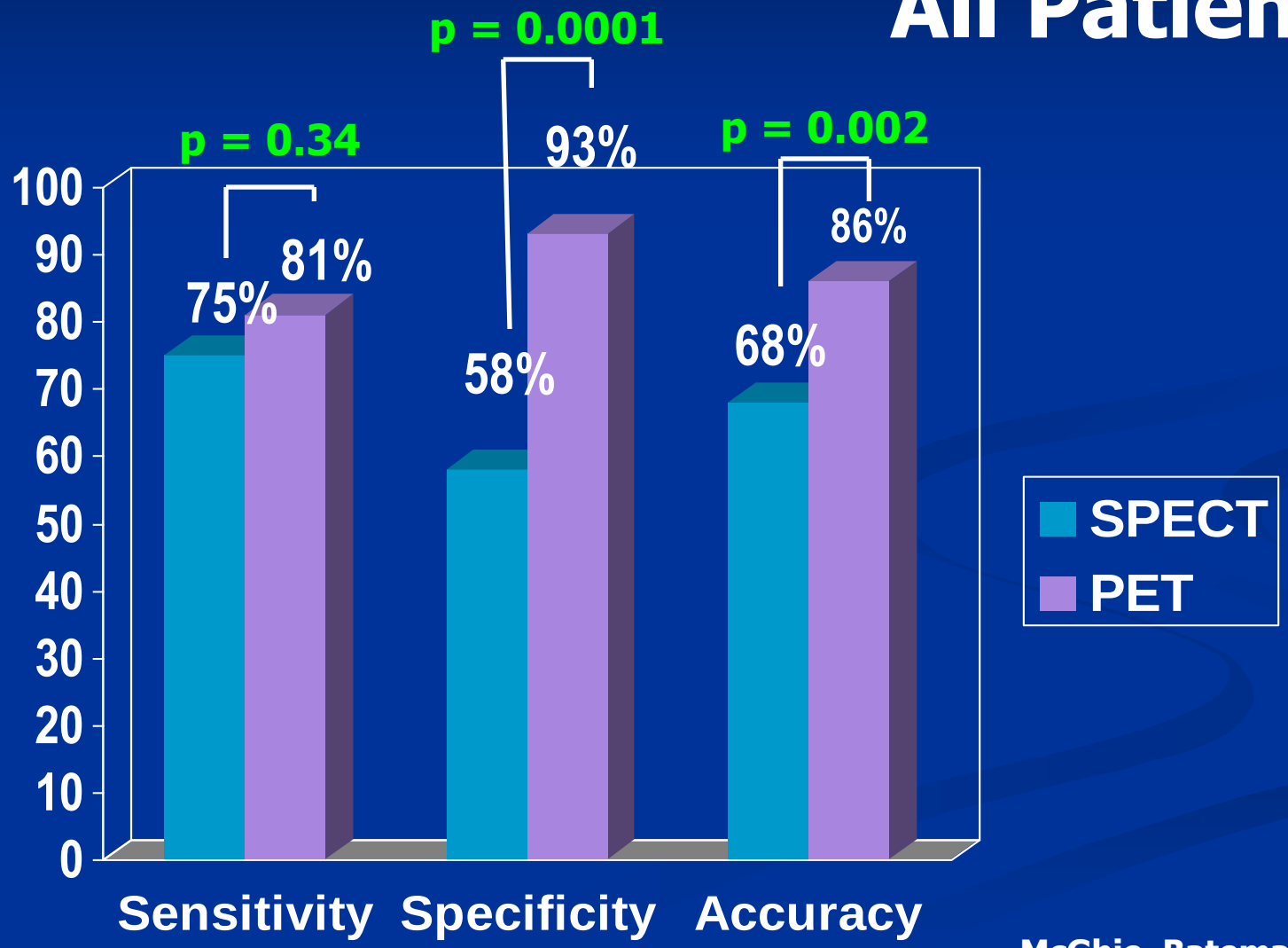
SPECT vs. PET


Medscape®
www.medscape.com
SPECT
PET
Stress
Rest
Source: J Invasive Cardiol © 2005 Health Management Publications, Inc.

