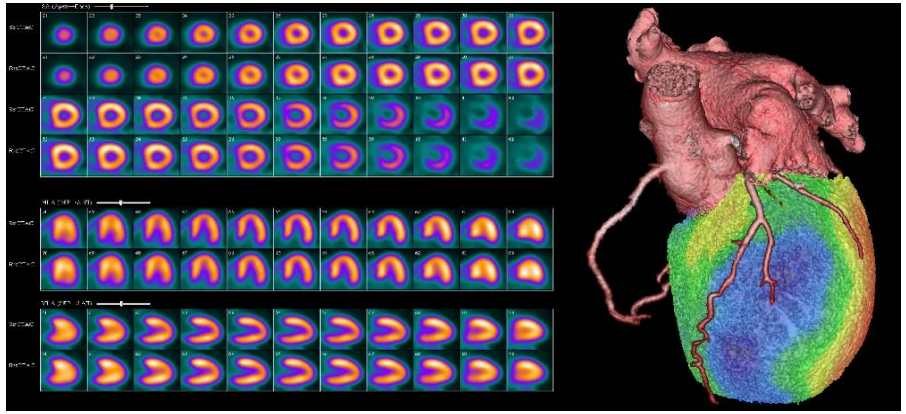

Myocardial Perfusion Imaging Protocols

Mouaz H. Al-Mallah, MD MSc

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Beverly B. and Daniel C. Arnold Distinguished Chair,
Professor of Cardiology, Houston Methodist Academic Institute
Professor of Medicine, Weill Cornell Medicine
Director, Cardiovascular PET
Houston Methodist DeBakey Heart and Vascular Center

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DEBAKEY HEART & VASCULAR CENTER

Disclosures

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- Research Support: Siemens, GE
- Consultant: Pfizer, Medtrace, GE, Jubilant

PET Radiotracers

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Characteristic	Rubidium^{82}	N^{13} ammonia	O^{15} water	^{18}Flurpiridaz
Supplied	Generator	Cyclotron	Cyclotron	Cyclotron/unit doses
Half-life	76 sec	9:96 min	2.09 min	109.7 min
Uptake mechanism	Active extraction	Active extraction	Freely diffusible	Active extraction
Positron range In water	1.7 mm	1.4 mm	1.5 mm	1 mm
Image quality	Very good	Excellent	Uninterpretable	Excellent
Radiotracer characteristics	Adequate	Very Good	Excellent	Very good
FDA approval	Yes	Yes	No	Yes

Relative Imaging Properties of PET Tracers Diagnostic Accuracy

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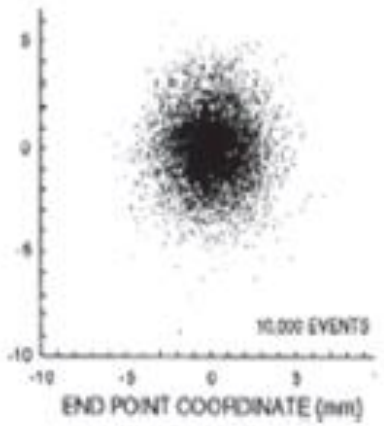
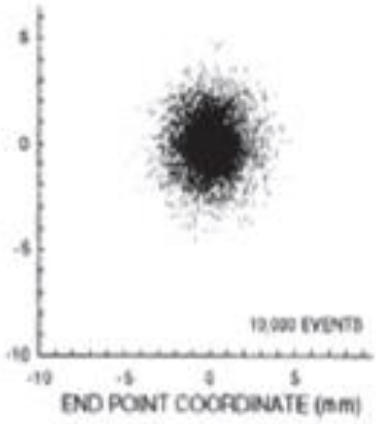
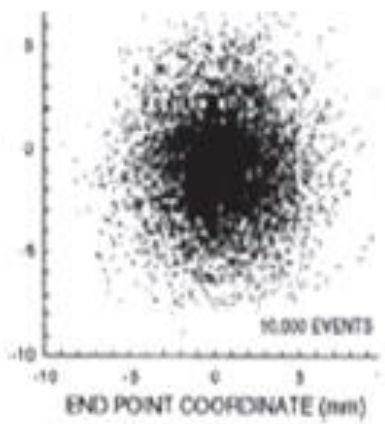
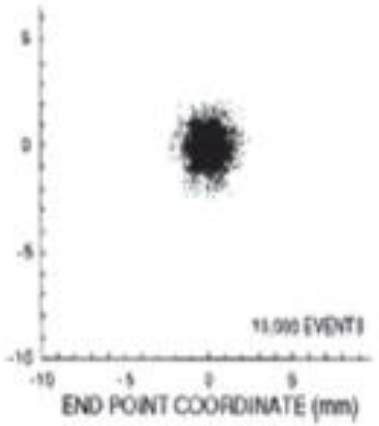
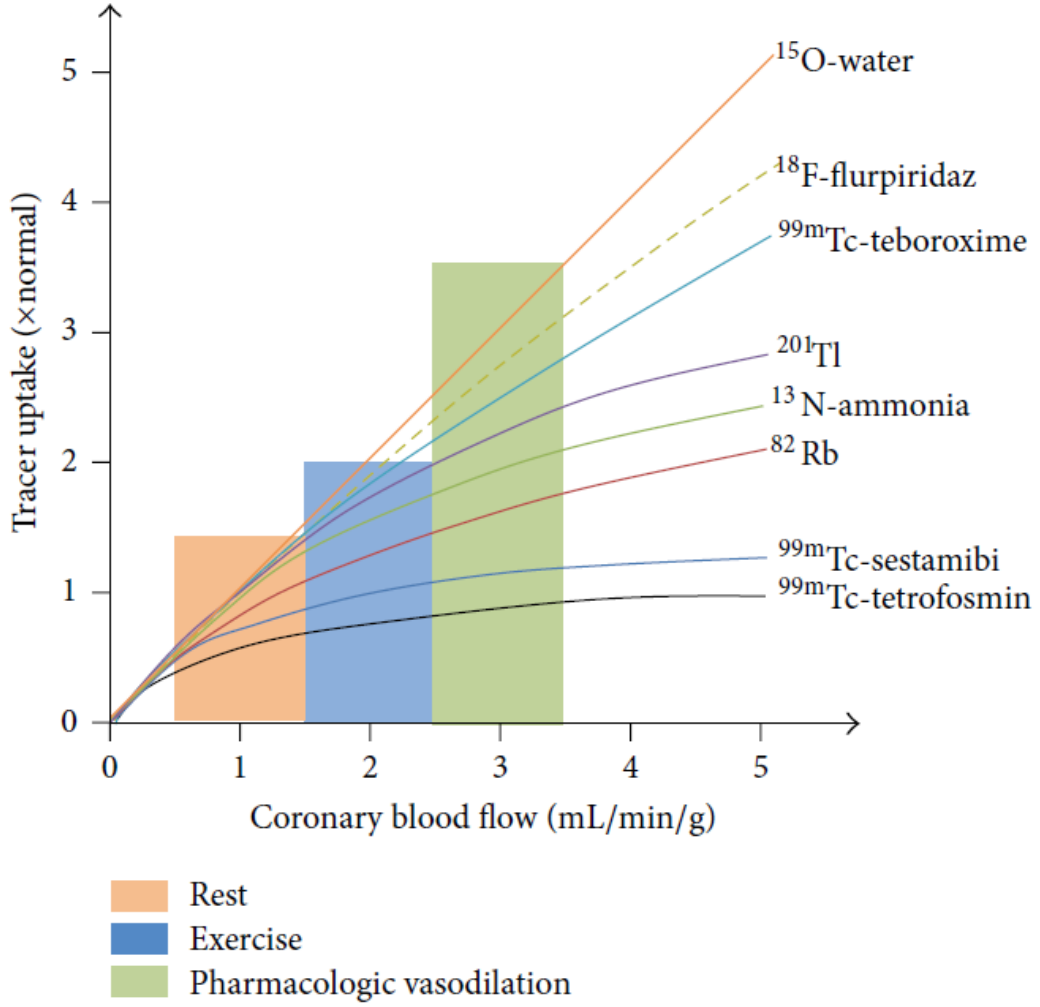
	^{15}O water	^{13}N ammonia	^{82}Rb	Flurpiridaz F 18
Positron range (mm)	4.14	2.53	8.6	1.03
End point coordinate				

Semin Nucl Med. 2014 Sep; 44(5): 333–343

Properties of PET Tracers



Radiopharmaceutical	Extraction Fraction
^{18}F-FPZ	0.9
^{13}N-Ammonia	0.8
^{15}O-Water	1.0
^{82}Rb	0.5

Patient Preparation

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- NPO for 6 hours
- No caffeine for 18-24 hours
- Avoid theophylline containing medications for at least 48 hours

Dilsizian, V. J. Nucl. Cardiol. (2016) 23: 1187

Patient Positioning

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- Ideally, the patient should be placed in the supine position, with the arms out of the camera's FOV.
- In patients with severe arthritis, whose arms cannot be positioned outside the camera's FOV, cardiac images should be obtained with the patient's arms resting on his/her side.
- Keep the patient positioned similarly for both studies

Dilsizian, V. J. Nucl. Cardiol. (2016) 23: 1187

PET Perfusion Imaging

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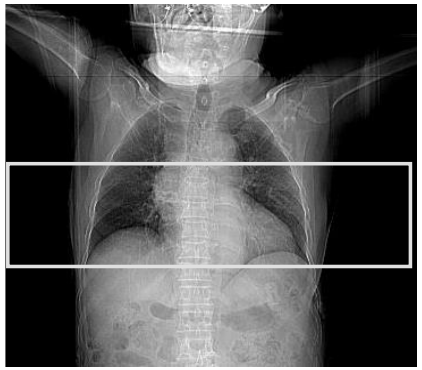
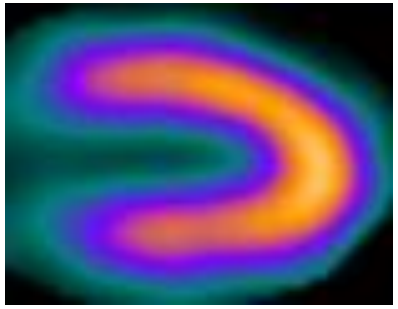
Scout



Transmission Scans

Emission Scans



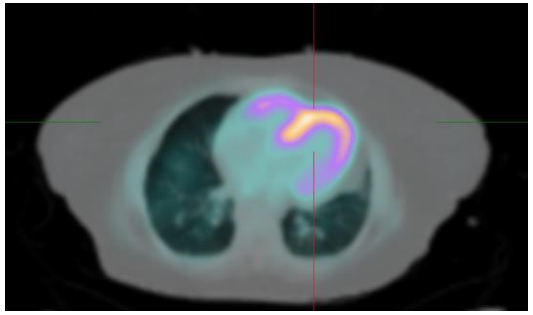


Image acquisition

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- Gated (ECG)
- Static
- Dynamic (Time)
- List mode (ECG and Time)

ECG Gated Acquisition

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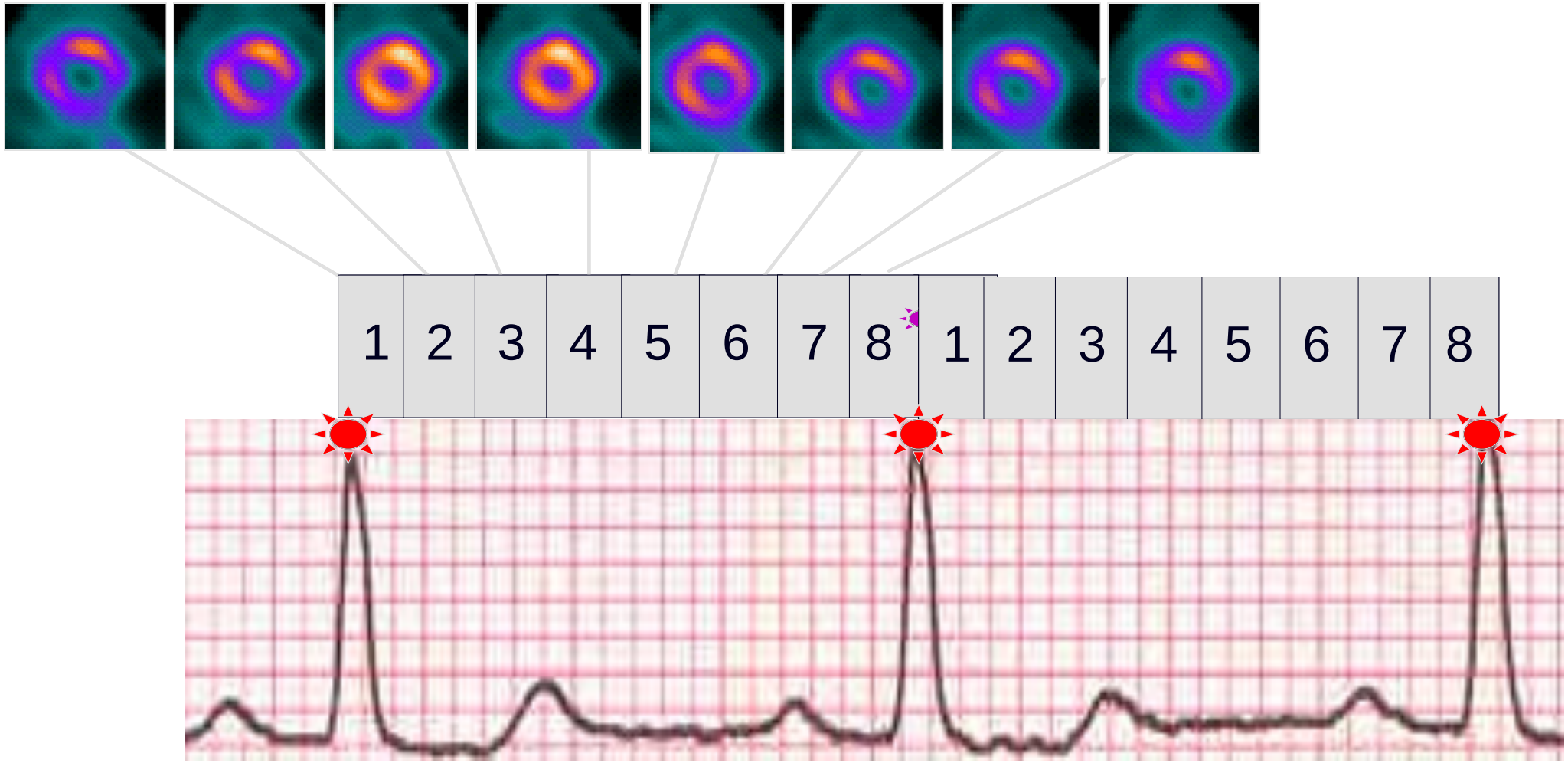

