Advances in PET/CT, SPECT/CT and SPECT for Cardiology



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OUTLINE

- Latest PET/CT hardware
- Latest SPECT hardware
- Low dose imaging
- Perfusion quantification
- Attenuation correction
- Kinetic modelling
- Motion
- Hybrid quantification

Cardiac PET/CT setup

ECG for gating

BP

12 leads ECG

82Rb generator

Cardiac PET/CT protocols



Imaging Med Nakazato et al 2013

2D vs. 3D PET acqusition



Most hybrid PET/CT systems are 3D

Time of flight



Townsend, PMB 2008

Time-of-flight (TOF) PET reconstruction

Improved contrast with TOF



HD= 3DOSEM PSF=resolution recovery TOFPSF =TOF + resolution recovery Bettinardi et al Med Phys 2011

TOF improves cardiac image quality



Figure 1. Comparison of images between TOF-OSEM and 3D-RAMLA. (A) A representative case of a 53-year-old normal, female volunteer. (B) A case with three-vessel coronary artery disease. There was a severe decrease of uptake in the inferior wall.

Tomiyama et al J Nucl Cardiol 2014

Saturation during Rb-82 infusion





Fan sum showing detector block saturation during rubidium-82 infusion in the (a) right and (b) left arm.





Taut et al. Nucl Med Commun 2012

NECRs of Discovery IQ and 710



NECR curves for the Discovery IQ, 5 ring configuration²

Digital Photon Counting in PET





SiPM

Digitial Silicon PMT (SiPM)



SiPM – faster timing resolution, insensitive to MR

Philips

Current PET/CT systems

	Ingenuity TF	Discovery 710	Biograph mCT	Vereos
Patient port [cm]	70 OpenView	70	78	70
Patient scan range [cm]	190	200	195	190
			3D S&S,	
Acquisition modes	3D S&S	3D S&S	continuous	3D S&S
Number of image planes	45 or 90	47	109	72
Plane spacing [mm]	2 or 4	3.27	2	1, 2, or 4
Crystal size [mm]	4 x 4 x 22	4.2 x 6.3 x 25	4 x 4 x 20	4 x 4 x 22
Number of crystals	28,336	13,824	32,448	23,040
Number of PMTs	420	256	768	23,040 SiPM's
Physical axial FOV [cm]	18	15.7	21.8	16.3
Detector material	LYSO	LYSO	LSO	LYSO
System sensitivity 3D, [%]*	0.74	0.75	0.95	2.2
Trans axial resolution @ 1 cm [mm]*	4.7	4.9	4.4	4.0
Trans axial resolution @ 10 cm [mm]*	5.2	5.5	4.9	4.5
	120	130	175	650
Peak NECR [kcps]	@19 kBq/ml	@29.5 kBq/ml	@28 kBq/ml	@50 kBq/ml
Time-of-Flight resolution [picoseconds]	591	544	540	307
Time-of-Flight localization [cm]	8.9	8.2	8.1	4.6
Coincidence window [nanoseconds]	4.5	4.9	4.1	1.5

Question 1. Which 3D PET/CT parameter will be most critical for ⁸²Rb imaging ______.

16%	a. Trans axial resolution
6%	b. Crystal size
3%	c. Patient port
72%	d. NECR
<mark>3%</mark>	e. Scatter fraction

Question 1. Which 3D PET/CT parameter will be most critical for ⁸²Rb imaging ______.

X



The correct answer is **D**: reference

Assessment of a protocol for routine simultaneous myocardial blood flow measurement and standard myocardial perfusion imaging with rubidium-82 on a high count rate positron emission tomography system. Tout D, Tonge CM, Muthu S, Arumugam P. Nucl Med Commun. 2012;33:1202-11

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Fast SPECT cameras



New collimators — high sensitivity

Solid state detectors



Improved spatial resolution 2x energy resolution 1.6 x to < 6%

Cadmium Zinc Telluride (CZT)

DSPECT: J Nucl Med 2009; 50:635–643 NM530c J Nucl Cardiol. 2008;15(suppl):S3.