SPECT vs PET

Overall CAD Detection

All Patients

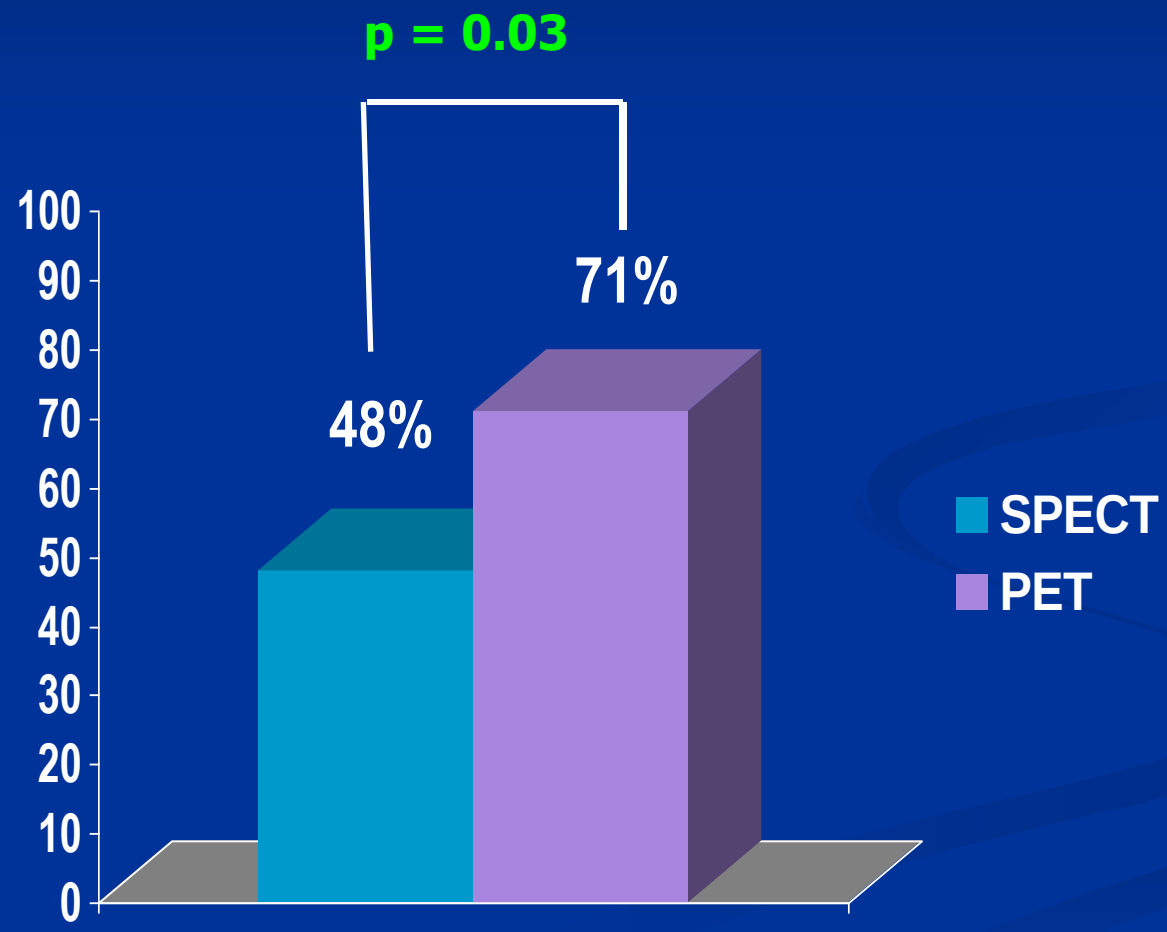


McGhie, Bateman et al, JNC 2007

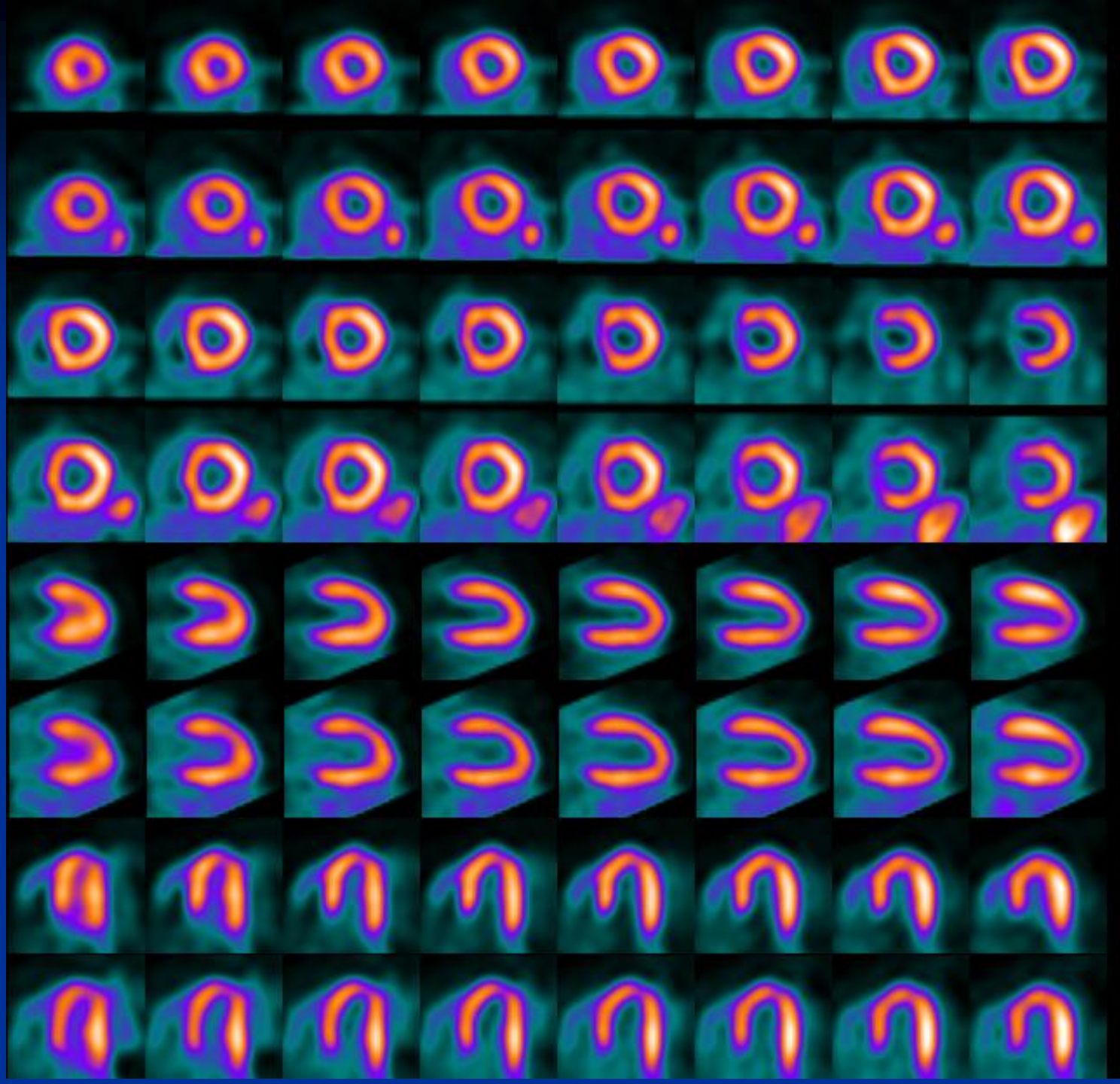
SPECT vs PET

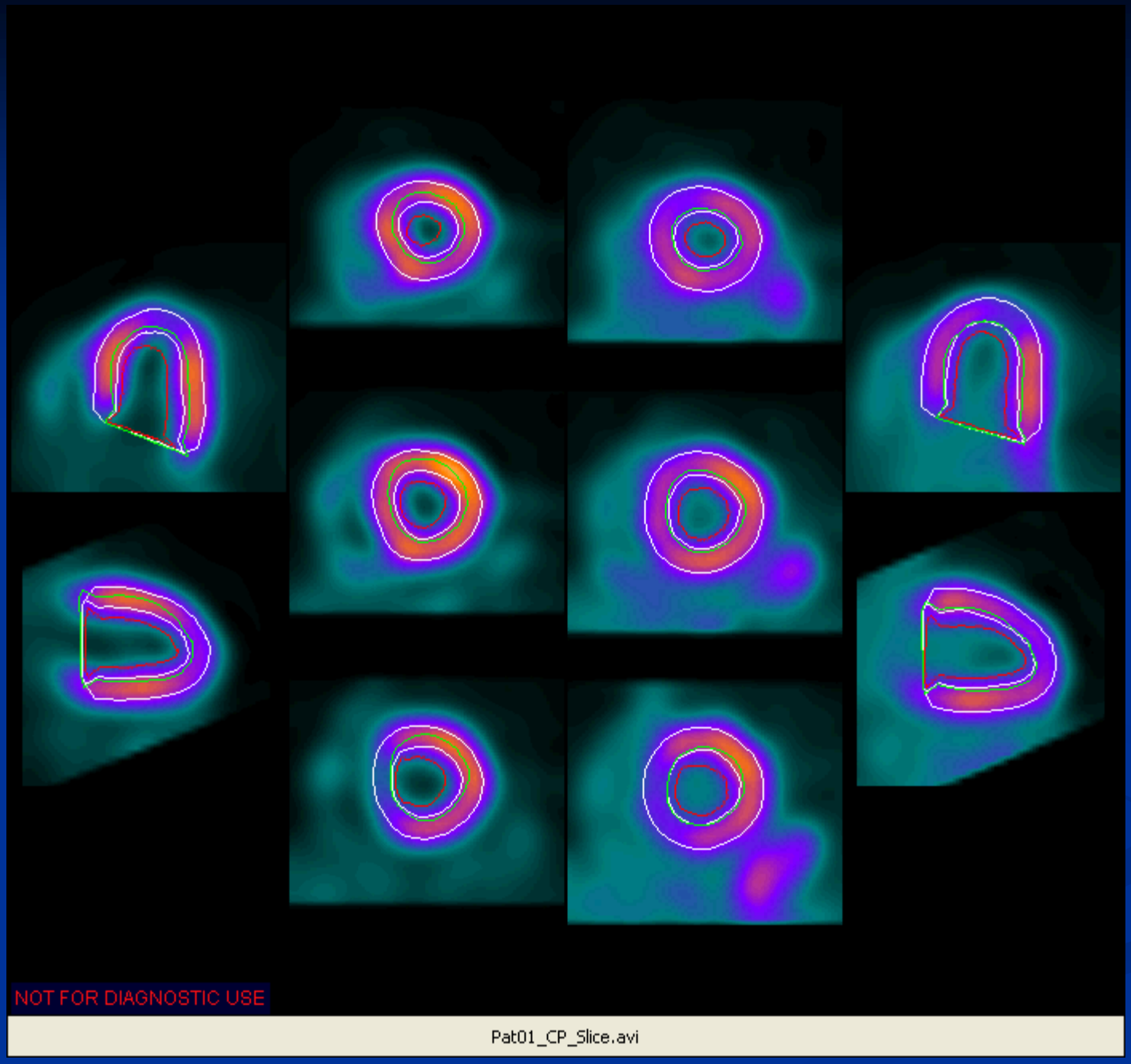