ECG Gated Acquisition

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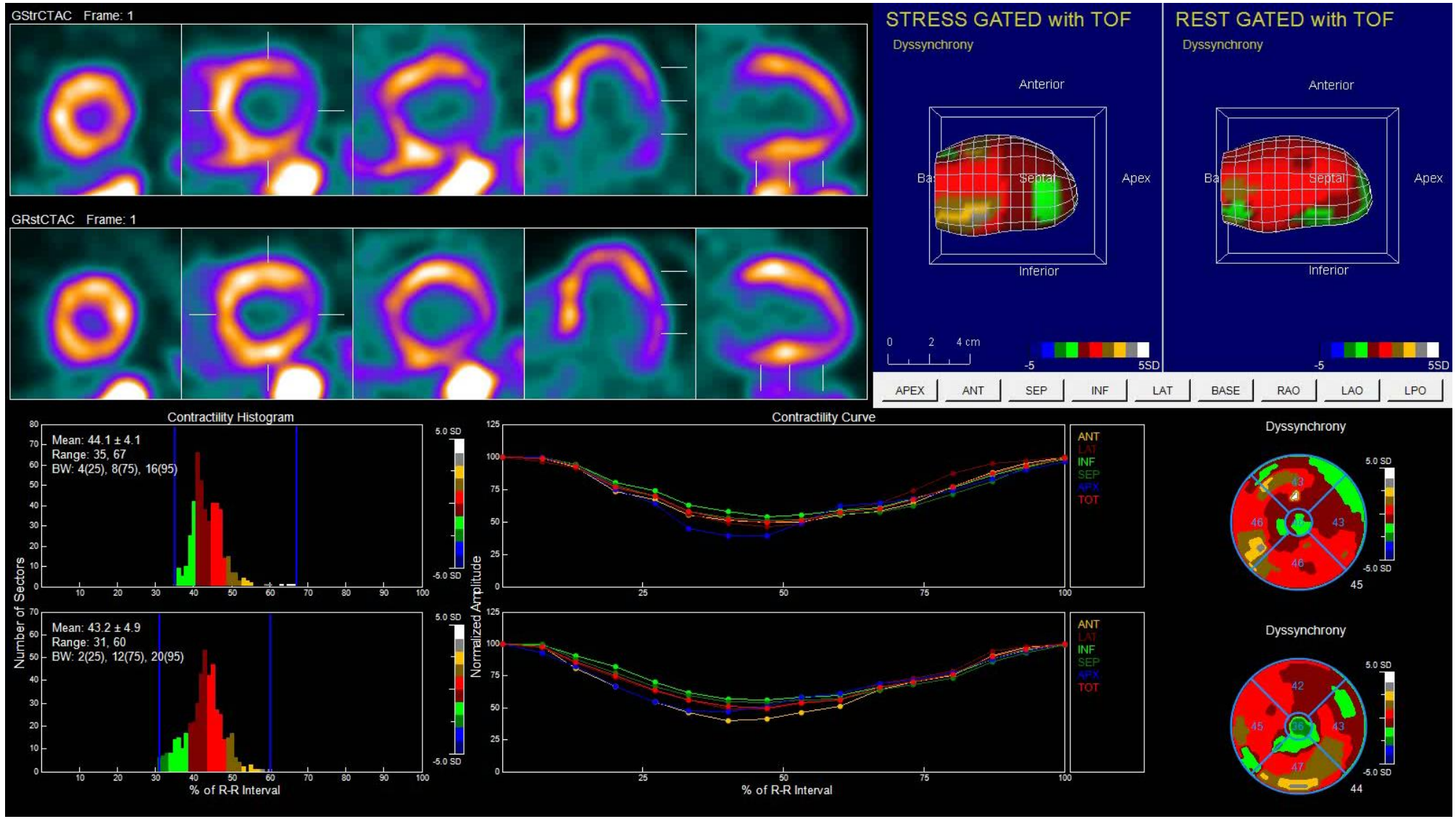
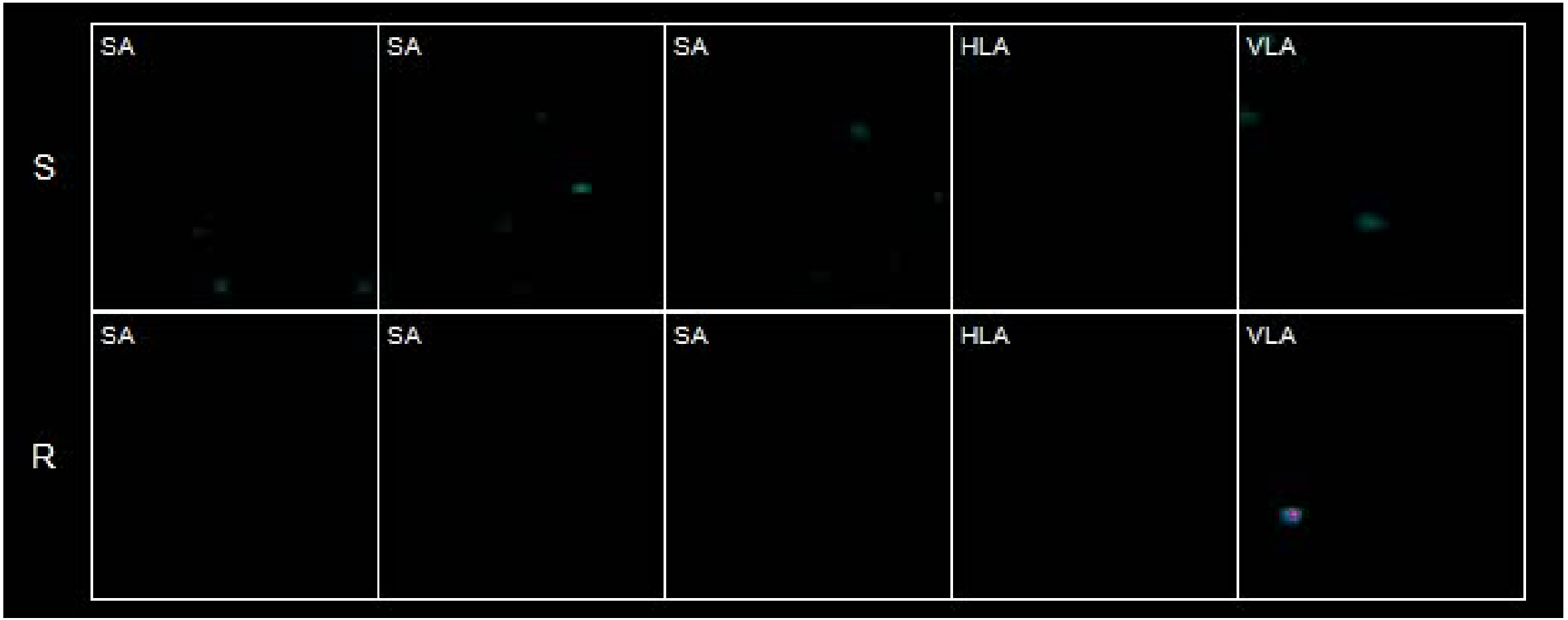
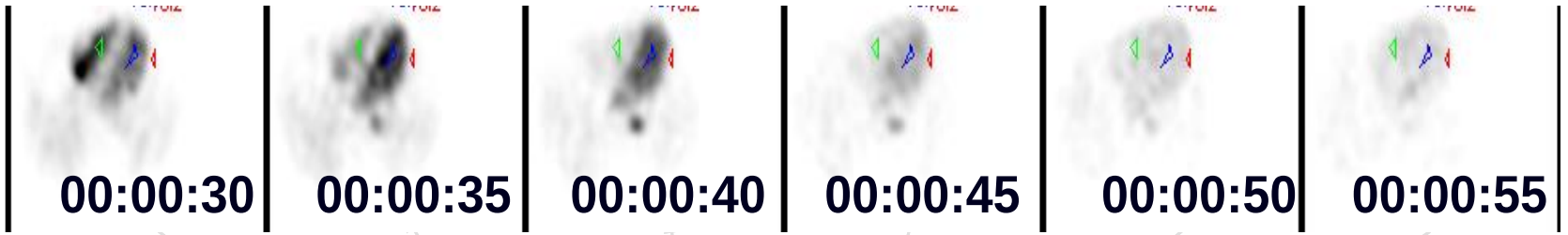


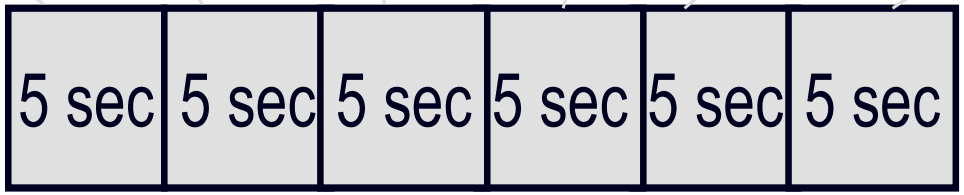
Dynamic Acquisition

HOUSTON Methodist
DEBAKEY HEART & VASCULAR CENTER



Dynamic Acquisition



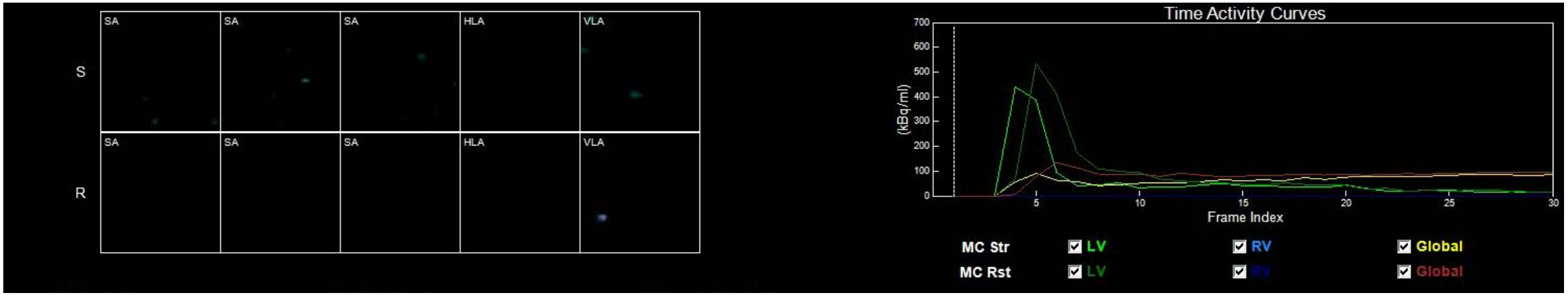


Dynamic data binned into 30 frames (16x5s, 6x10s, 3x20s, 4x30s, 1x80s)

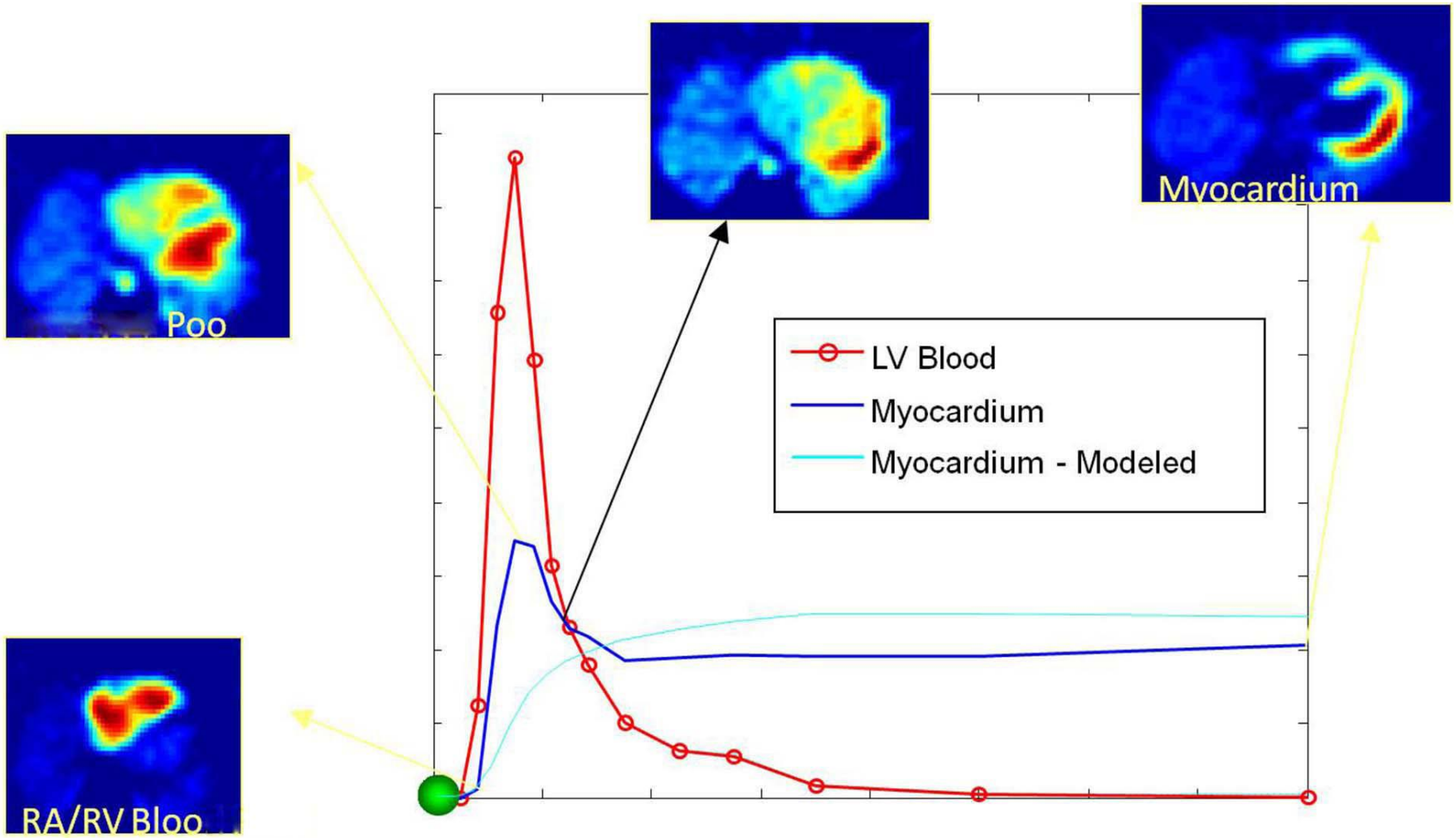
Other bins used 9x10s, 3x30s,1x60s,2x120s