Improved spatial resolution

Cesium Iodide (Csl)

Digirad Bai et al. JNC 2010;17:459-69



CZT not the reason for increased sensitivity for new scanners

Photon efficiency: solid-state vs Nal (TI)



Lee Y-J et al Journal of the Korean Physical Society, 2014;64:1055~1062

Solid-state superior intrinsic



DePuey EG J Nucl Cardiol 2012 56119;551-81

CZT superior energy resolution



Overlay of ^{99m}Tc and ¹²³I spectra, showing greater crosstalk between two peaks for the Anger camera with its poorer energy resolution

Multi-pinhole collimation with CZT



Focusing high sensitivity paralell collimators







Sharir et al, JACC imaging 2008; 1: 156 Kacperski et al IEE MIC 2008

Reduced cost CZT



6 rotating detectors (instead of 9)

Sensitivity reduced approximately 33%

Future designs: Improved Detector Sensitivity

Curved Detectors with Pinhole:

- Increase Sensitivity (> 2 times) by opening pinhole
- Maintain same resolution



21 Pinholes arranged in surface-sectors around upper torso of body; Pinholes are pointed towards the heart
J. Dey, IEEE TNS, *vol.59,no.2,Apr 2012,pp.334-347*

Fan beam collimators with indirect conversion solid state detectors



Triple head and Fan beam allow Increase sensitivity

Courtesy of Richard Conwell Digirad

Anger camera: technologies for efficiency improvements **Cardiofocal collimation**

4 x more counts from the heart

No truncation



Heart is the center of rotation

diverging

Cardiofocal





Fast-MPS resolution and sensitivity



Counts in high-sensitivity SPECT Myocardial fraction of injected activity (MFI) vs body weight MFI 9 times higher for high-sensitivity SPECT



MFI (ppm)= 10⁶ x myocardial counts per second /injected activity

Verger et al. Eur J Nucl Med Mol Imaging 2014;41-522-528

Fast-MPS sensitivity vs. PET

Sensitivity %



Slomka et al JNC 2014 based on Imbert et al J Nucl Med 2012, Mawlawi et al J Nucl 2004

Question 2. The primary reason for improved photon sensitivity in newer cardiac cameras is

34% a. The use of new cadmium zinc telluride (CZT) detectors

0% b. Faster digital processing by the camera electronics

59% c. New collimators and optimized camera geometry

- 3% d. Closer position to the patient
- 3% e. Better energy resolution

Question 2. The primary reason for improved photon sensitivity in newer cardiac cameras is _____.



The correct answer is **C**, because:

- Newer cameras: more sensitive collimators & optimized geometry
- CZT detectors are about <u>2 times thinner</u>
- Overall photon efficiency: similar to <u>scintillation crystals used in a</u> <u>traditional Anger camera</u>.

Slomka PJ, Berman DS, German G. New cardiac cameras: single-photon emission CT and PET. Semin Nucl Med. 2014;44:232-51

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Radiation dose

U.S. Lawmakers Want to Know More About Low-Dose Radiation, Draft Bill for Further Research

By James Maynard, Tech Times | January 13, 9:00 AM

Low-dose radiation will be studies by the Department of Energy, to determine health risks to Americans. What brought about this new study? (Photo : Getty Images / Sean Gallup)

Low-dose radiation is the subject of a new investigation initiated in Congress. The news study was spurred by concerns over radiation, following the 2011 accident at the Fukushima nuclear plant in Japan.

🛫 TWEET(9)

0 COMMENTS

SHARE(20)

Radiation constantly bombards everyone. The Earth itself contains radioactive elements, and air travelers receive additional doses every time they fly. Many medical treatments and tests also involve the use of low-level ionizing radiation.

"The research program involves using advances in modern molecular biology and instrumentation unavailable during the previous 50 years of radiation biology research. Scientists will be able to examine - at a systems level - the relationship between normal oxidative damage and radiation-induced damage, using studies conducted at very low doses and dose-rates," the Department of Energy (DOE) reports.

United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) highlighted the need for caution in extrapolating the effects of low radiation doses on large populations. Dec 2012





Slomka et al. Curr Cardiol Rep (2012) 14:208–216

Ultra-low dose (ULD) cardiac SPECT

OPTION 1



Einstein A. et al. J Nucl Med 2014 :1430-7
Ultra-low dose (ULD) cardiac SPECT enabled by high-sensitivity

101 patients ULD rest scans on high-efficiency scanner Average ULD:3.6 mCi -injected 1.16 mSv-received

		Short axis			Long axis		Image assessment				Received dose	
		Apical	Mid	Basal	Vertical	Horizontal	Study quality	Extracardiac activity	SRS	Total perfusion defect (%)	Activity (MBq)	Effective dose (mSv)
Brigham and Women's Hospital: case 003	HE-SPECT	0	Q	0	1	{ }°	Excellent	None	18	27.2	134	1.15
	A-SPECT	8	Q	0	11	•	Good	Mild and probably without any interference with scan interpretability	14	23.2	497	4.29
Cedars- Sinai Medical Center: case 033	HE-SPECT	0	0	0	n:	5	Excellent	None	5	6.3	134	1.16
	A-SPECT	0	0	0	0	5	Good	None	4	4.4	248	2.14