Multi-vessel Disease

All Patients



McGhie, Bateman et al, JNC 2007

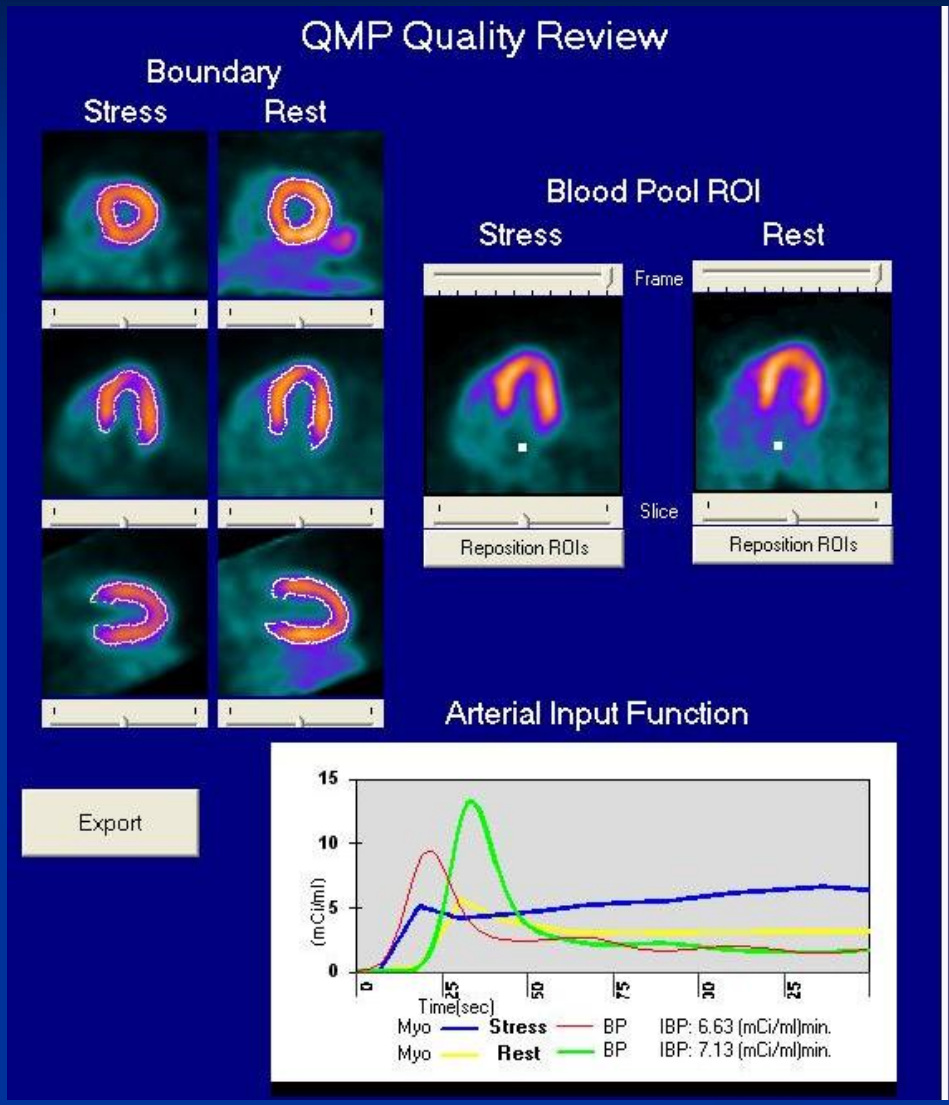


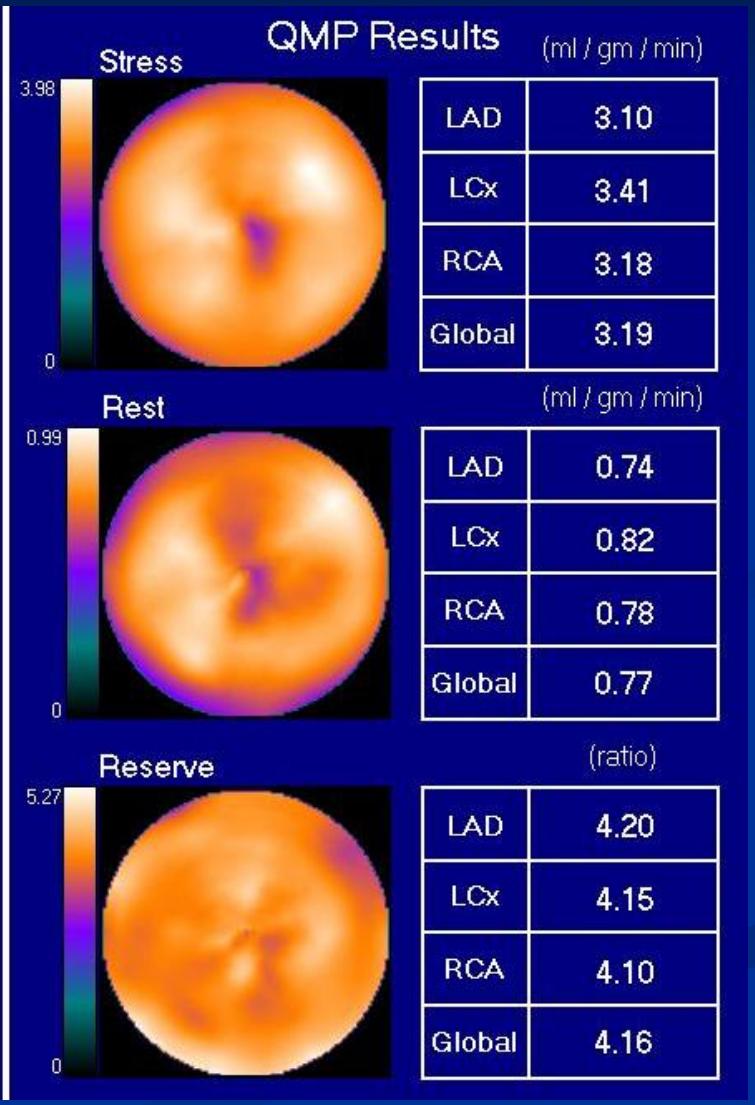


Stress= 71%

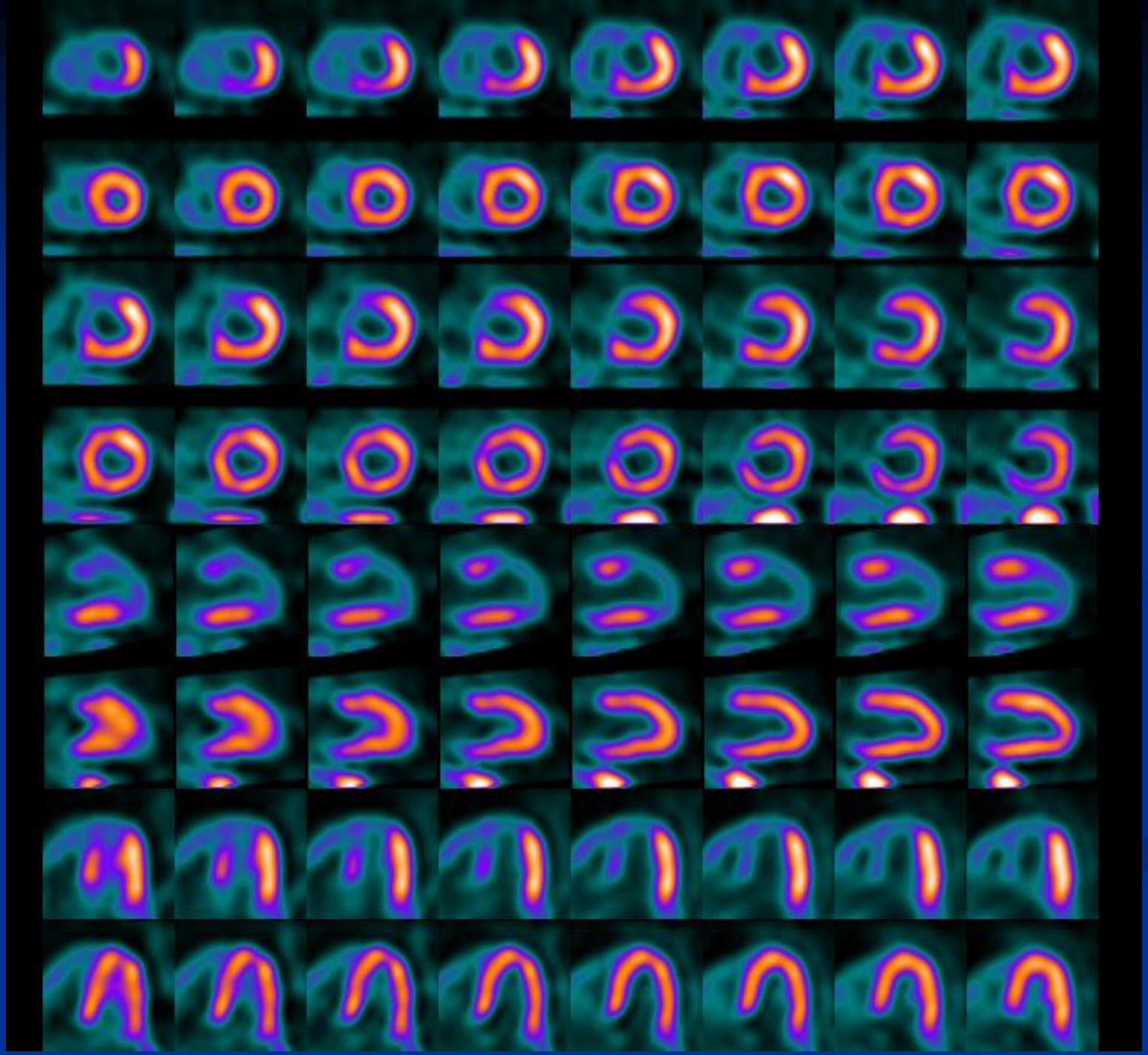