Dynamic Acquisition

HOUSTON Methodist DEBAKEY HEART & VASCULAR CENTER

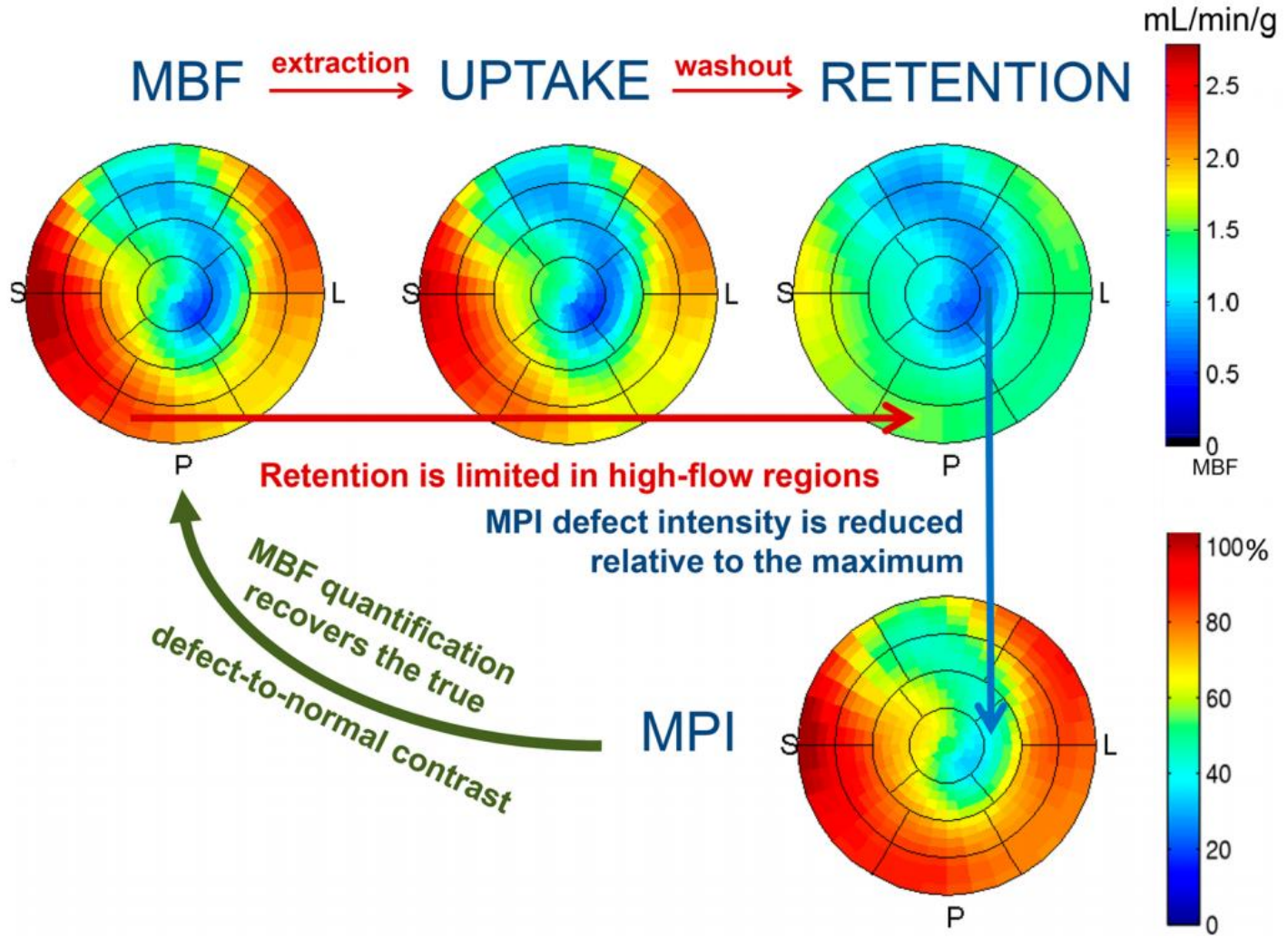


Dynamic Imaging



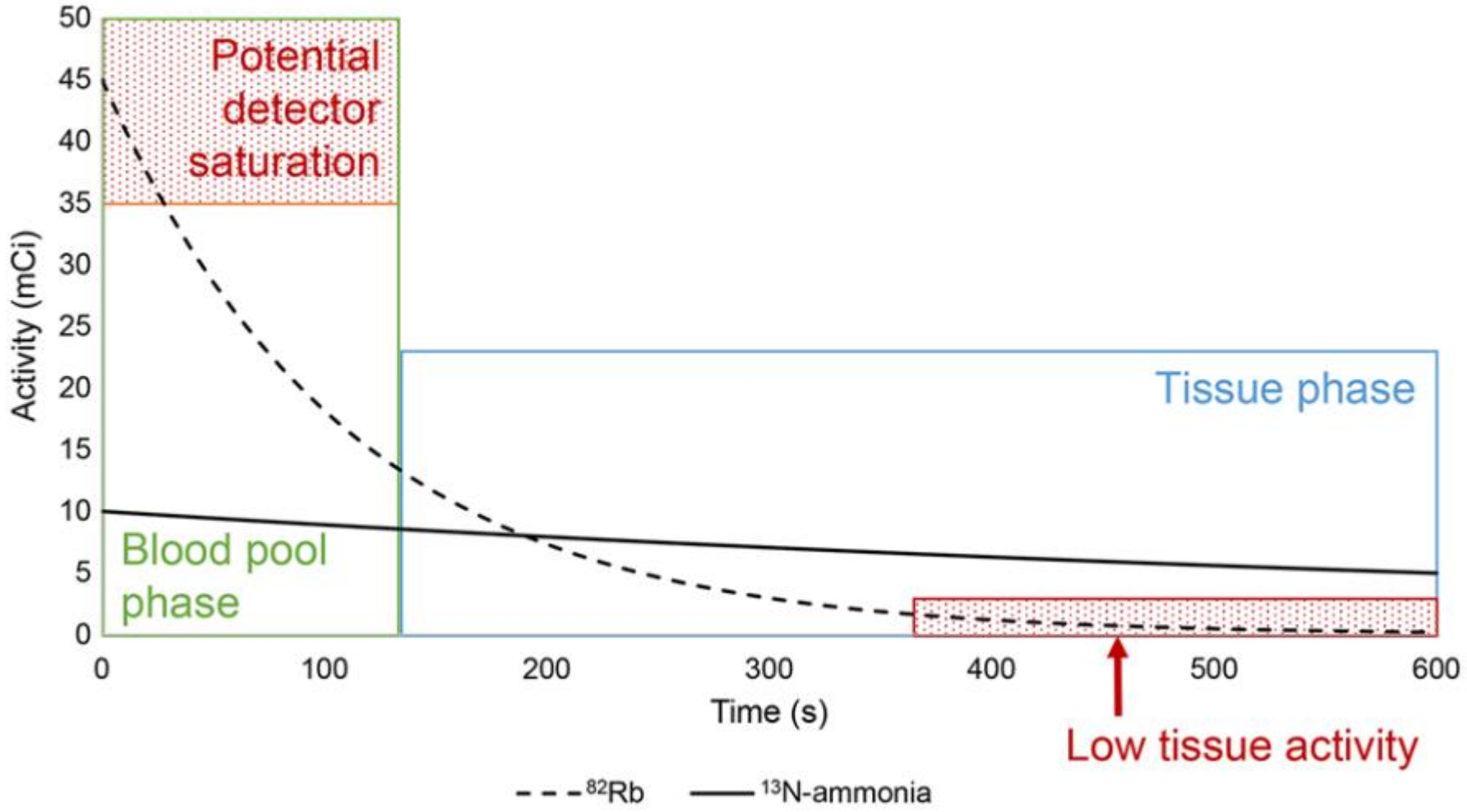
Ziadi *Cardiovasc Diagn Ther* 2017;7(2):206-218

MBF Assessment



Murthy, Di Carli, J Nucl Cardiol 2018;25:269–97.

How Much to Inject?



Murthy, Di Carli, J Nucl Cardiol 2018;25:269–97

MBF and MFR reference ranges for ^{13}N-ammonia PET

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Publication	Sample size (*n*)	Age (y)	Stress agent	Rest MBF (mL/minute/g)	Stress MBF (mL/minute/g)	MFR
Hutchins et al.[212]	7	24 ± 4	Dipyridamole	0.88 ± 0.17	4.17 ± 1.12	4.80 ± 1.30
Chan et al.[213]						4.00 ± 1.30
Czernin et al.						4.1 ± 0.90
Czernin et al.						NR
Nagamachi et						NR
Yokoyama et						4.13 ± 1.38
Böttcher et al						3.16 ± 0.80
Campisi et al.						3.16 ± 0.85
Nitzsche et al						NR
Dayanikli et a						4.27 ± 0.52
Sawada et al.						3.50 ± 0.69
Beanlands et						4.10 ± 0.71
Muzik et al.[21						4.60 ± 0.90
Muzik et al.[88						4.28 ± 0.65
Lortie et al.[22						4.25 ± 0.91
DeGrado et a						3.61 ± 1.06
Tawakol et al						NR
Schindler et a						NR
Quercioli et al.[70]	21	43 ± 11	Dipyridamole	0.71 ± 0.10	2.37 ± 0.49	3.38 ± 0.67
Valenta et al.[220]	26	38 ± 10	Dipyridamole	0.71 ± 0.13	2.29 ± 0.51	3.28 ± 0.70
Prior et al.[68]	50	42 ± 13	Dipyridamole/ adenosine	0.64 ± 0.12	1.98 ± 0.44	3.40 ± 1.00
Renaud et al.[221]	14	31 ± 6	Dipyridamole	0.68 ± 0.12	2.86 ± 1.14	4.15 ± 1.57
Slomka et al.[27]	15	NR	Adenosine	0.85 ± 0.16	2.77 ± 0.65	3.39 ± 1.22
Weighted mean	363 (total)	37.6		0.71	2.58	3.54

Weighted Average:

Rest 0.71 ml/min/g

Stress 2.58 ml/min/g

MFR 3.54

Murthy, Di Carli, J Nucl Cardiol 2018;25:269–97.

MBF and MFR reference ranges for ^{82}Rb PET

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Publication	Sample size (*n*)	Age	Stress	Rest MBF	Stress MBF (mL/minute/g)	MFR
Lin et al.[222]	11				2.50 ± 0.54	NR
Lortie et al.[22]	14				2.83 ± 0.81	4.25 ± 1.37
Manabe et al.[223]	15				3.35 ± 1.37	4.47 ± 1.47
Prior et al.[224]	22				3.82 ± 1.21	3.88 ± 0.91
Sdringola et al[225]	56				2.89 ± 0.50	4.17 ± 0.80
Johnson et al.[171]	241				2.71 ± 0.58	4.02 ± 0.85
Germino et al.[226]	9				3.65 ± 0.64	NR
Renaud et al.[221]	14				2.96 ± 0.89	4.32 ± 1.39
Weighted mean	382 (total)	28.6		0.74	2.86	4.07

Weighted Average:

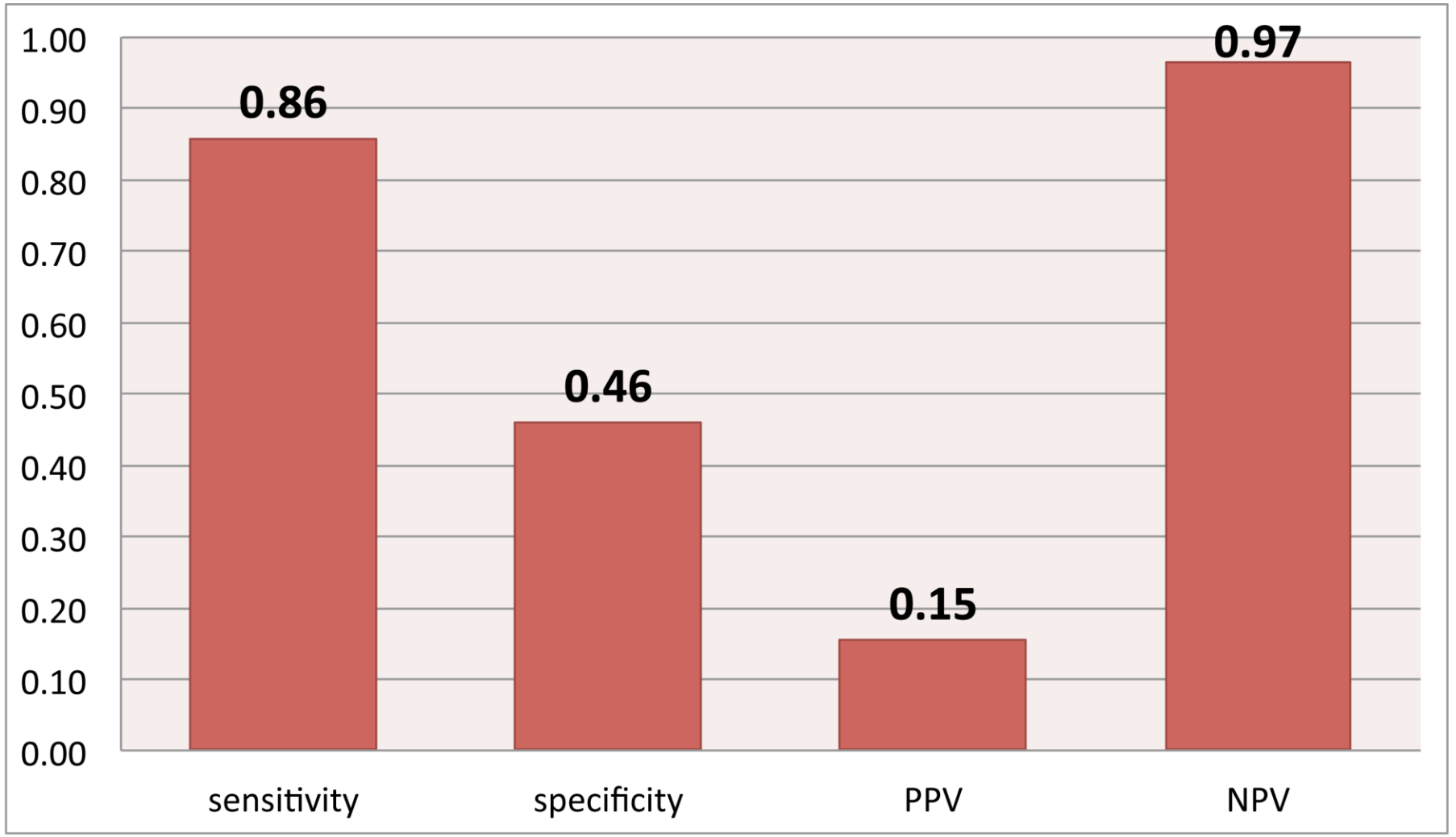
Rest 0.74 ml/min/g

Stress 2.86 ml/min/g

MFR 4.07

Murthy, Di Carli, J Nucl Cardiol 2018;25:269–97.

Coronary flow reserve and obstructive CAD



Sources: Naya et al, JNM 2014;55:248-55

MBF/CFR Most Helpful in

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1. Patients without known prior history of cardiac disease who present with symptoms suspicious for myocardial ischemia.

2. Patients with known CAD, in whom more specific physiological assessment is desired.

3. Identifying an increased suspicion for multivessel CAD.

4. Disparity between visual perfusion abnormalities and normal angiography, in order to assess microvascular dysfunction.