ULD image quality superior to low-dose (2x ULD) Anger-SPECT Einstein A. et al. J Nucl Med 2014:1430-7

Optimal lowest dose can be determined from list-mode data



79 patients Full dose 21.7 ± 5.4 mCi full time 14 min

Nakazato et al JNM 2013:373-9



Nakazato .. Slomka PJ et al J Nucl Med 2013 :373-9

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Perfusion: weakness of visual analysis

~7 mln scans per year in US Inter observer agreement 2 expert observers (core readers)

Summed stress score





Diagnostic agreement (normal-abnormal) 87% 995 pts with no known CAD Unpublished data (NIH R0HL089765)



Slomka et al. J Nucl Cardiol 2005;12:66-77

Relative perfusion quantification Perfusion Extent (%) Severity (0 - 10sd) Score





INF

APEX









Review Slomka et al. JNC 2012;19:338-46.

Infarct sizing and detection: DE MRI vs. SPECT 27% by DE-MRI, 31% by SPECT



Sizing: N=26, r =0.85 Detection: N=82, Sens =87%, Spec=91% Slomka et al J Nucl Med. 2005;46:728-35.

MPI diagnostic accuracy: Experts vs. software per-vessel etection of > 70% stenosis n=2985



S	oftware	ROC-AUC	ROC-AUC
	NC-TPD	0.83	-
	AC-TPD	0.84 *	-
Readers		Reader 1	Reader 2
	V1	0.82	0.78 #
	V2	0.83 *	0.79 * <mark>#</mark>
	V3	0.84 *	0.80 #
	V4	0.84	0.80 *#

*Comparison to prior step *P* < 0.01 #Auto vs. visual *P* < 0.01 Red = auto better than visual V1 = NC only V2 = NC + AC V3 = NC + AC + computer V4 = NC + AC + computer + clinical

Arsanjani et al J Nucl Med 2013:221–8

Automatic PET perfusion analysis High diagnostic performance with PET



* 3D PET/CT

Nakazato et al. Imaging Med. 2013;1:35-46

Quantitative automatic prognosis from perfusion n=1613 consecutive pts



Question 3. Total perfusion deficit is a measure of _____.

- 7% a. Absolute myocardial blood flow (at stress or rest)
- 41% *b. Relative* myocardial perfusion (vs normal region)
- 3% c. Myocardial flow reserve
- 45% d. Difference between stress and rest perfusion
- e. Ejection fraction reserve

Question 3. Total perfusion deficit is a measure of _____.

(a) Absolute myocardial blood flow (at stress or rest)
(b) Relative myocardial perfusion (vs normal region)
(c) Myocardial flow reserve
(d) Difference between stress and rest perfusion
(e) Ejection fraction reserve

The correct answer is **B**, because:

- Total perfusion deficit is estimated by comparing with the normal regional reference database
- Normalization of counts is with an arbitrary # in a patient study
- Thus, it is a measure of relative perfusion of the myocardium

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PET/CT – AC misregistration



Ready

Registration increases correct alignment



Severe misalignment 📕 Mild/moderate misalignment 📕 Good * p < 0.0001 # p < 0.05

JNC 2015 (in press) vs. Experienced radiologist

Improved detection of CAD with automatic registration

Slomka et JNC 2015 (in press)

False positive resolved by CTAC alignment

44 y/o male with SOB

Stress alignment. None.

Stress alignment. Rigid.

Stress perfusion before alignment TPD = 12%

Stress perfusion after alignment TPD =1.8% JNC 2015 (in press)

False negative resolved by CTAC alignment

60 y/o male with atypical chest pain

Stress perfusion after alignment TPD =9% JNC 2015 (in press)

Attenuation correction methods: SPECT/CT approach

External CT attenuation correction for fast MPS

Reset 1

NM Coronals REST

CT Sagittals REST

CT Transaxials REST

NM Sagittals REST

NM Transaxials REST

Courtesy Aharon Peretz (GE Medical Systems) Schepis et al Eur J Nucl Med Mol Imaging 2007

Automatic alignment of Calcium CT scan for attenuation correction

Zaidi et al. Int J Cardiovasc Imaging 2013

100

before after

Fast MPS Deep Inspiration Breath-Hold Acquisition

- Study of 40 pts
- Patients imaged 9-18 breath-hold intervals
- No respiratory motion
- Improved image quality
- Potential to utilize improved CZT image resolution

UniversitätsSpital Zürich

Oliver Cleric et al SNM 2014 Abstract #1767

Abdominal activity correction

Quantitative Upright–Supine High-Speed SPECT Myocardial Perfusion Imaging for Detection of Coronary Artery Disease: Correlation with Invasive Coronary Angiography J Nucl Med. 2010 Nov;51(11):1724-31

Ryo Nakazato^{*1–3}, Balaji K. Tamarappoo^{*1–3}, Xingping Kang^{1–3}, Arik Wolak^{1–3}, Faith Kite^{1–3}, Sean W. Hayes^{1–4}, Louise E.J. Thomson^{1–4}, John D. Friedman^{1–4}, Daniel S. Berman^{1–4}, and Piotr J. Slomka^{1–4}

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Alternative to attenuation correction ?