Rest=61%

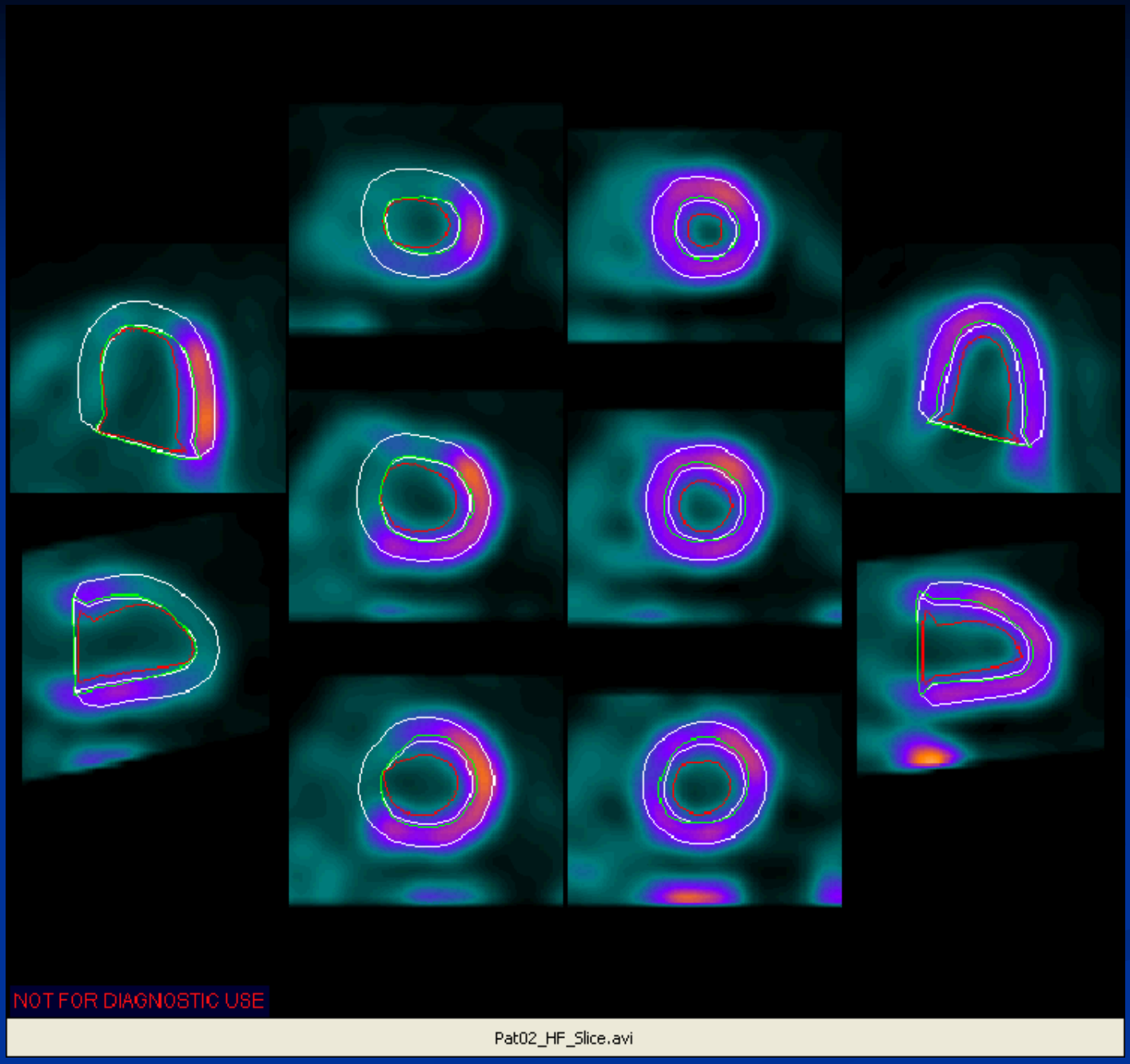
New PET Application: Myocardial Blood Flow Quantitation (ml/g/min)





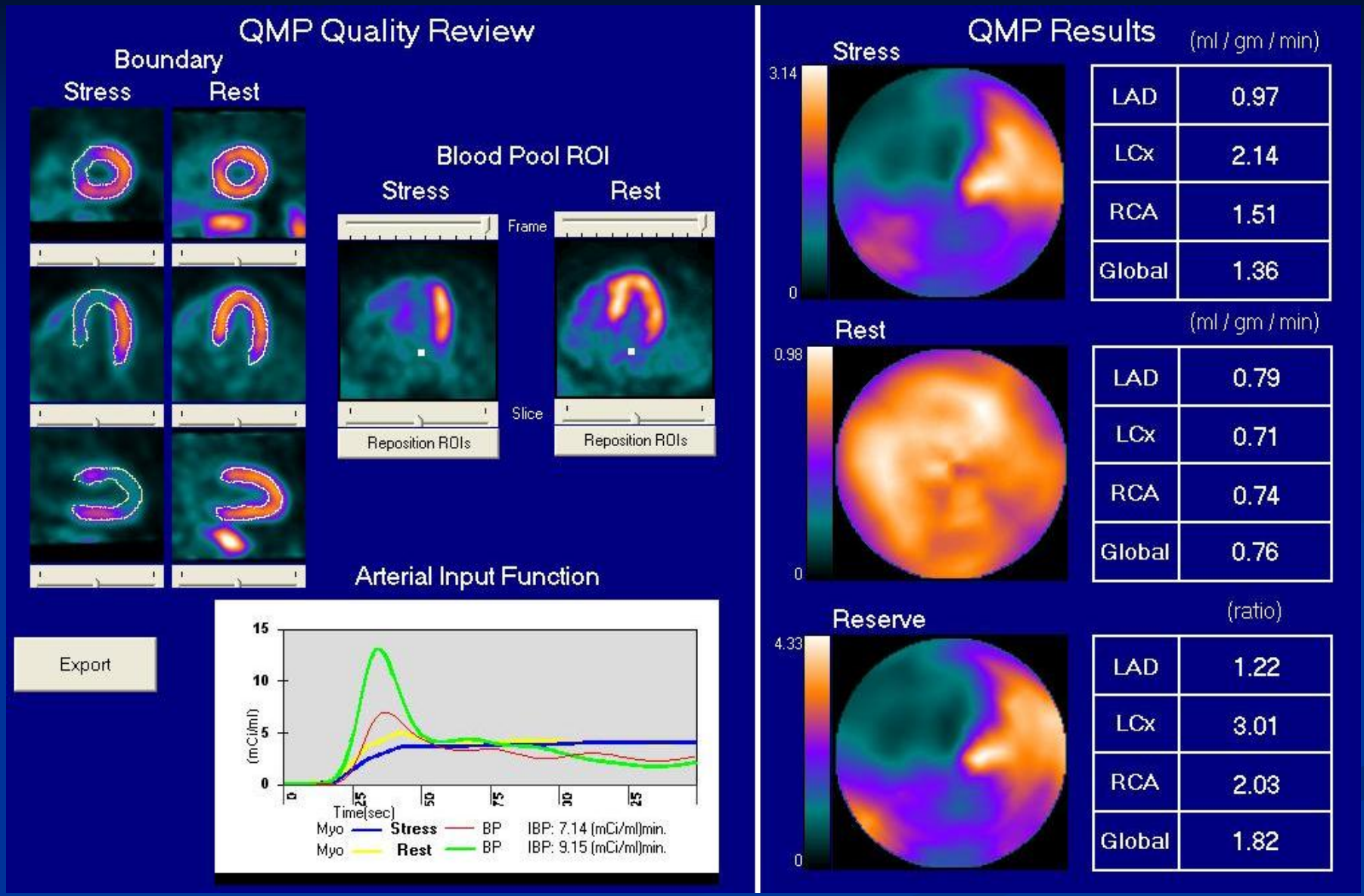
Cardiovascular Imaging Technologies, Kansas City, USA