5. Heart transplant when there is a question of vasculopathy.

Dilsizian et al PET Guidelines Journal of Nuclear Cardiology 2016

MBF/CFR Need Careful Assessment

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1. Patients post-CABG who can have diffuse reduction on MBF despite patent grafts.

2. Patients with large transmural infarcts where resting flow may be severely reduced such that small increases in flow lead to normal or near-normal flow reserve.

3. Patients with advanced severe chronic renal dysfunction who likewise often have diffuse coronary disease.

4. Patients with severe LV dysfunction.

Dilsizian et al PET Guidelines Journal of Nuclear Cardiology 2016

Rubidium-82

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- Parent: Strontium-82 generator every 42 days
- Half life: 75 seconds
- Dosing: equal dose for rest and stress
  - 40-60 mCi for 2D
  - 25-30 mCi for 3D LSO
  - 10 – 20 mCi for Digital PET
- Injection: Rapid bolus infusion in 30 sec preferably to follow by Saline Chase

Cardiac PET-CT Protocol
Rest - Stress ^{82}Rb MPI

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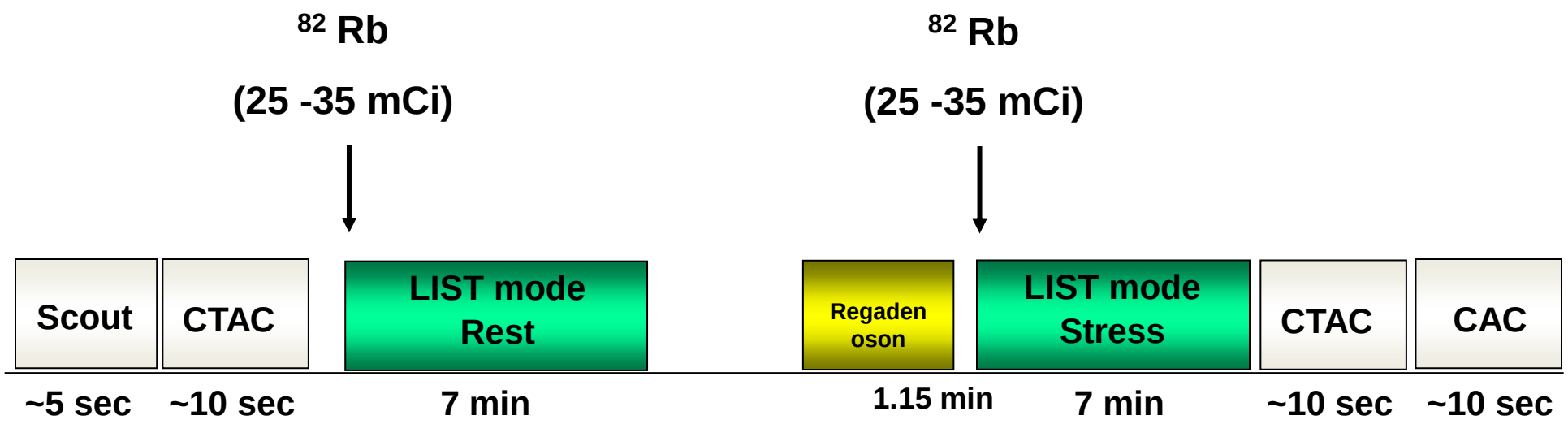
Regadenoson



~ 25 minutes

Cardiac PET-CT Protocol
Rest - Stress ^{82}Rb MPI

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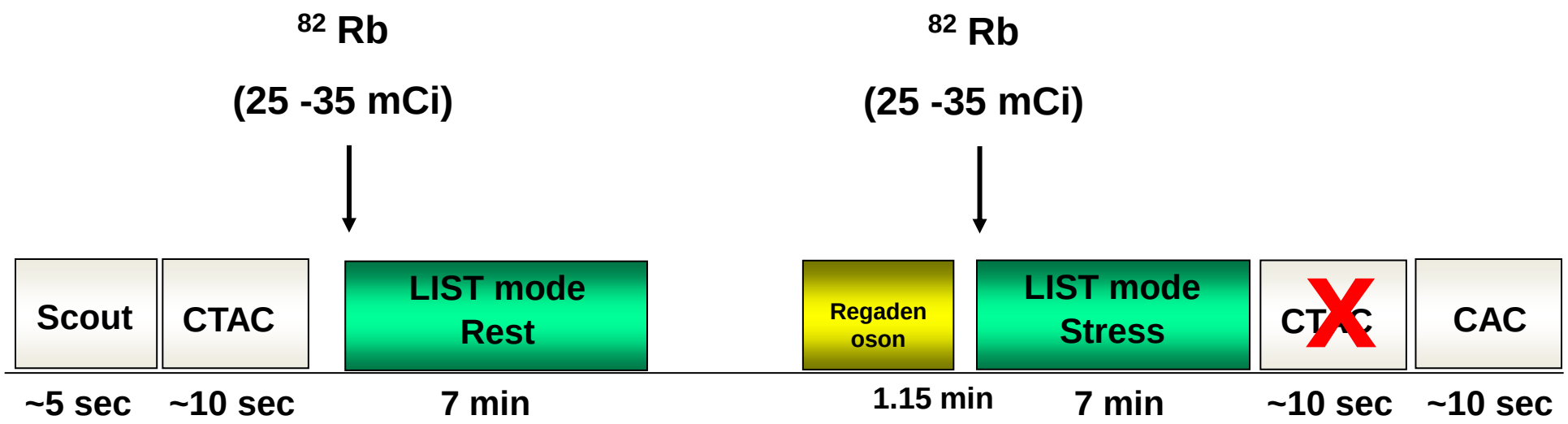
Regadenoson



~ 25 minutes

Cardiac PET-CT Protocol
Rest - Stress ^{82}Rb MPI

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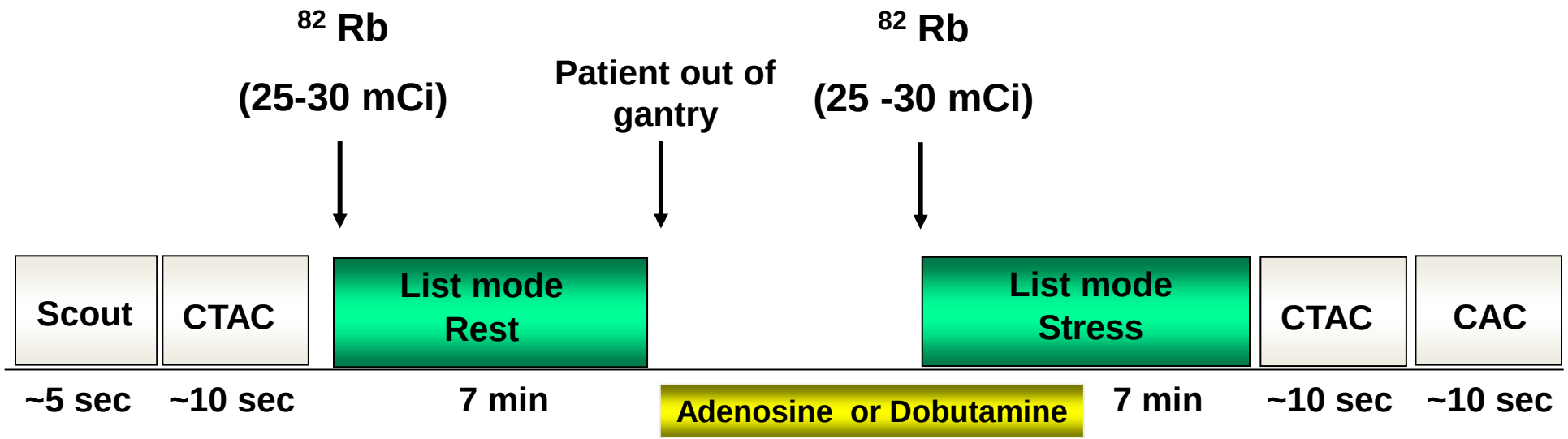
Adenosine or Dobutamine



2 IV Lines Required

~ 30-35 minutes

Cardiac PET-CT Protocol
Rest - Stress ^{82}Rb MPI

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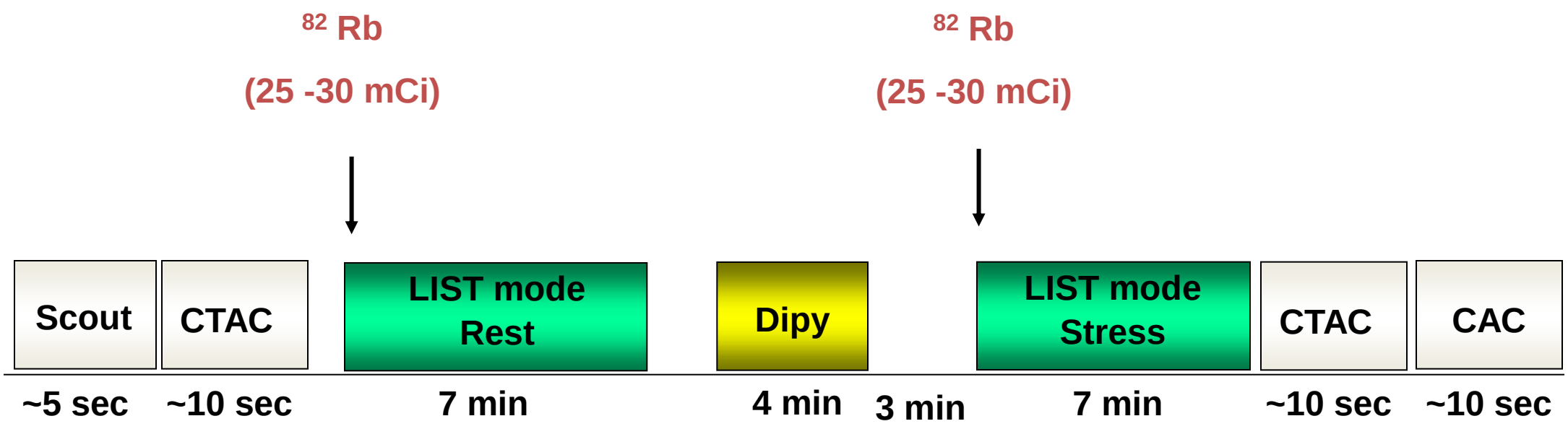
Dipyridamole



~ 25-30 minutes

Practical Considerations

- Staff exposure could be high because of the limited effectiveness of shielding and the potential for large doses (e.g., 82 Rb PET).
- A lead apron is not helpful in shielding the 511-keV photons.
- Large patients may benefit from higher doses.
- 3D imaging requires less dosage than 2D imaging due to the improved sensitivity of the system.

Dilsizian, V. J. Nucl. Cardiol. (2016) 23: 1187

Cardiac PET-CT Protocol
Rest - Stress ^{82}Rb MPI

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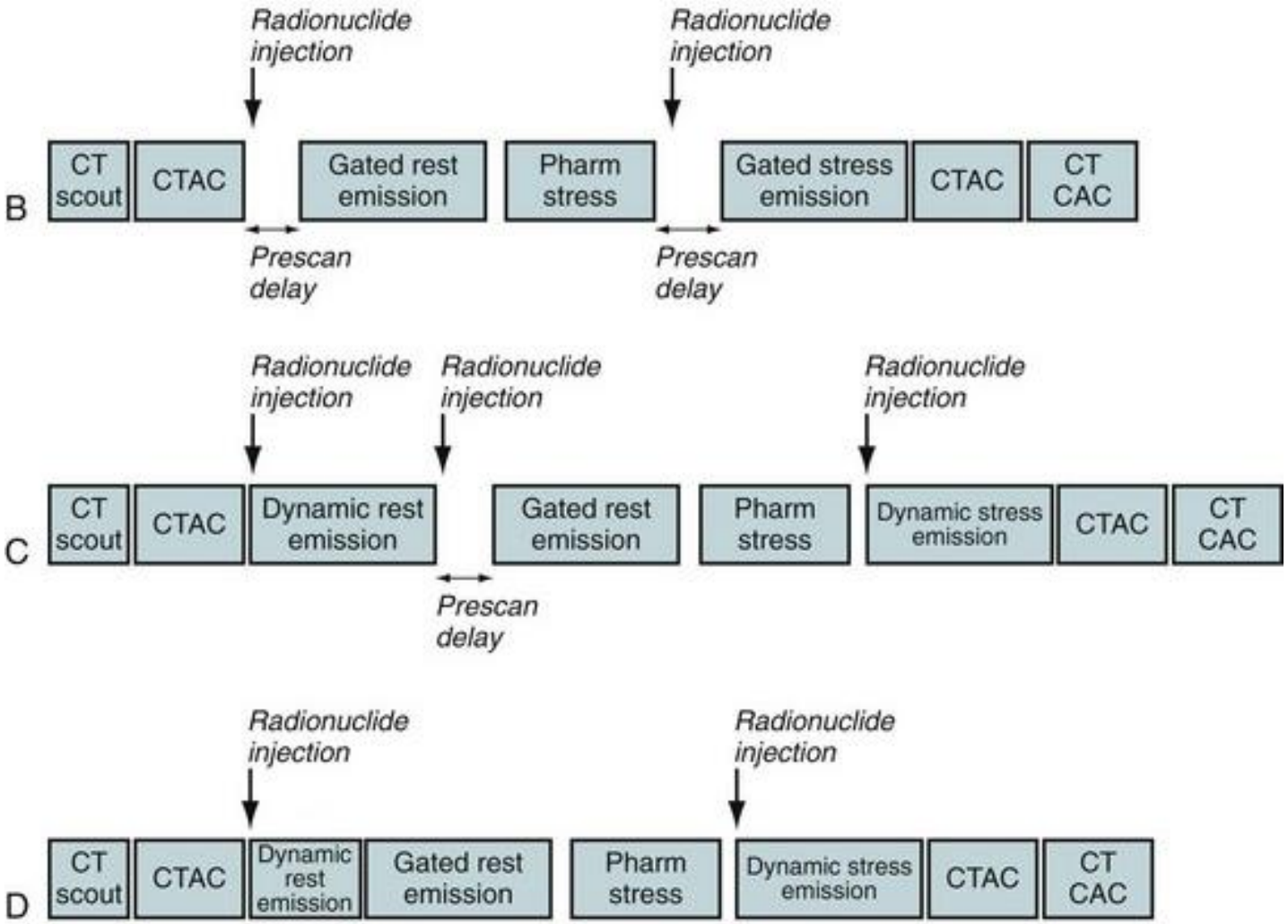

Marcelo F. Di Carli, Mouaz H. Al-Mallah, Clinical Techniques of Positron Emission Tomography and PET/CT 2011