Upright/supine fast MPS imaging

J Nucl Med. 2010 Nov;51(11):1724-31.

Combined upright/supine fast MPS

Nakazato R... Slomka PJ. J Nucl Med. 2010 Nov;51(11):172

Combined upright supine in obese patients

N=67 BMI = 41±6

67 Y M BMI =43 RCA and LCX disease on angio

Nakazato et al JNC 2015

3D sensitivity variation of stationary CZT scanners Sensitivity gradient > 8%/cm

2-position imaging may help

Kennedy et al. J Nucl Cardiol 2014

Two position imaging on multi-pinhole system

Courtesy Dr Henzlova Mount Sinai

Two position imaging on multi-pinhole system improved specificity for detection of CAD

Nishiyama et al Circulation Journal May 2014

Also Duvall et al J Nucl Cardiol 2013

Question 4. Combined 2-position imaging & quantification can be used to mitigate

33%	a. Attenuation artifacts
10%	b. Patient motion artifacts
13%	c. Patient positioning artifacts
0%	d. Truncation artifacts
43%	e. All of the above

Question 4. Combined 2-position imaging & quantification can be used to mitigate _____

The correct answer is **E**, because:

- <u>2-position imaging</u>: technique where 2 SPECT scans (Supine + Prone <u>or</u> Supine + Upright) are quantified or visually analyzed *simultaneously*
- A true defect will be present at the same location in both scans
- If only 1-position: Any shifting of the defect or presence of the hypoperfusion area could indicate: attenuation artifact, motion artifact present **OR** truncation artifact (due to the incorrect patient position)

Nakazato R, Tamarappoo BK, Kang X, et al. Quantitative upright-supine high-speed SPECT myocardial perfusion imaging for detection of coronary artery disease: Correlation with invasive coronary angiography. J Nucl Med. 2010;51:1724-1731.

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From Perfusion to Flow:

- The key measurements for calculating Quantitative Myocardial Perfusion are
 - Arterial Concentration
 - Myocardial Uptake

Arterial concentration Myocardial Uptake

Courtesy: James Case, CVIT

Adenosine

Dynamic 82Rb PET imaging reconstructed from list mode data

Dynamic imaging Myocardial compartmental model

Figure 7. Myocardial compartmental model consisting of blood and tissue and the transport of tracer between compartments.

Klein et. al J Nucl Cardiol Volume 17, Number 4;555–70
Kinetic Modeling: Increasing Complexity

Net Retention: Uses Blood Concentration and and extraction to determine flow (Yoshida, J Nucl Med 37: 1701–1712)

Single Compartment: Fits blood concentration (t), tissue uptake (t) and washout model (k₂): (Lortie M, EJNM,2007; 34:1765-1774)

Two Compartments: Fits blood concentration (t), tissue uptake into two tissue compartments interstitial intercellular (K1,K3) and washout model (k_2): (Herrero, Circ Res, 1992; 70(3); 496)







Classic Definitions

- "Absolute blood flow" is measured in units like volume per time (i.e. ml/min).
- "Relative blood flow" is measured in units of volume/time/volume of tissue (i.e. ml/min/g).
- ml is a unit of volume
- g of myocardium = ml of myocardium * density
- Density of myocardium = 1.05 g / ml
- ml/min/g = ml·min⁻¹·(1.05 ml)⁻¹ = 1/1.05 min
 ≈ min⁻¹

Courtesy Dr. Arai, NIH

Zierler KL Circ Research 196210:393-407

Kinetic modeling -Flow quantification



Outlier 9

PET ⁸²Rb blood flow analysis



⁸²Rb flow PET/CT quantification: comparison of 3 tools, data from 3 PET/CT centers