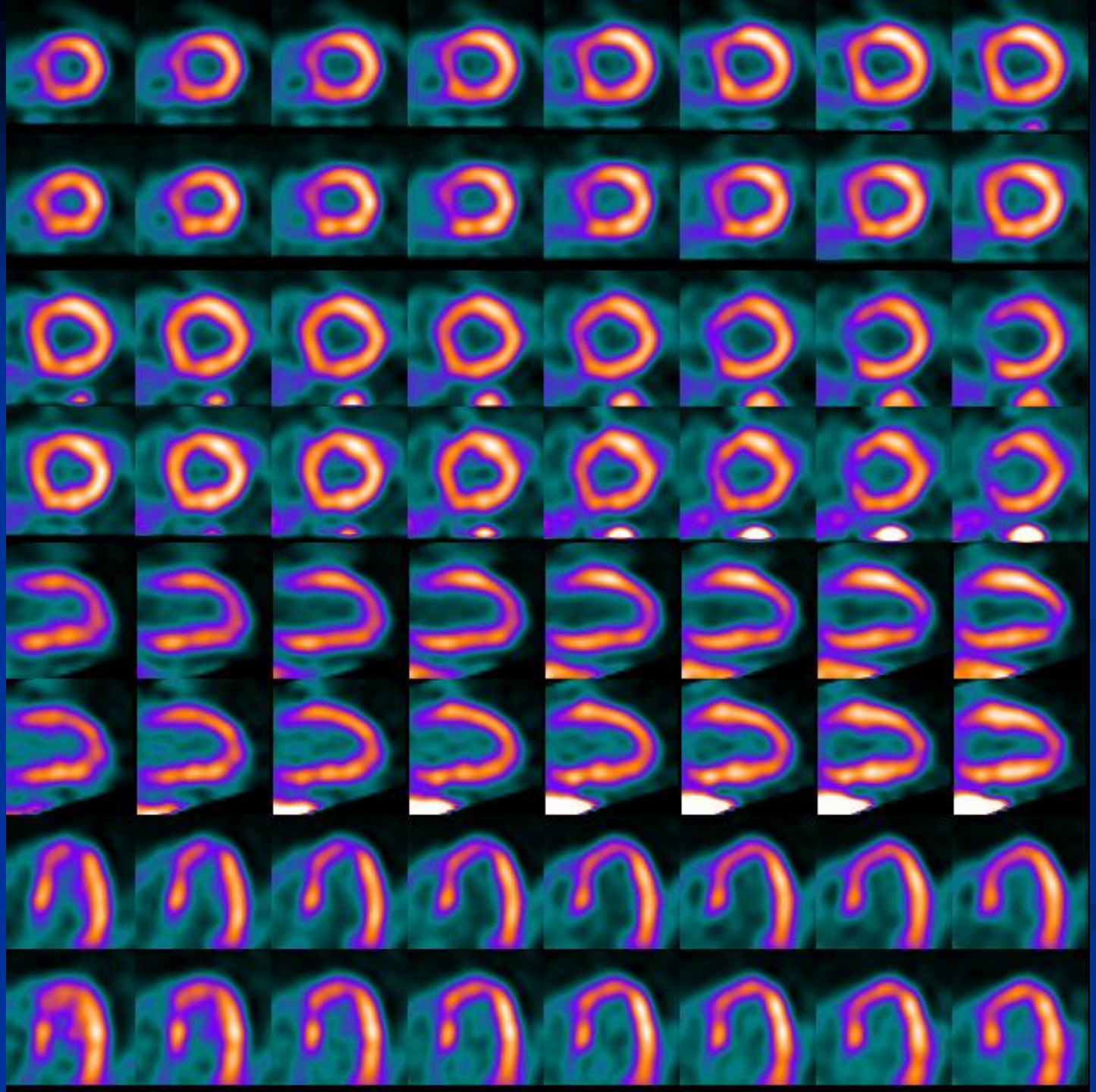


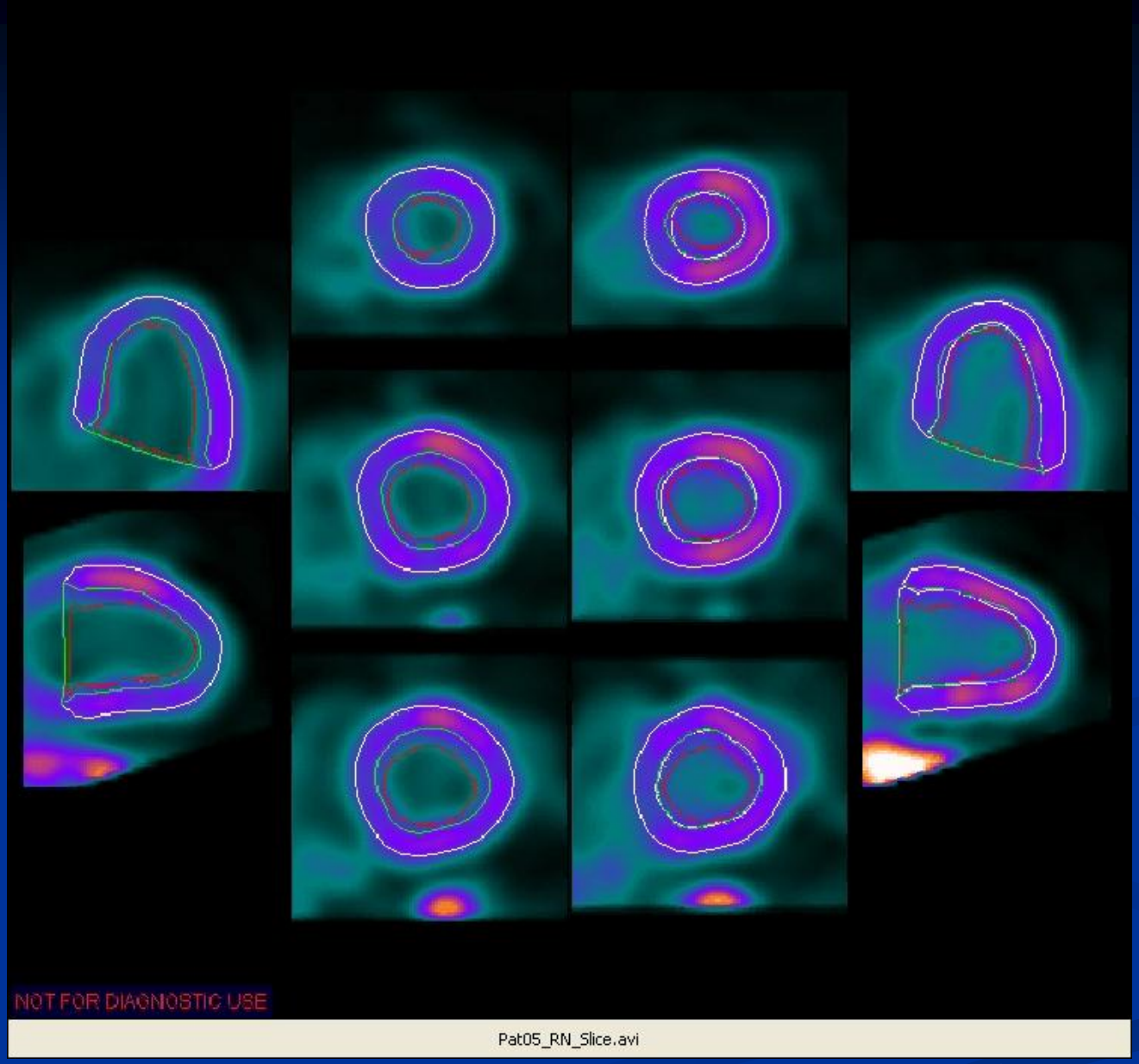


Stress= 43%

Rest=65%

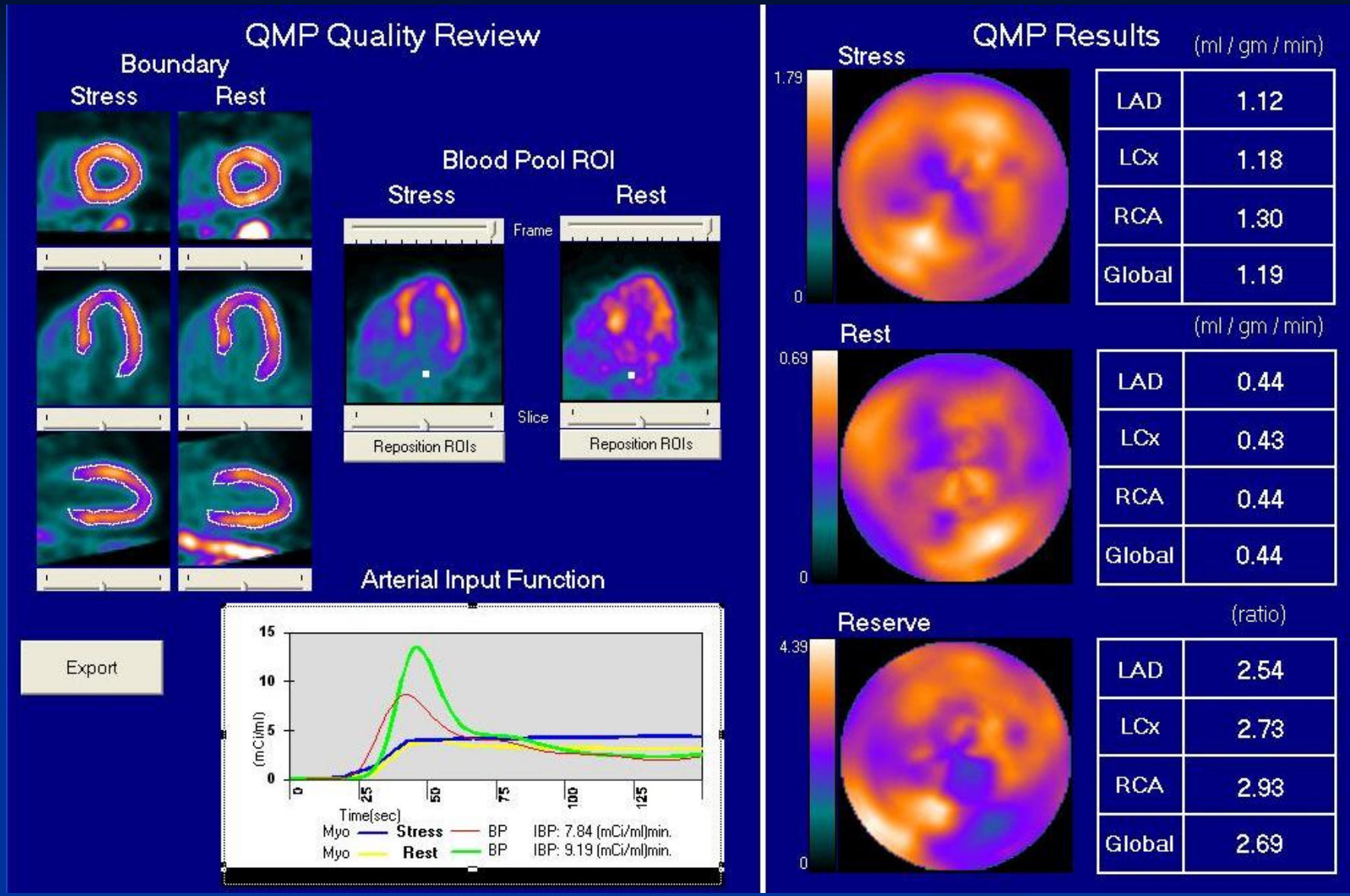

QMP Quality Review
Boundary
Stress
Rest
Blood Pool ROI
Stress
Rest
Frame
Slice
Reposition ROIs
Reposition ROIs
Arterial Input Function
Export
15
10
5
0
(mCi/ml)
0
25
50
75
100
125
Time(sec)
Myo Stress BP IBP: 7.14 (mCi/ml)min.
Myo Rest BP IBP: 9.15 (mCi/ml)min.
QMP Results
(ml / gm / min)
Stress
3.14
0
LAD 0.97
LCx 2.14
RCA 1.51
Global 1.36
(ml / gm / min)
Rest
0.98
0
LAD 0.79
LCx 0.71
RCA 0.74
Global 0.76
(ratio)
Reserve
4.33
0
LAD 1.22
LCx 3.01
RCA 2.03
Global 1.82