Pre Scan Delay

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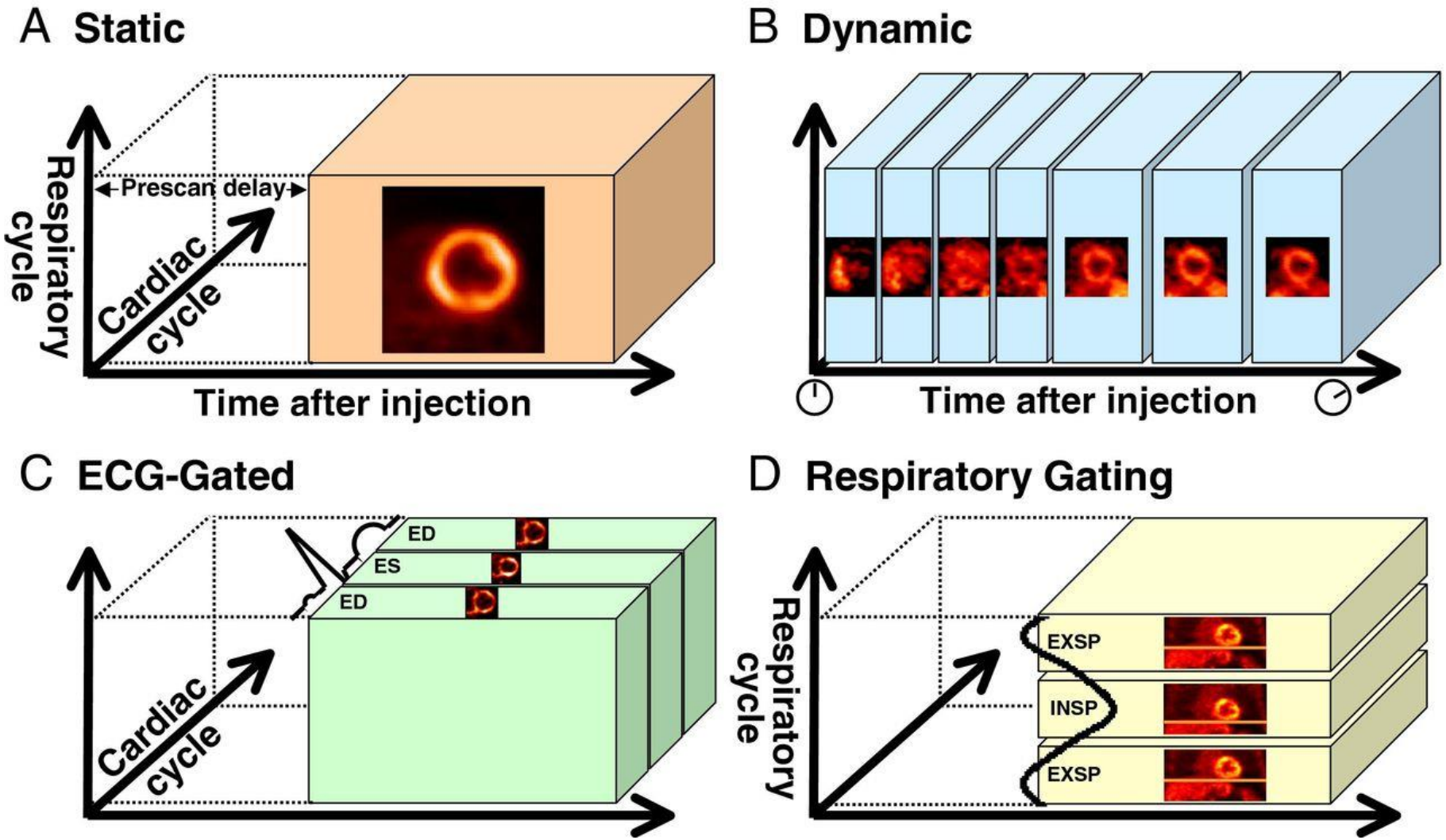

J Am Coll Cardiol 2009;54:1–15

Pre Scan Delay 120 secs in low flow

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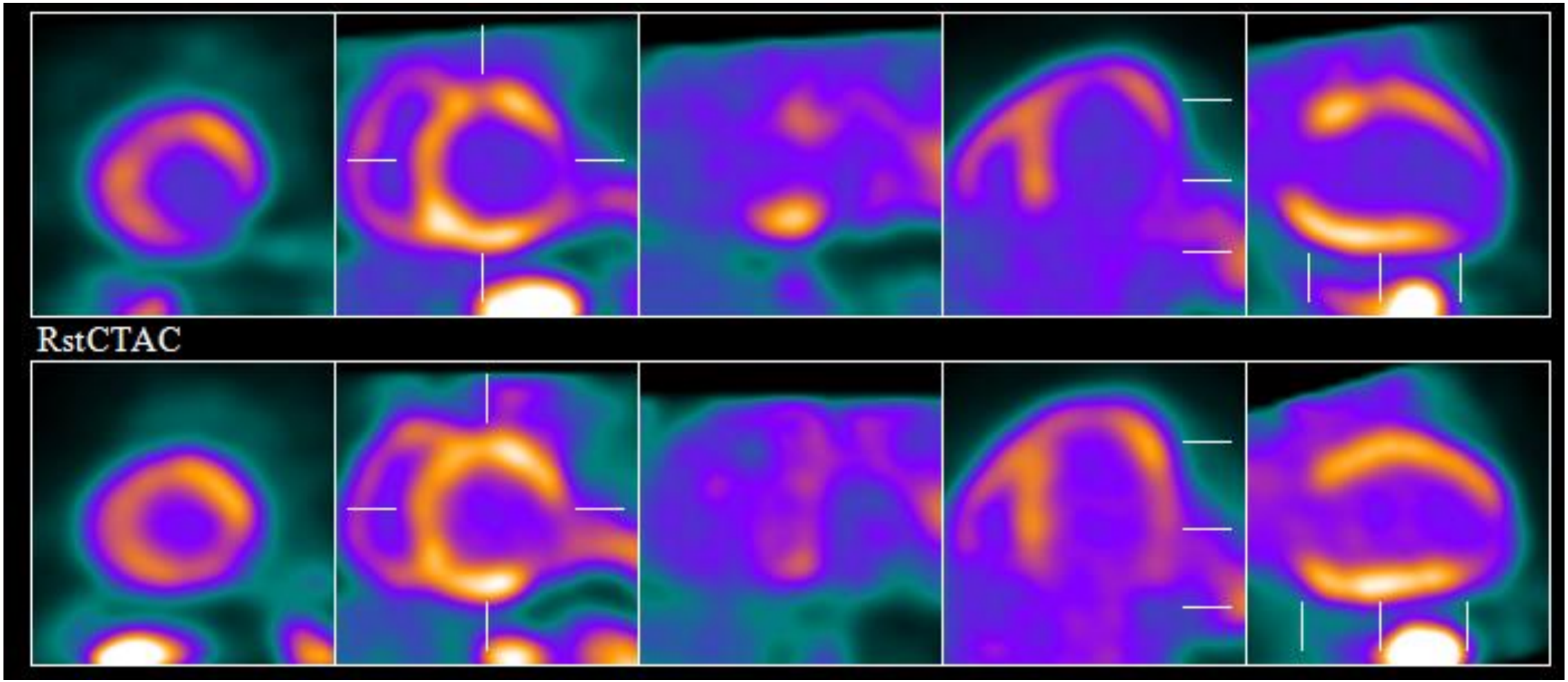
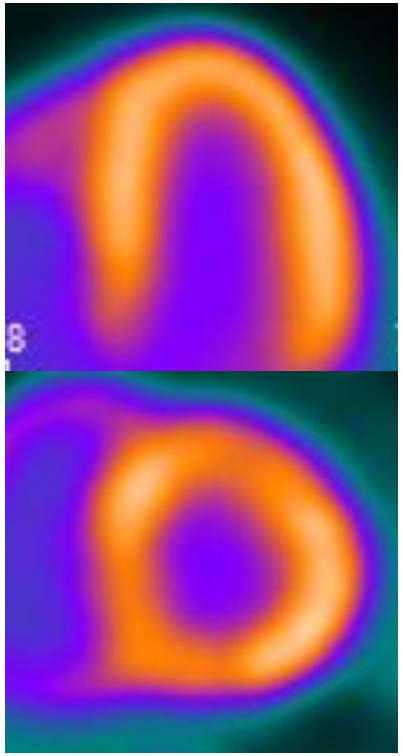


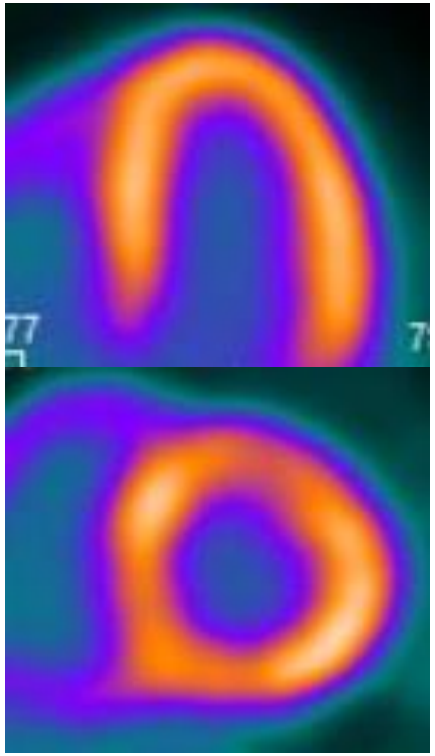
Pre Scan Delay 120 secs in low flow

HOUSTON Methodist DEBAKEY HEART & VASCULAR CENTER



120 sec

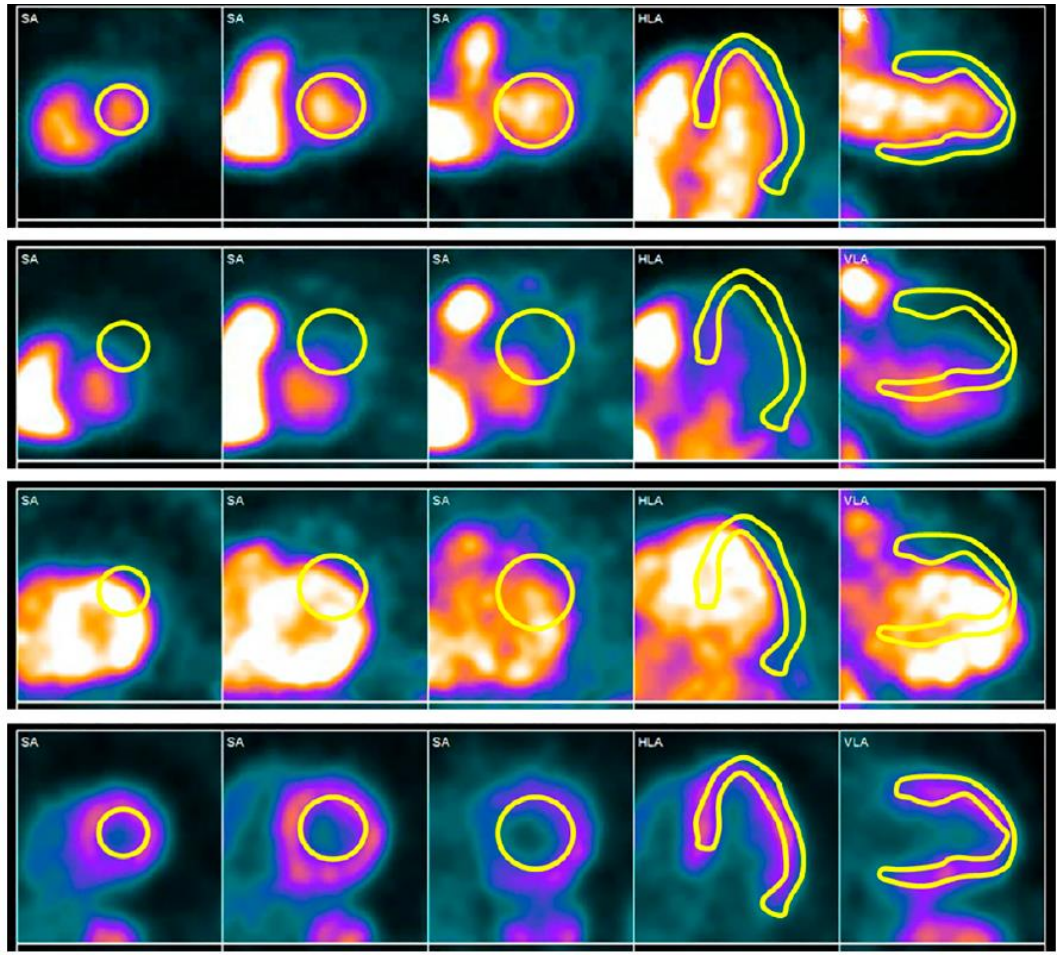
Additional 30 seconds Delay



150 sec

Motion Correction

- At the beginning of the acquisition, the blood pool and myocardial ROIs are in correct place
- As scan progresses, ROIs no longer positioned over their respective regions
- To obtain accurate blood flow measurements, motion during the dynamic phase must be corrected



Bateman TM et al. J Nucl Cardiol 2021; 28:768–787.