Myocardial Flow



De Kemp et al J Nucl Med. 2013;54:373-379

Example: Flow reserve In triple vessel disease







MFR





Flow + perfusion case 2



Flow + perfusion case 2

TPD



S-TPD: 4% R-TPD: 0%



Cath 60 % LAD negative FFR Multiple risk factors. Prob micro vascular

Added value of myocardial flow reserve mortality predicition



Murthy V, <u>Circulation</u>. 2011;124:2215-2

Dynamic SPECT Tc^{99m} imaging

Scanning method:



- 10 VIEWS / FRAME
- 3.5 SECONDS / FRAME
- 70 FRAMES
- 4 MIN SCAN

Dynamic FRAMES





TIME ACTIVITY



Fast-MPS sensitivity vs. PET

Sensitivity %



Slomka et al JNC 2014 based on Imbert et al J Nucl Med 2012, Mawlawi et al J Nucl 2004

Dynamic CZT SPECT Protocol

^{99m}Tc-sestaMIBI/tetrofosmin



Sakakibara Heart Institute Japan



Dynamic SPECT: contour detection



DYNAMIC SPECT with Fast SPECT Cameras ? 1.52**10 sec** 30 sec 2 min 1.47 **Myocardial perfusion reserve index** unamic LV / BV Innu Input curves Stress/rest tissue curve 1.2e4 1.0e4 1.0e7 5.0e8 Breult et al ASNC 2010

Dynamic SPECT blood flow analysis



INSTITUTE

^{99m}Tc-sestamibi CZT SPECT microspehere validation



17-segment comparison of microsphere MBF to MBF measured with attenuation- and scatter-corrected 201TI (A), 99mTc-tetrofosmin (B), and 99mTc-sestamibi (C).

Wells et al JNM 2014

Question 5. Myocardial flow measurements in PET use the following units: ______.

- 14% a. ml/sec
- 0% b. Bq/min
- 0% **c.** ml/cm²
- 62% d. ml/g/min
- 24% e. Bq/ml/sec

Question 5. Myocardial flow measurements in PET use the following units: _____



The correct answer is **D**, reference: Quantification of myocardial blood flow and flow reserve: Technical aspects. Klein R, Beanlands RS, deKemp RAJ Nucl Cardiol. 2010;17:555-70.

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Cardiac motion-frozen perfusion

84 y/o patient BMI = 27 with a history of myocardial infarction



0.

0.2

0.4

0.6

0.8

MF-TPD

S-TPD



Respiratory motion



Normal patient breathing. low-dose cine no contrast CT scan Average radiation dose ~ 1.7 mSv

Respiratory motion















Cardiac PET/CT respiratory gating



 The histogram (right) shows the amount of breathing amplitudes for the entire 24 min list-mode acquisition. The Optimal Gating method selects the narrowest bandwidth (shaded area) containing 35% of the respiratory signal



Cardiac motion frozen in each respiratory gate

Respiratory motion frozen

Dual-gated cardiac perfusion PET



MF motion frozen

F, 42 y/o BMI:34.7, 7.7 mCi 18 F Flurpiridaz

High resolution hybrid PET/CT dual motion frozen PET



SNM 2010

PET/CT limitations: patient motion



PET: patient motion correction



Woo Med Phys 2011

F18 Flurpiridaz

Simultaneous PET/MR systems



Motion compensation in Cardiac PET/MR



Dramatic Improvement in cardiac image quality as compared to conventional PET





Courtesy Georges EL Fakhri, PhD, DABR

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Automated PET/CTA fusion



C JNM 09, Med Phys 09

Automated PET/CT fusion



JNM 09, Med Phys 09

Example: Mitral Valve plane position adjustment







3.5



416.2





63.5

416.2



Example: Mitral Valve plane position adjustment


SPECT/CTA volume/surface fusion

CATH: proximal RCA 100%, no significant LAD, LCX disease



CTA-guided MPS quantification



Slomka et al. J Nucl Med 2009

Coronary calcium scoring

- Non-contrast imaging
 of the heart
- Coronary Calcium Score predicts cardiovascular events



Hybrid imaging: ischemia and calcium scans



Brodov et al JNM 2015 in press



Summary 1/2

- New PET/CT systems include Time of flight. Digital PET is introduced. Cardiac PET is growing
- High-sensitivity SPECT in clinical use (>300 systems) Sensitivity 7-9x, resolution 2x of Anger SPECT
- Most SPECT scanners <u>do not use</u> AC. 2-position is essential without AC. May correct other problems
- New tools for registration of CT maps with PET
- Ultra-low-dose stress-only SPECT imaging ≈1 mSv

Summary 2/2

- Flow quantification can be automated and reproducible
- dynamic SPECT enabled by high sensitivity
- Patient motion has a big effect on perfusion and flow: needs to be corrected
- Integration CT with PET and SPECT can improve accuracy