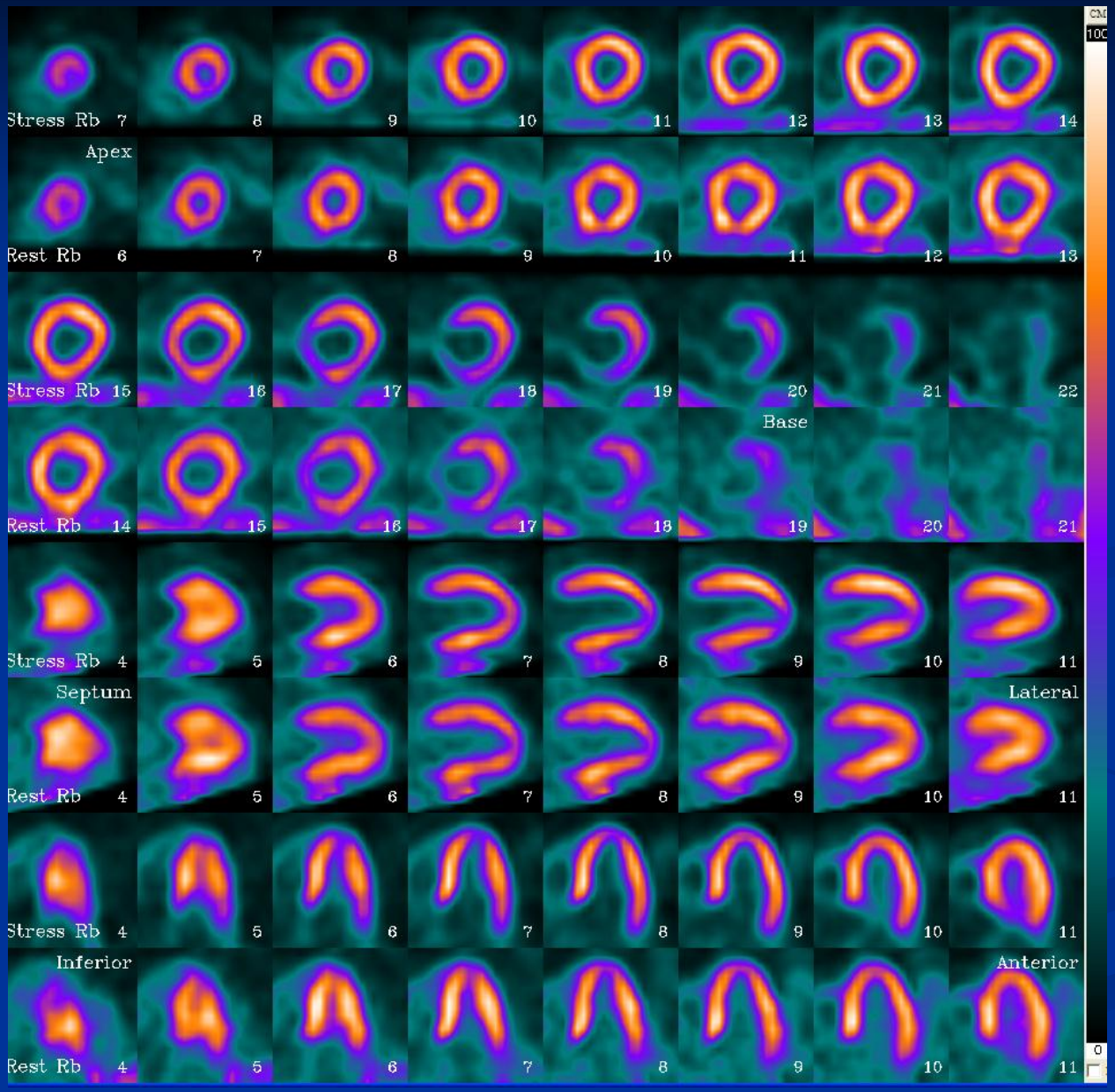


Stress=43%

Rest=39%


QMP Quality Review
Boundary
Stress
Rest
Blood Pool ROI
Stress
Rest
Frame
Slice
Reposition ROIs
Reposition ROIs
Arterial Input Function
Export
15
10
5
0
(mCi/ml)
0
25
50
75
100
125
Time(sec)
Myo Stress BP IBP: 7.84 (mCi/ml)min.
Myo Rest BP IBP: 9.19 (mCi/ml)min.
QMP Results
(ml / gm / min)
Stress
1.79
0
LAD 1.12
LCx 1.18
RCA 1.30
Global 1.19
(ml / gm / min)
Rest
0.69
0
LAD 0.44
LCx 0.43
RCA 0.44
Global 0.44
(ratio)
Reserve
4.39
0
LAD 2.54
LCx 2.73
RCA 2.93
Global 2.69