^{13}N Ammonia

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- Cyclotron produced
- Half life is 9.8 minutes

- Intravenous dose is 20 mCi per Injection
- Possible to be combined with Exercise
- Need 50 minutes between rest and stress

Cardiac PET-CT Protocol
Rest – Stress MPI

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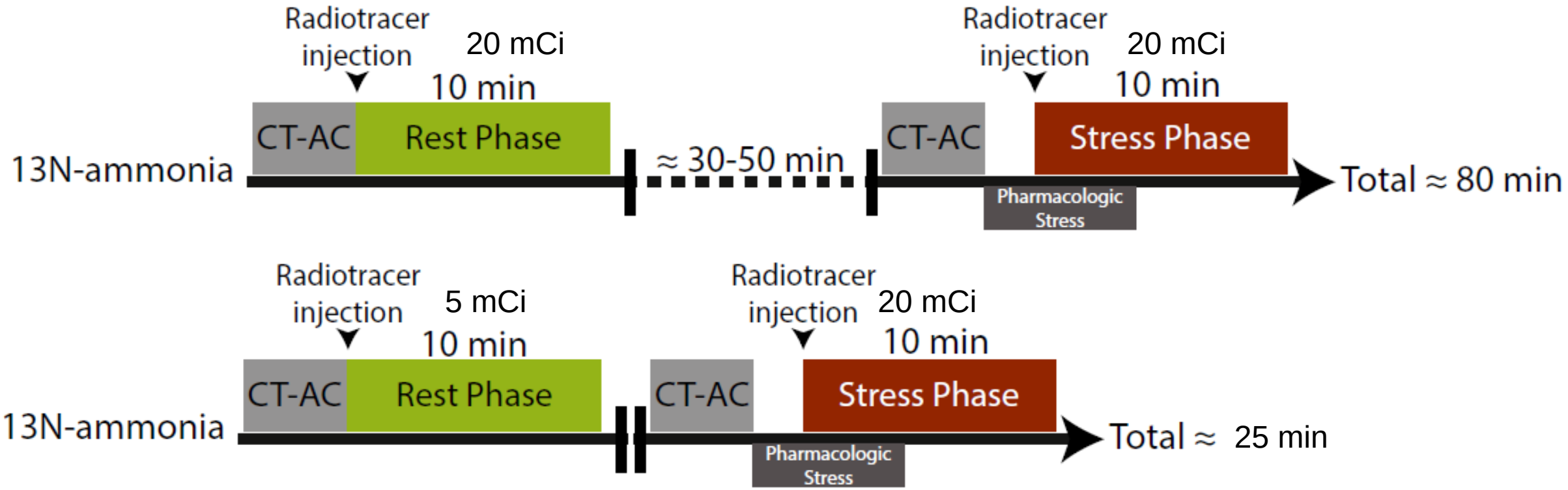

Clinical and Translational Imaging (2018) 6:47–60

Rubidium-82 Versus Ammonia

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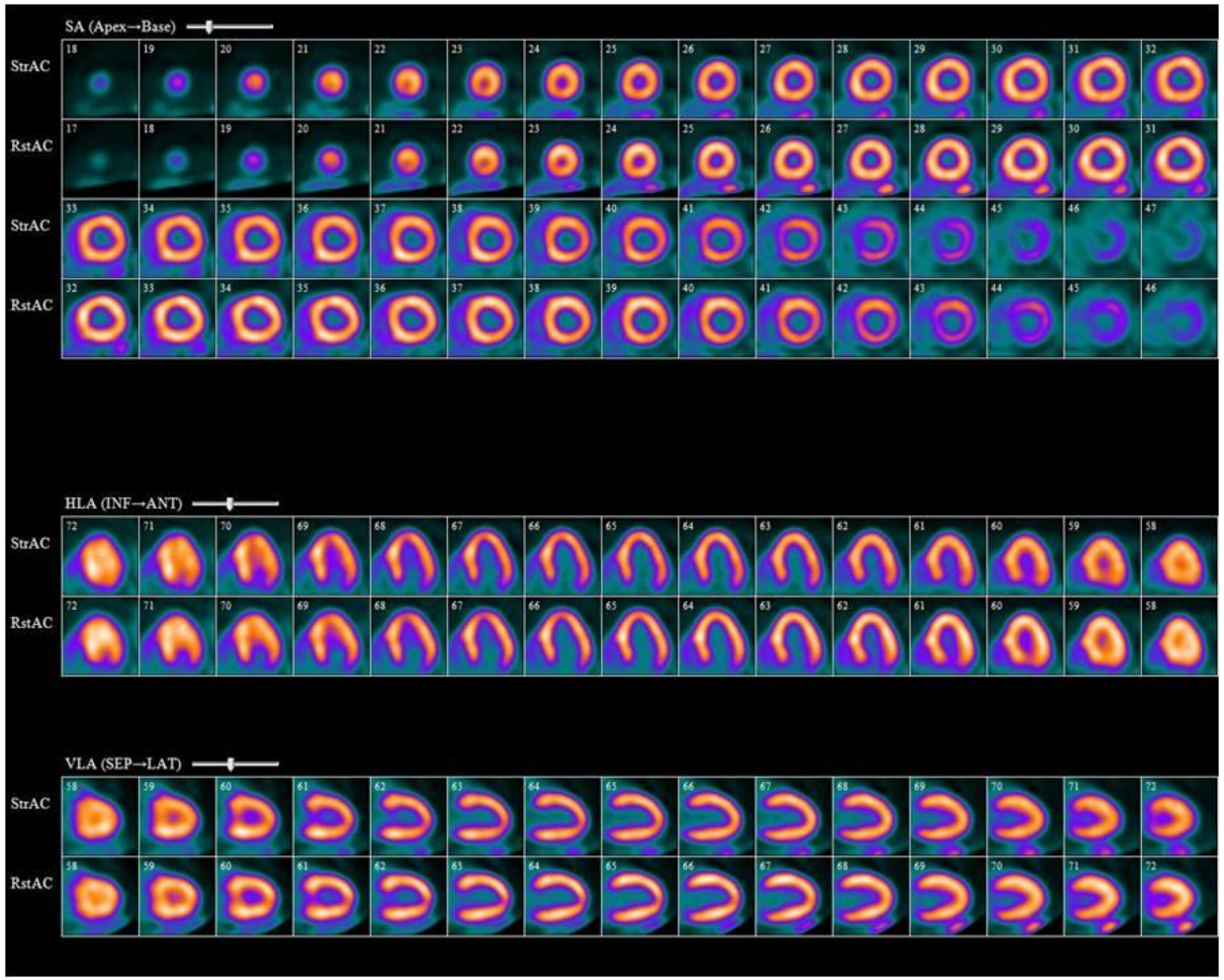
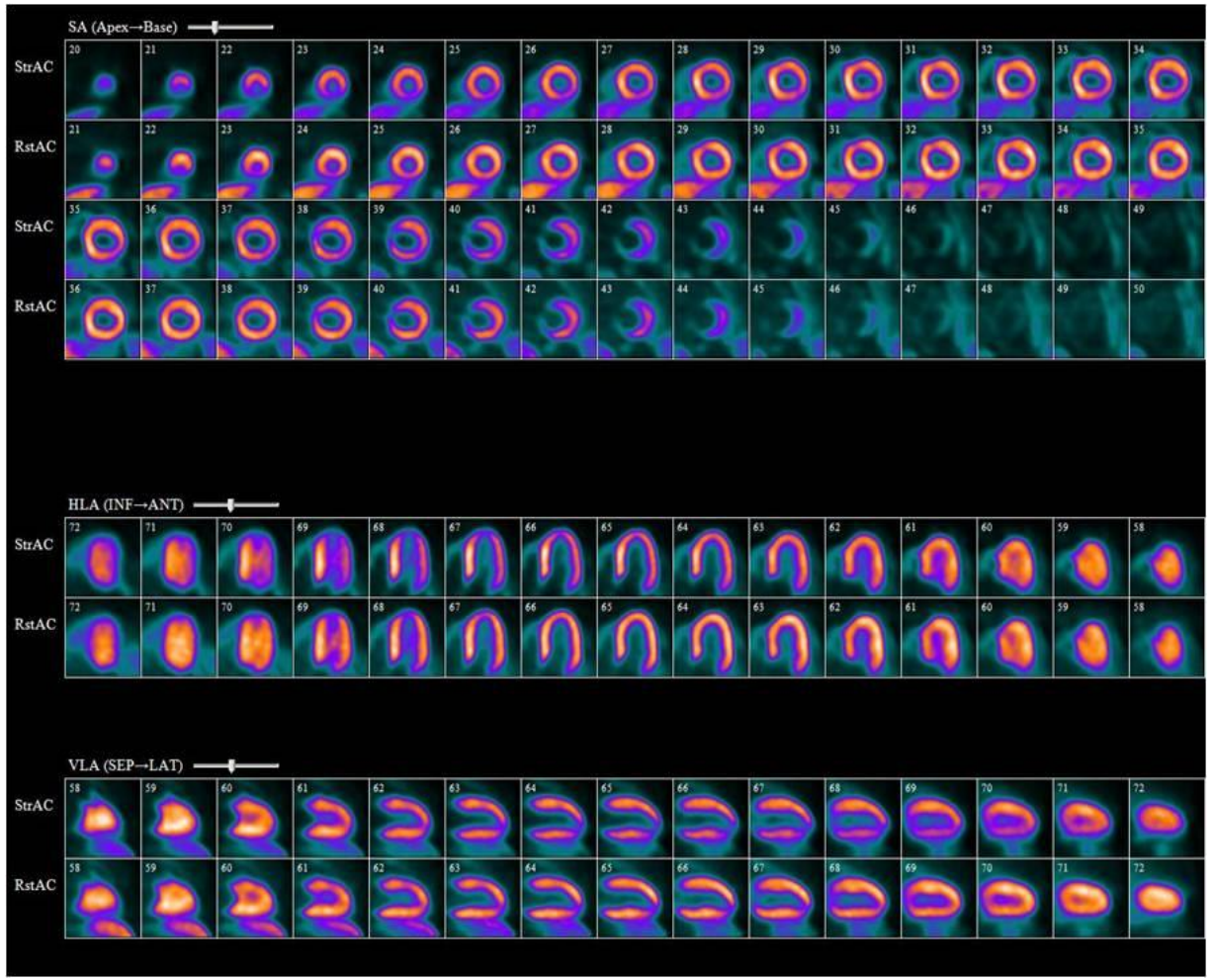


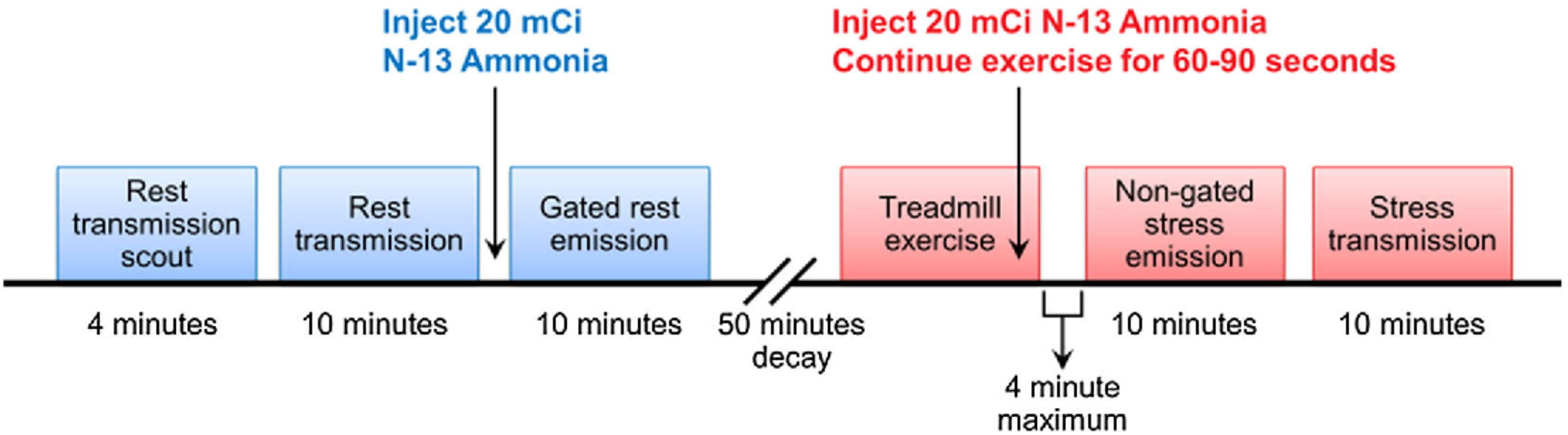
Rubidium Imaging



Ammonia Imaging

Courtesy of Sharmila Dorobala

Exercise Ammonia



J Nucl Cardiol. 2015 Dec;22(6):1273-80

[^{18}F] Flurpiridaz

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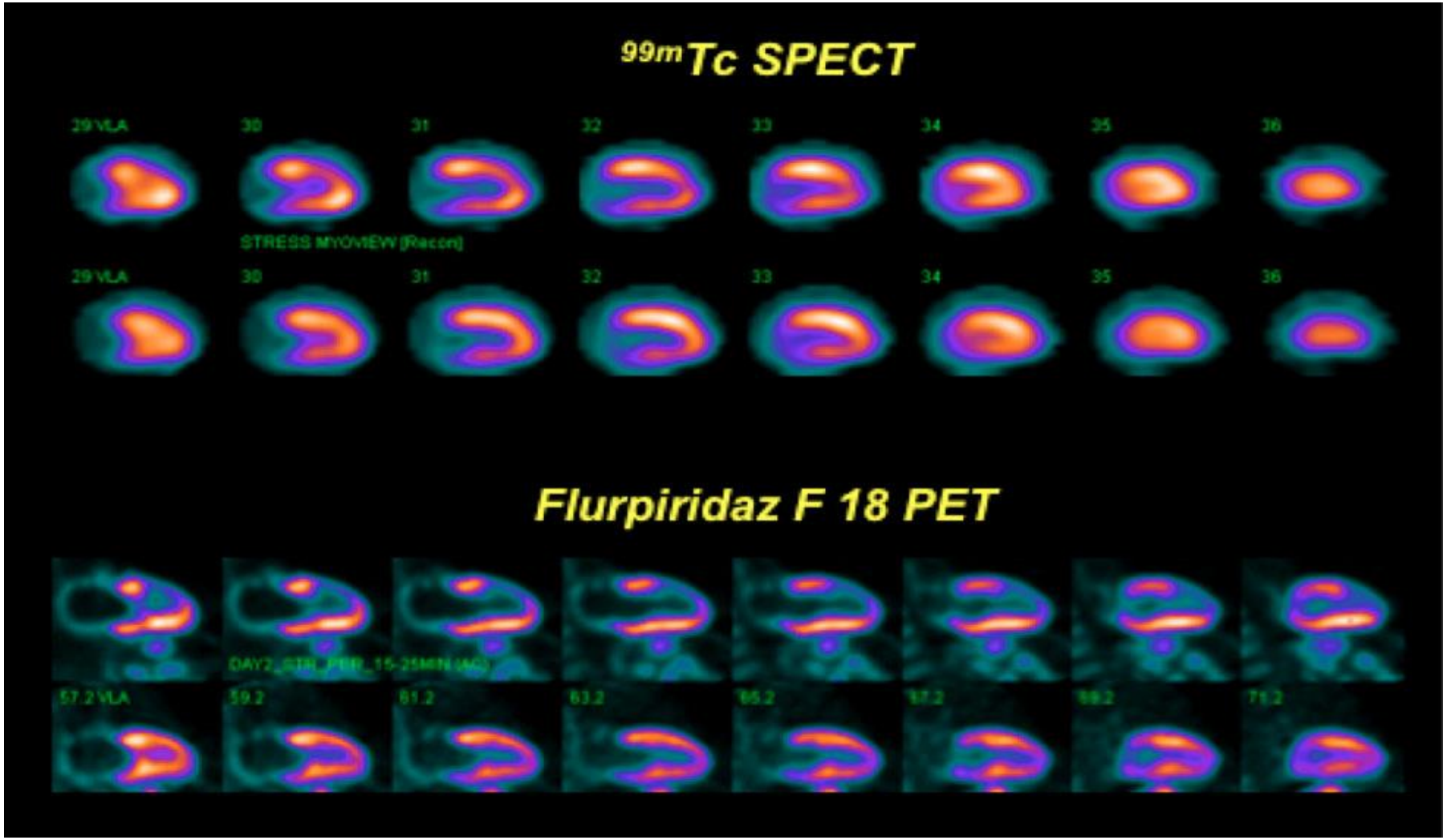

J Nucl Cardiol 2012;19:S30–7.

^{18}F Flurpiridaz

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- High heart/non-target ratio; minimal redistribution
- Superior image quality and disease detection
- Near linear uptake vs. flow
- Absolute quantification of MBF
- Effective with exercise stress
- Good safety profile in clinical trials
- Centralized production with unit dose distribution

Yu M, et al. Semin Nucl Med 2011; 41: 305-13.

^{18}F Flurpiridaz PET 303 Study (Aurora)

Key Endpoint: PET vs. SPECT for Overall Detection of CAD

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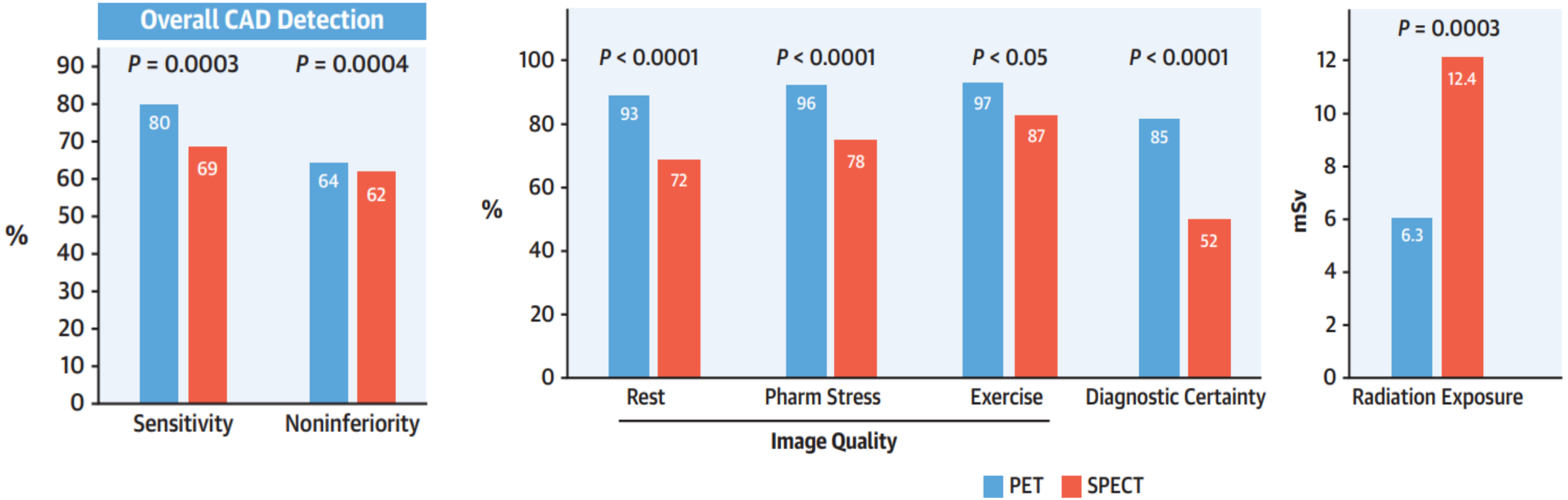
^{18}F flurpiridaz PET has a greater diagnostic efficacy than ^{99m}Tc SPECT



FDA approval in 2024

Maddahi. J Am Coll Cardiol 2020;76:391–401

^{18}F Flurpiridaz Pharm Stress Protocol

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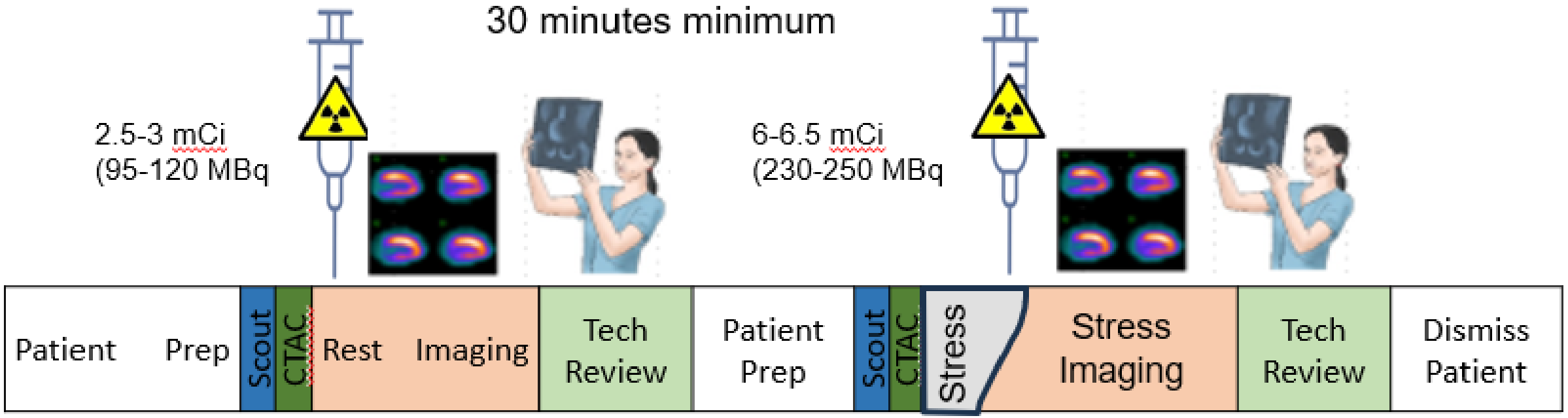

57-year-old female with chest pain

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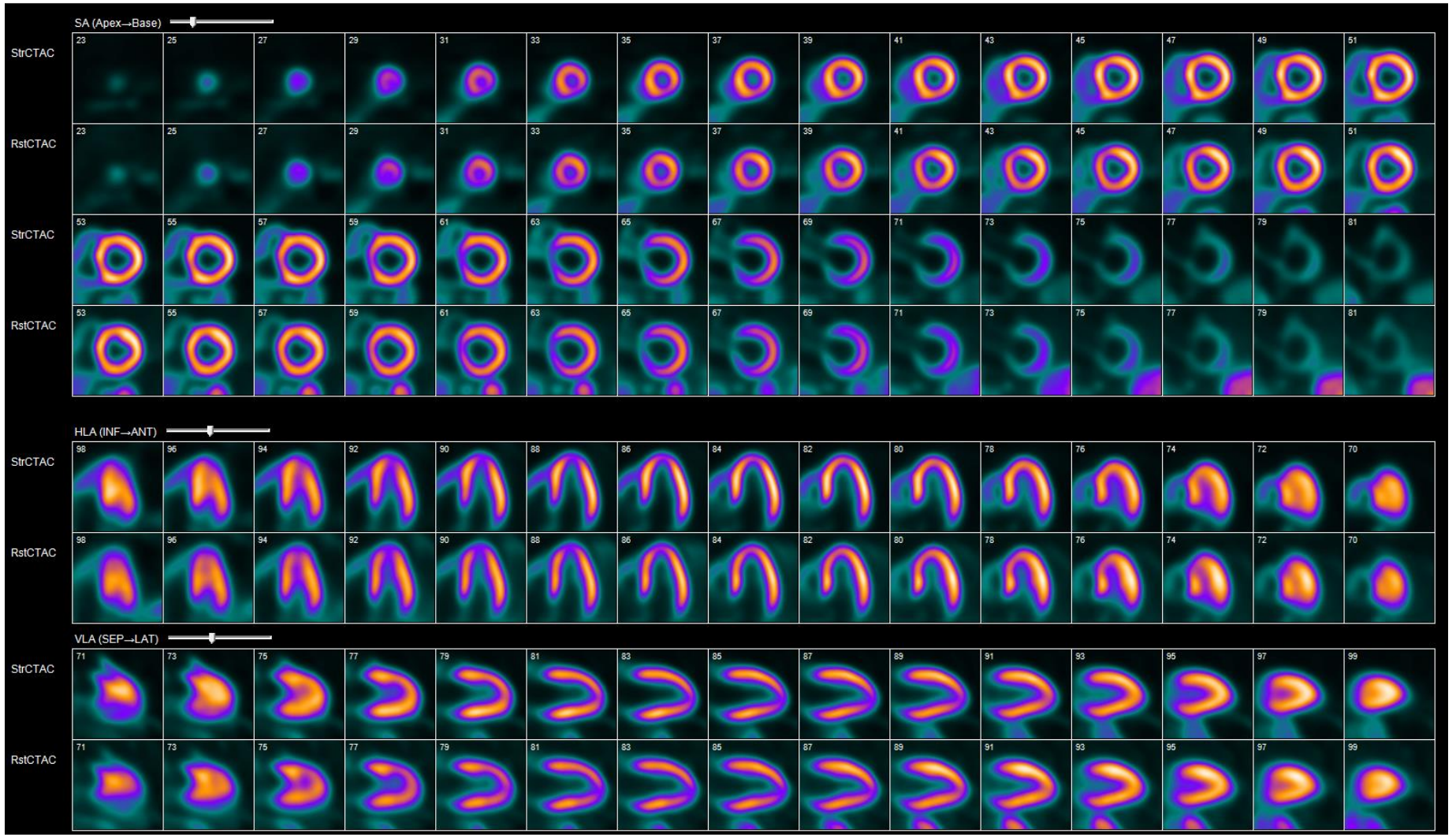

Tech Considerations

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- Prepare patient well; Cost and logistic issue with repeating the studies
- Dose will be supplied in small volume: 0.5ml for rest and 1ml for stress
  - We use 30 ml of normal saline for flush
  - No FDA approved solutions for automatic injections YET
- After injection, you may want to flush or measure residual activity
  - Residual activity may be as high as 0.5mCi
- Injection of rest and stress doses of F-18 Flurpiridaz should be at least 30 min apart
- F-18 Flurpiridaz and adenosine must be administered through separate lines or separate ports of the same IV line. Three way IV if using Regadenoson

IV Setup

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Tech Considerations

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- For the second dose, need to start the PET imaging prior to injection to allow for adequate residual activity subtraction
  - Arms down ? effect on residual activity

Residual Subtraction

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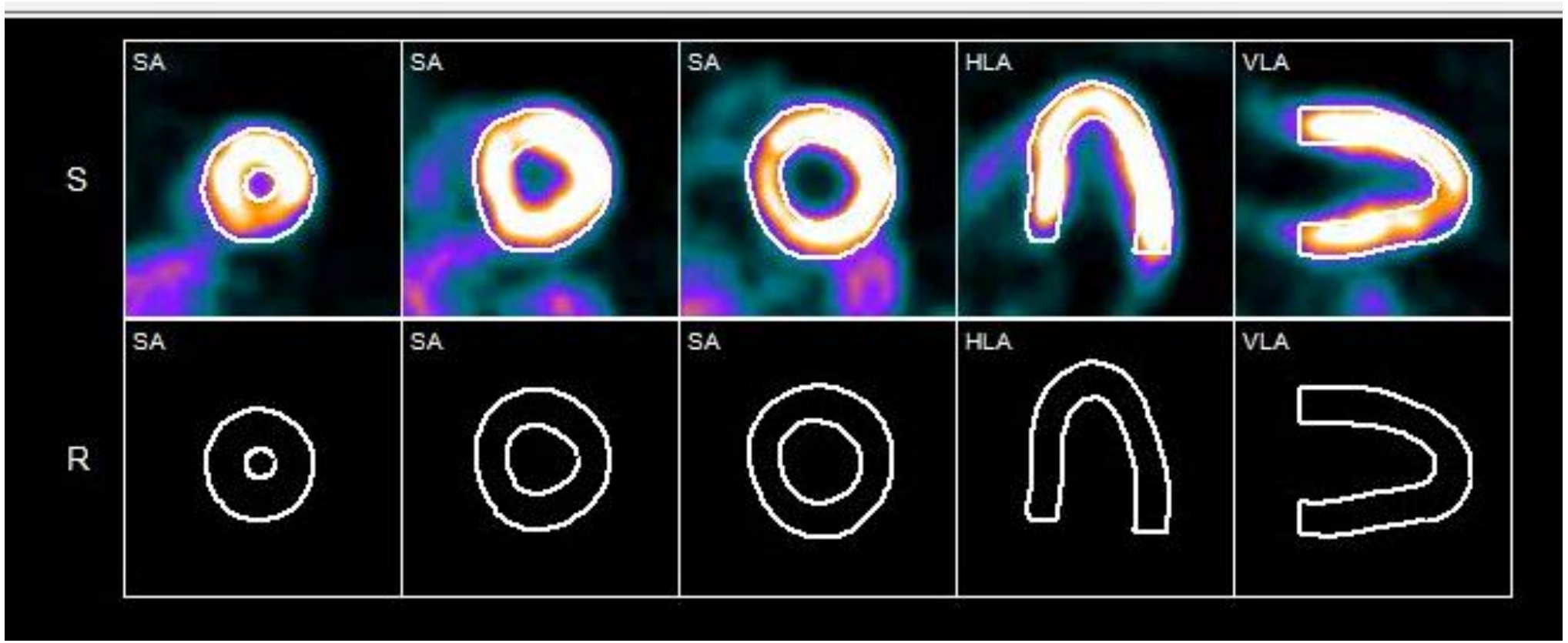
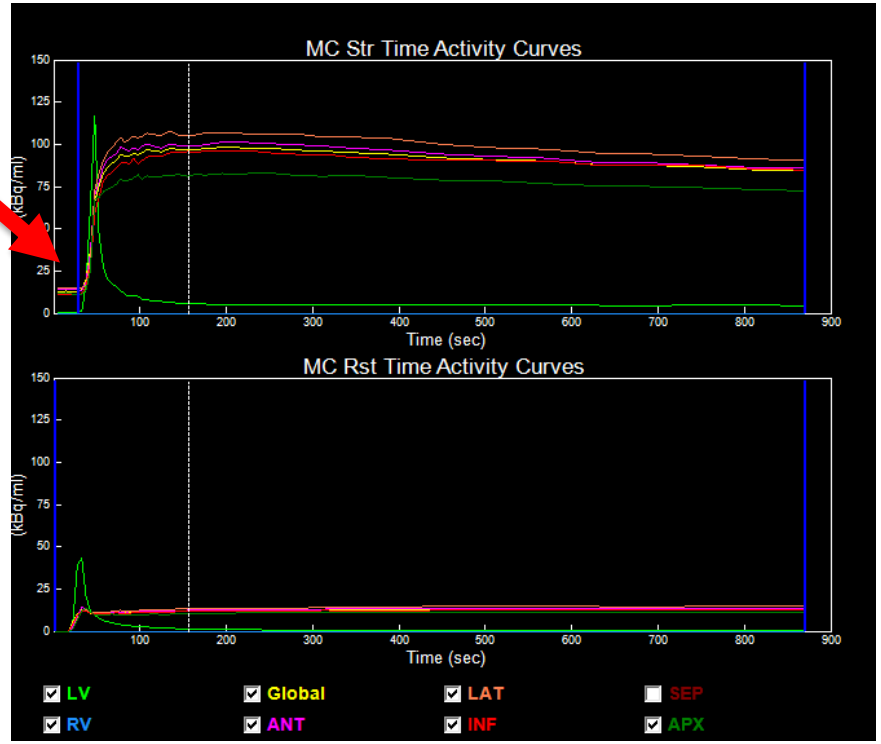