N13-Ammonia

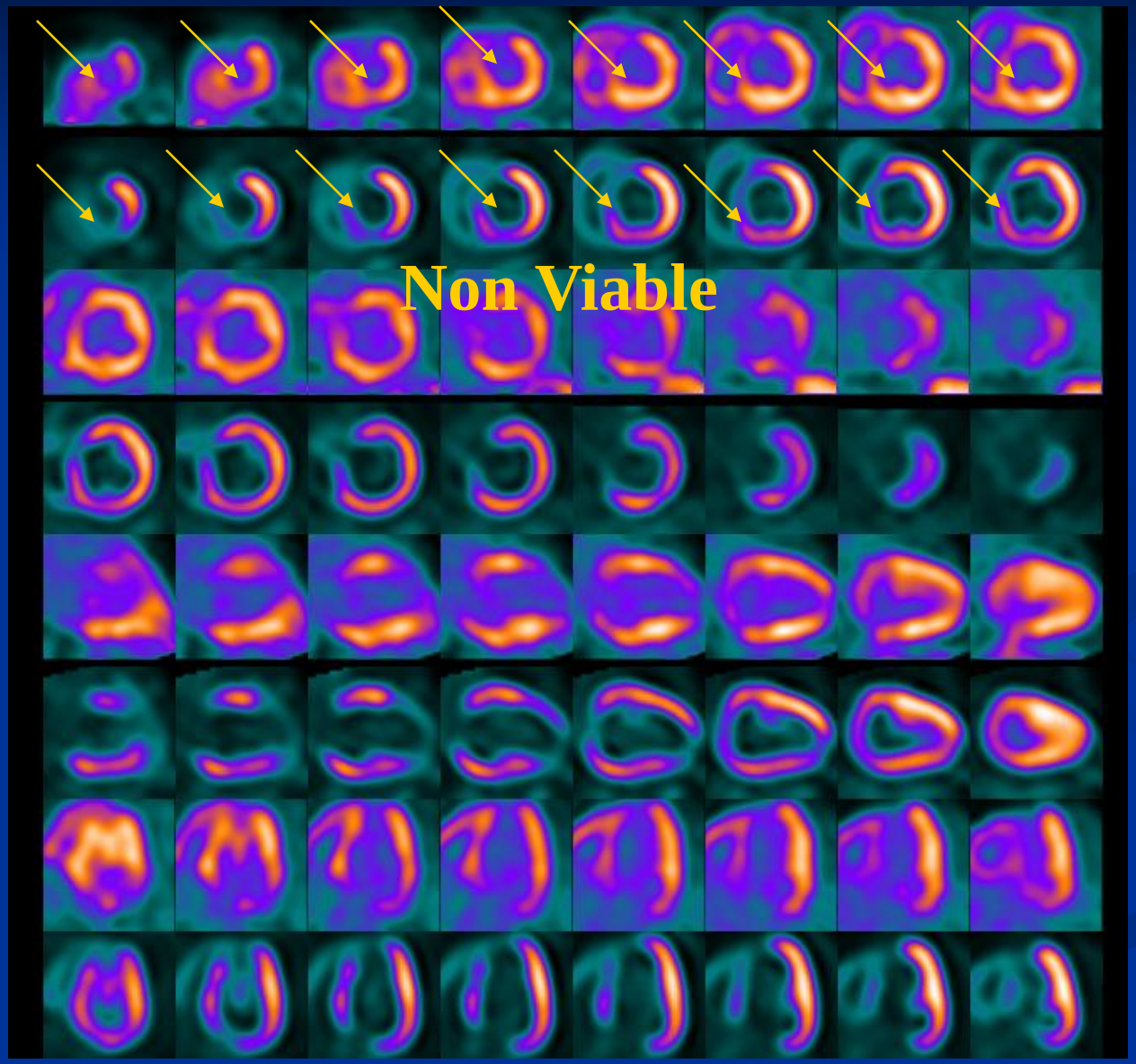


Pat06

200 lbs male
Volunteer
32 mCi stress
8 mCi rest

PET FDG Viability

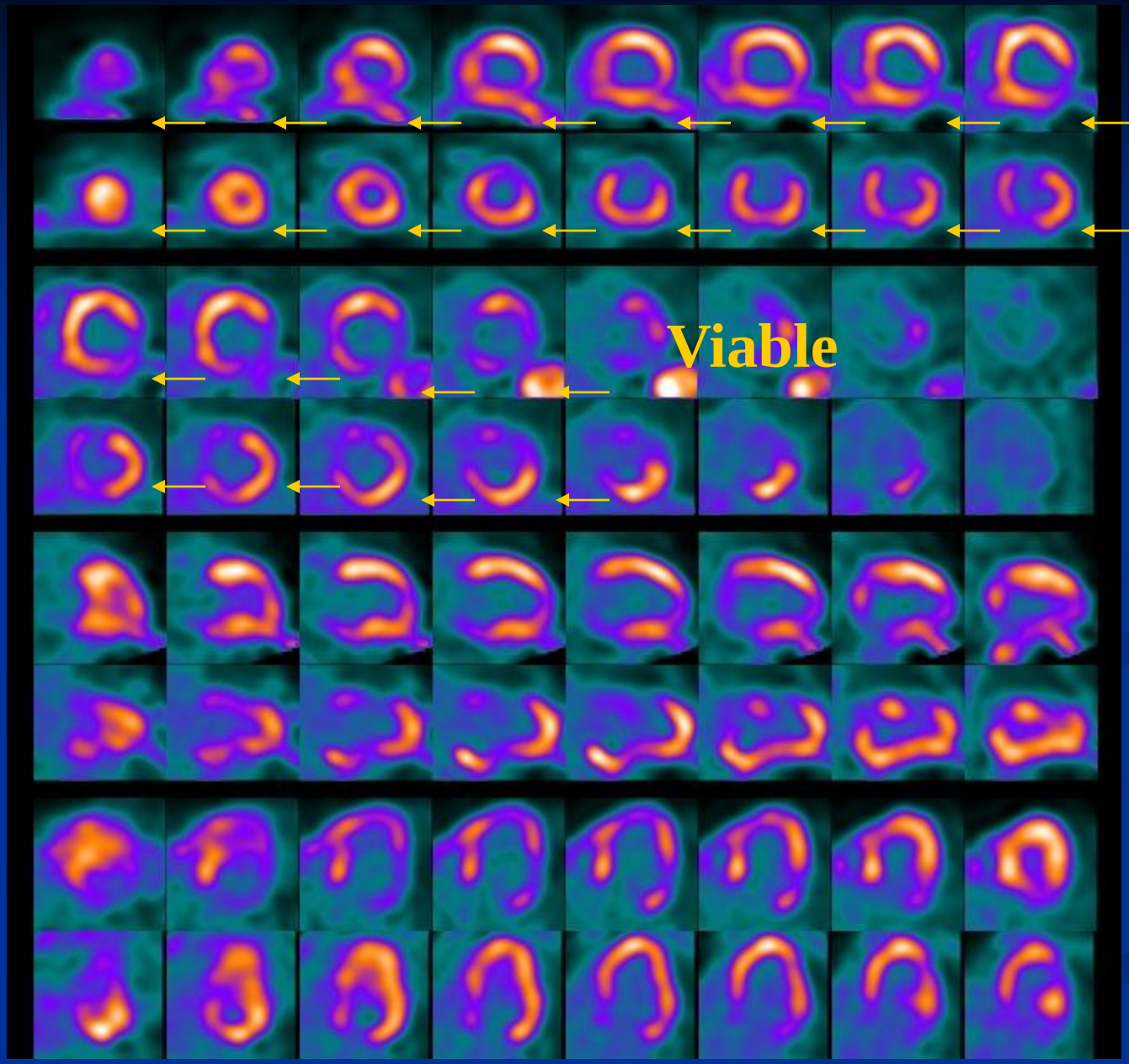
Pat07



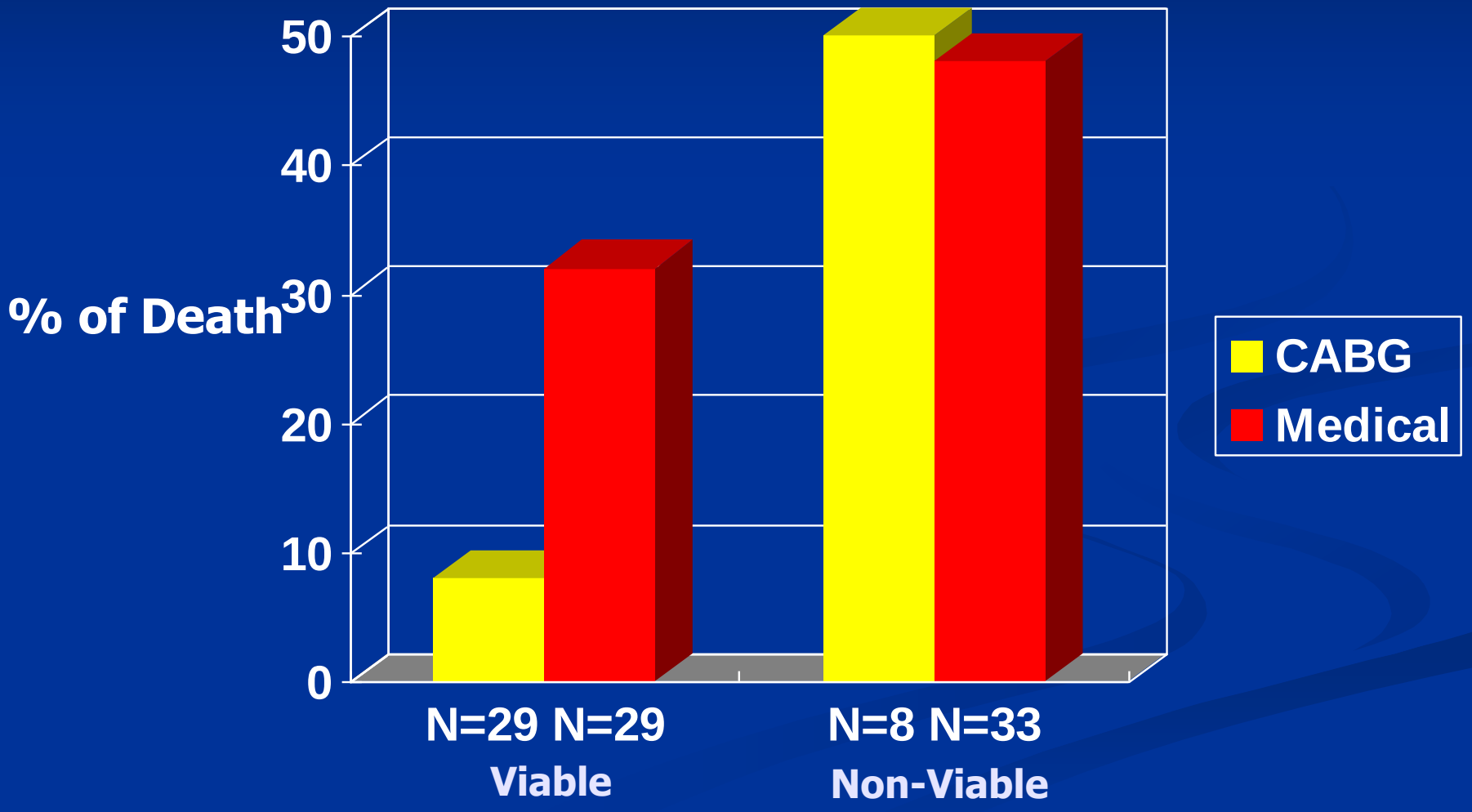
Rest Rb-82

FDG

Pat08



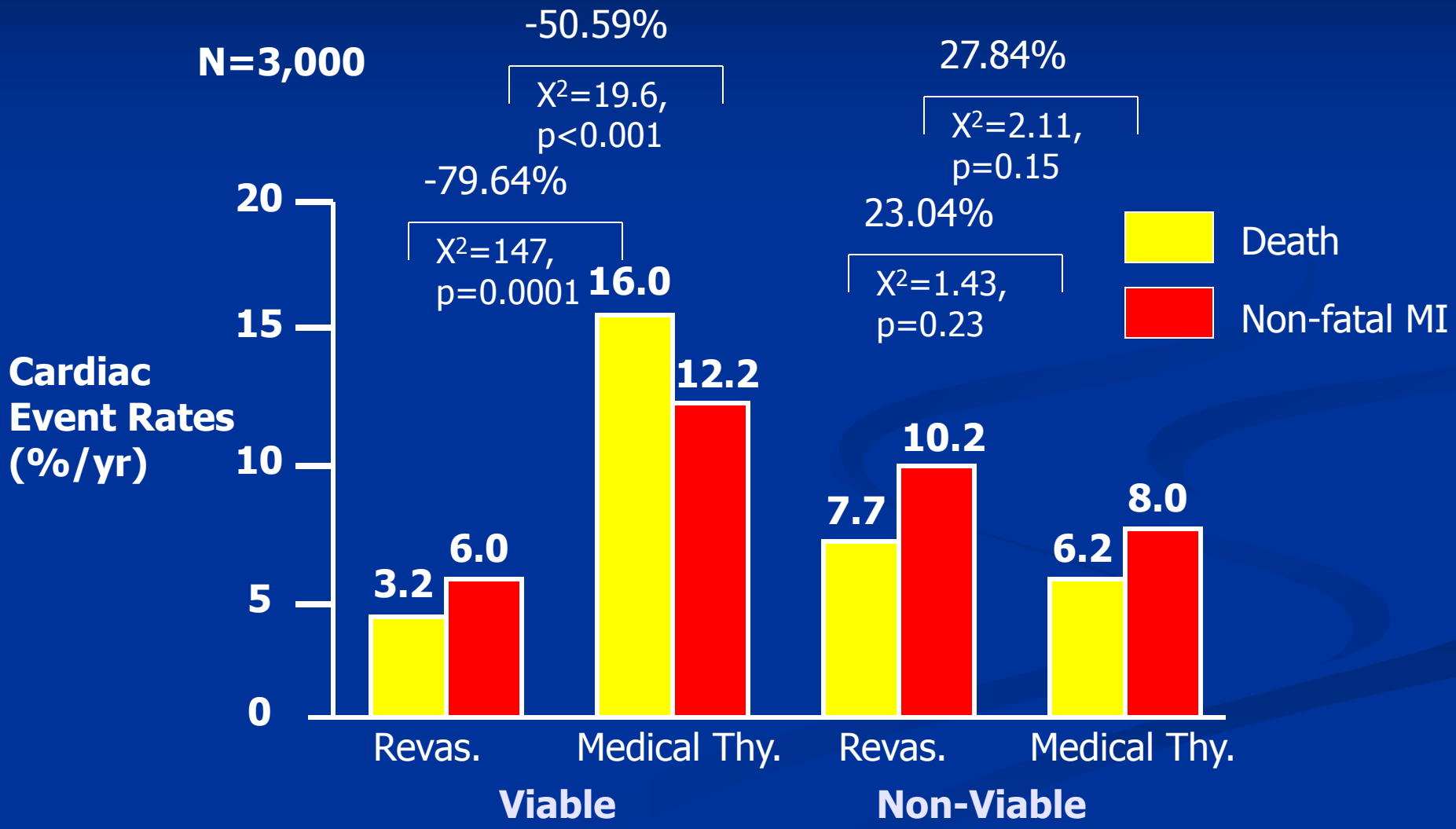
Rehospitalization of CHF by Viability and Treatment Mode



Rohalgi et al, Am J Cardiol;87:109

All Event Rates with and w/o Viability

Revascularization vs Medical Therapy



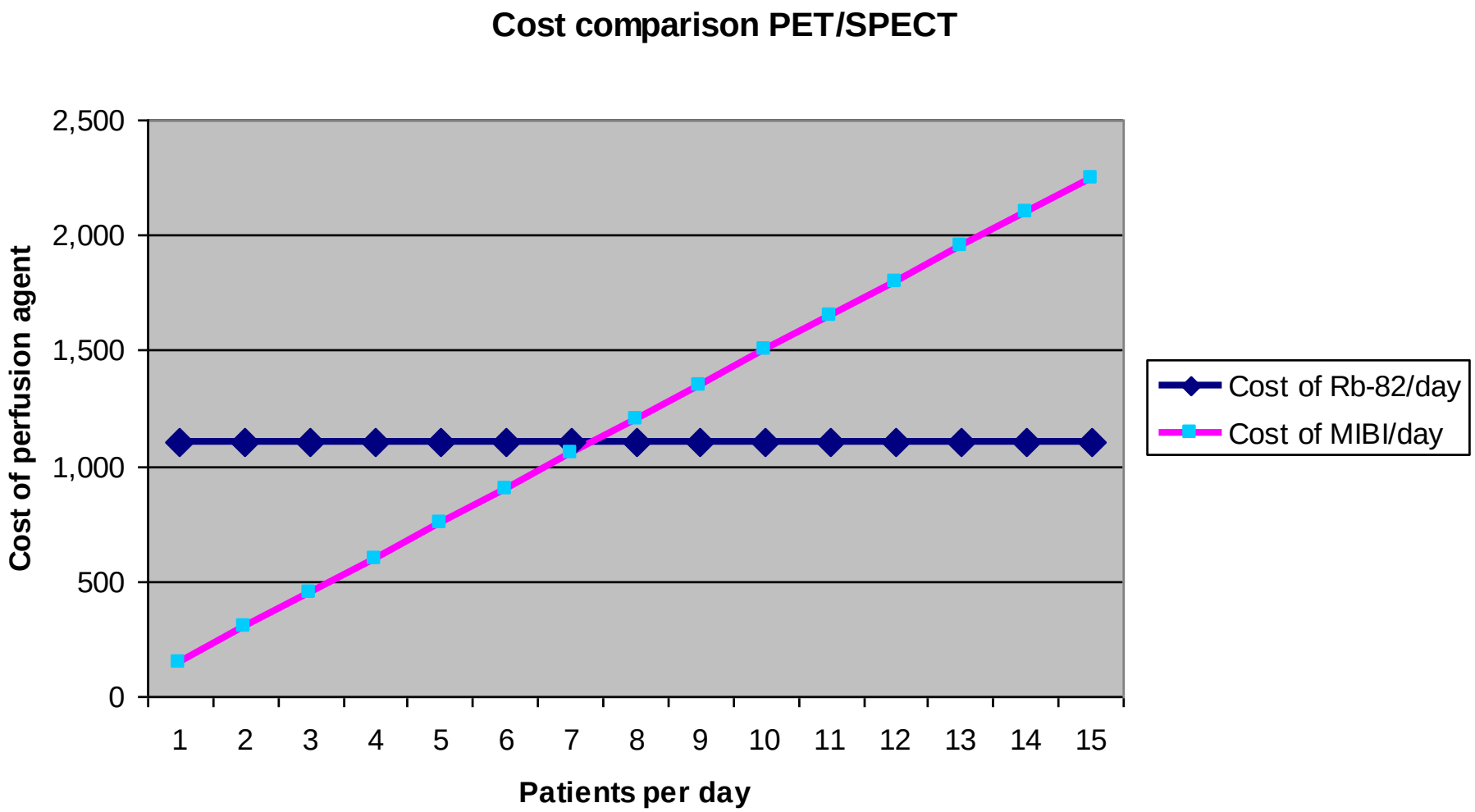
Allman K et al, JACC 2002

Economic impact on society

- Single missed diagnosis of CAD-$90,000
- Comparison of SPECT and PET
  - 300 patients
  - SPECT over 32% referred for coronary angiography
  - PET only 10% referred for coronary angiography
  - Additionally 20% of catheterization were normal in the face of a abnormal SPECT study (false positives)
  - PET imaging lead to a cost savings of 30-40%

Impact of PET on health care cost prepared for General Motors 1996

The Myth of Rb-82



Quick note on Generator Recall (it is temporary thus far)

- **What precipitated FDA's concern about CardioGen-82?**
  - The U.S. Department of Homeland Security recently notified the FDA about two separate incidents where individuals crossing U.S. borders triggered gamma ray emissions sensors, which detected radiation that was analyzed to have come from strontium-82 (Sr-82) and strontium-85 (Sr-85). Both of these radioisotopes are normally present in the generator that produces CardioGen-82. In both cases, the individuals had been imaged at facilities using CardioGen-82. The role of CardioGen-82 has not yet been determined

Quick note on Generator Recall (it is temporary thus far)

- **What is the risk of harm to the two patients?**
  - Based on the results of a full body scan of one of the patients, conducted by the Oak Ridge National Laboratory, it has been determined that the health risk, if any, to the scanned individual is minimal. The estimated amount of unexpected radiation the two patients received is similar to what other patients may receive with cumulative exposure to certain other types of cardiac imaging procedures. It would take more radiation to possibly cause adverse health effects in patients. In its July 15 Drug Safety Communication, FDA stated that "At this time, FDA believes that the risk of harm from this exposure is minimal, although any unnecessary exposure to radiation is undesirable."