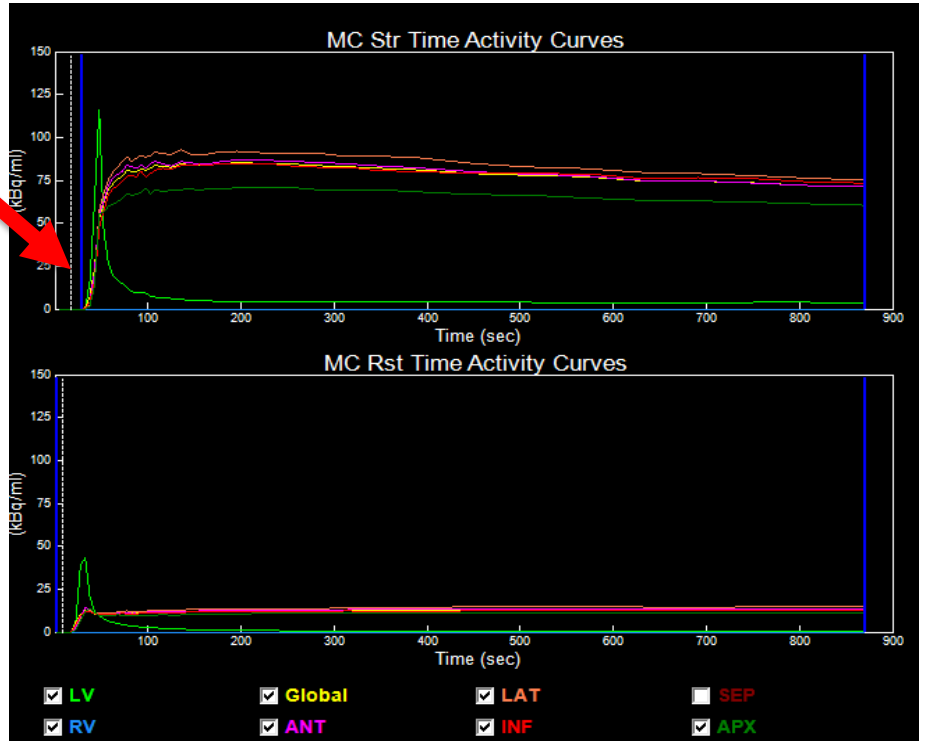
Residual Subtraction



Algorithm (MC Str): INVIA F-18 FPZ ROI 1:1
Algorithm (MC Rst): INVIA F-18 FPZ ROI 1:1

Global Results

Region	Mean MC Str	Mean MC Rst	Flow (ml/min/g) MC Str	Flow (ml/min/g) MC Rst	Ratio
LAD	82%	79%	4.62	0.92	5.02
LCX	91%	90%	4.81	0.98	4.93
RCA	82%	77%	4.06	0.92	4.43
TOT	85%	82%	4.58	0.93	4.92



Algorithm (MC Str): INVIA F-18 FPZ ROI 1:1 / Residual Subtracted
Algorithm (MC Rst): INVIA F-18 FPZ ROI 1:1

Global Results

Region	Mean MC Str	Mean MC Rst	Flow (ml/min/g) MC Str	Flow (ml/min/g) MC Rst	Ratio
LAD	82%	79%	3.59	0.92	3.90
LCX	91%	90%	3.75	0.98	3.84
RCA	82%	77%	3.27	0.92	3.56
TOT	85%	82%	3.54	0.93	3.80

Tech Considerations

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- Important to limit motion: cannot repeat injection in same setting and quantify flow
  - Importance of motion correction
  - Can repeat imaging and obtain static and gated imaging

- Be careful of **contamination**: PET machine will be down for a significant time in the day

Tech Considerations

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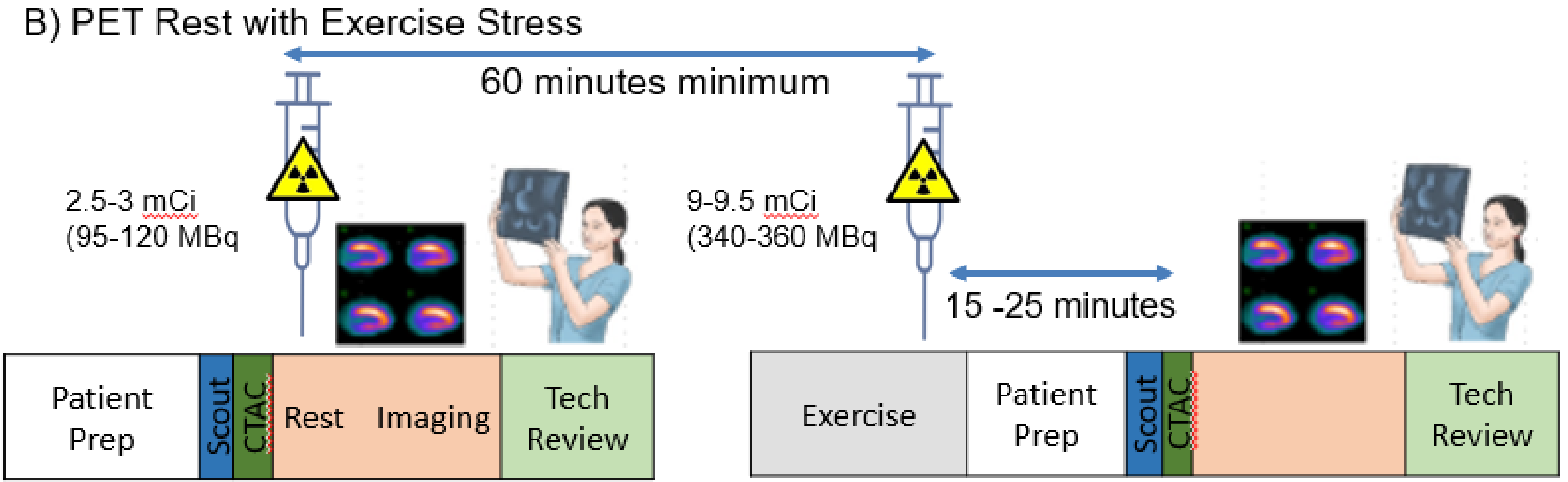
- Total activity not to exceed 14 mCi for an individual subject

- Always wear you dose badges

Stress Protocol	Rest Dose	Stress Dose	Typical Study Dose (rest & stress)
Pharmacologic stress	2.5 -3.0 mCi (95-120 MBq)	6.0-6.5 mCi (230-250 MBq)	**6.2 mSv**
Exercise stress	2.5 -3.0 mCi (95-120 MBq)	9.0-9.5 mCi (340-360 MBq)	**6.9 mSv**

Exercise Protocol



Other PET agents vs Flurpiridaz

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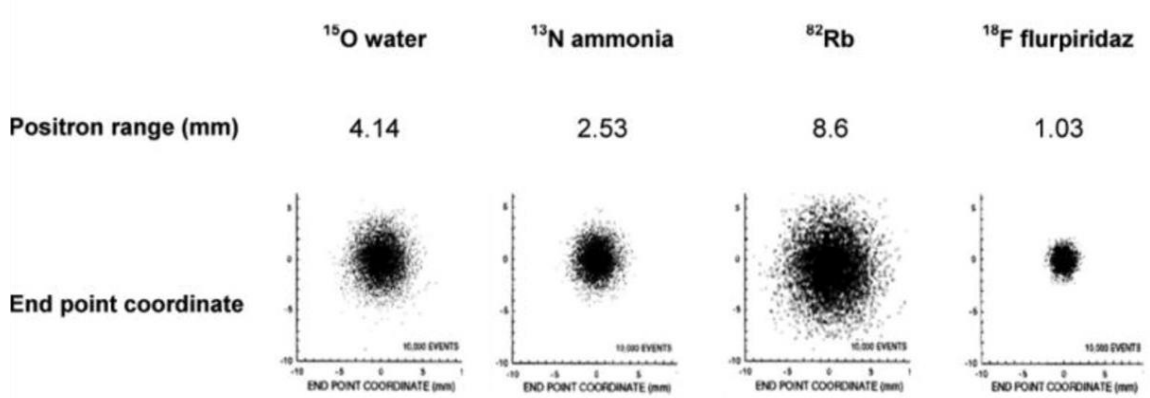
Table Characteristics of Various Cardiac PET Perfusion Tracers

	^{15}O Water	^{13}N Ammonia	^{82}Rb	Flurpiridaz F 18
Half-life (min)	2.06	9.96	1.25	109
Production	Onsite cyclotron	Onsite or nearby cyclotron	Generator	Regional cyclotron
Positron range (mm)	4.14	2.53	8.6	1.03
Image resolution	Intermediate	Intermediate-high	Lowest	Highest
Myocardial extraction fraction (%)	100	80	65	94
Perfusion defect contrast	Intermediate*	Intermediate	Lowest	Highest
Pharmacologic stress imaging protocol	Feasible	Feasible	Feasible	Feasible
Treadmill exercise imaging protocol	Not feasible	Feasible but not practical	Not feasible	Feasible

*Theoretically, 100% myocardial extraction fraction of ^{15}O water should result in the highest perfusion defect contrast. However, poor myocardial-to-background ratio reduces defect contrast.



^{15}O-water PET Protocol

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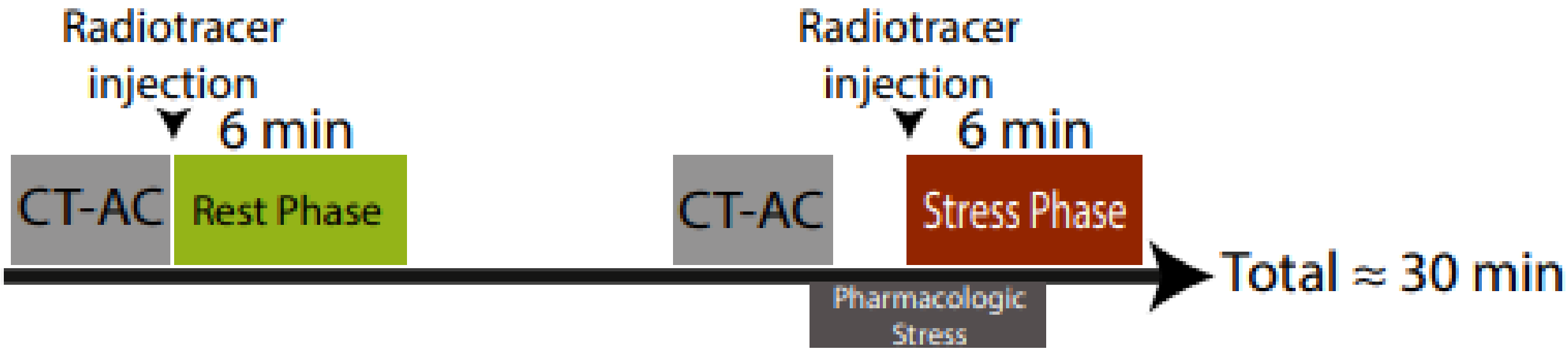

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Analyzing 15O-water scans

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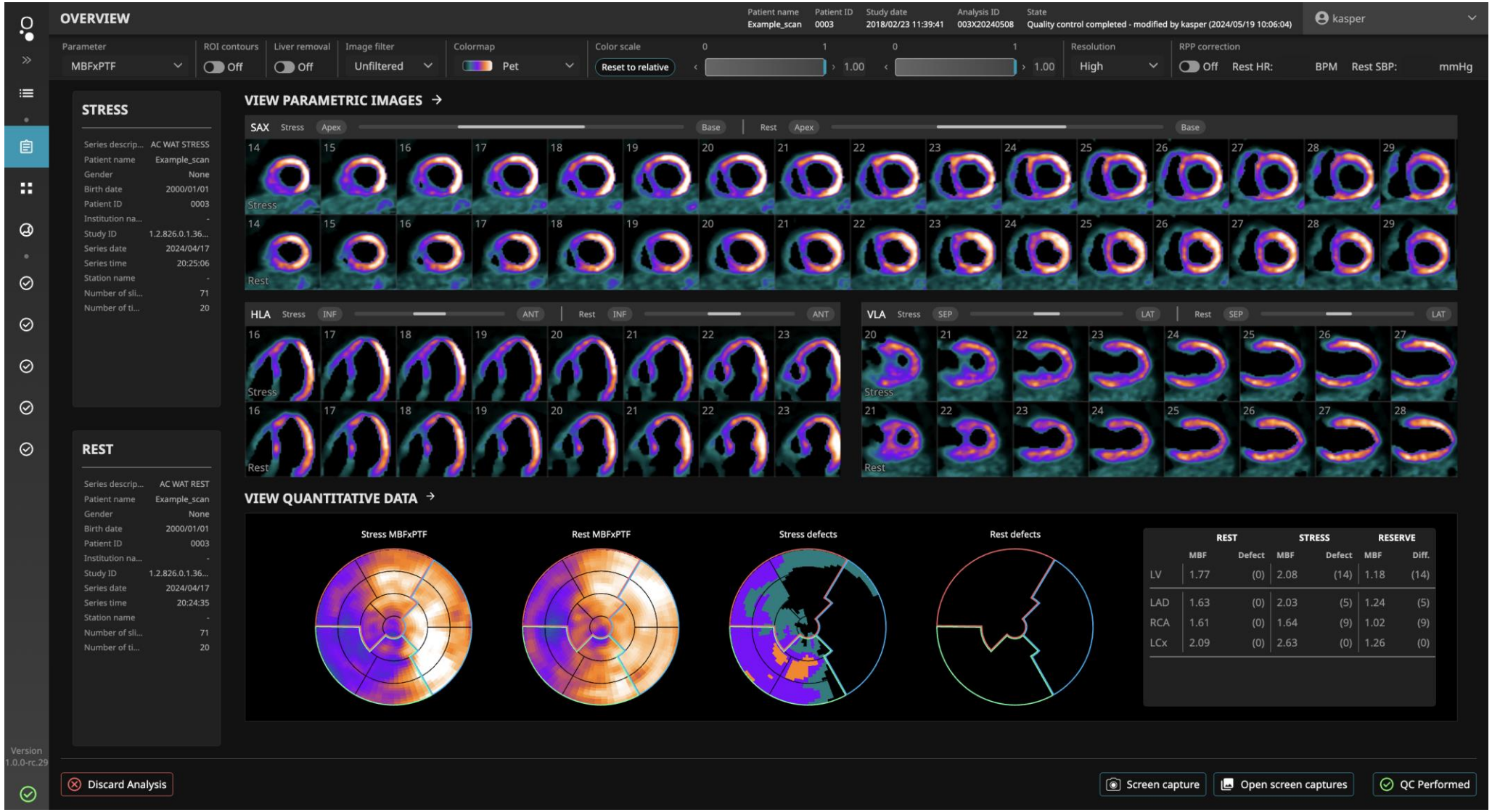

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