Quick note on Generator Recall (it is temporary thus far)

- **Why was CardioGen-82 recalled?**
  - Bracco voluntarily recalled and suspended distribution of CardioGen-82 following discussions with the FDA regarding reports of unexpected radiation exposure in two individuals who underwent cardiac positron emission tomography (PET) scans with CardioGen-82. The reported unexpected radiation exposure is being further investigated. This work is being conducted in collaboration with the FDA and the respective state nuclear regulatory agencies

Quick note on Generator Recall (it is temporary thus far)

- **What else has Bracco done to address concerns about CardioGen-82?**
  - Bracco arranged for the two patients to receive full body scans at the Oak Ridge National Laboratory in order to determine the actual levels of radiation exposure. The full body scan results for the first patient were very favorable with minimal exposure levels. Our experts state that the total amount of exposure was found to be less than what would be expected from a thallium imaging procedure. Arrangements for testing the second patient are underway, with testing projected for August 12, 2011

Quick note on Generator Recall (it is temporary thus far)

- **Will patients who were treated at the same facilities as these two patients be notified of the incidents?**
  - FDA and Bracco are both working with the States of Nevada and Florida and with the two healthcare facilities to determine whether other patients may also have been exposed to unexpected radiation levels, and what further steps to take regarding any who were

Would anyone like to guess on the time frame for the return of the generator?

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Is it time to make our escape yet???

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