KU LEUVEN

PRISMAP School on Radionuclide Production

Quality Control in Nuclear Medicine

31/05/2024

prof. dr. Kristof Baete

KU Leuven & UZ Leuven – kristof.baete@uzleuven.be

UZ LEUVEN

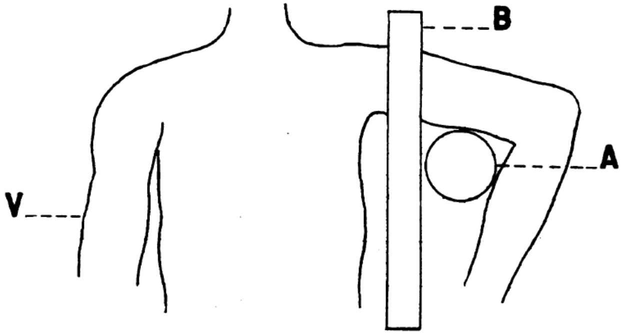
27 EU PRISMAP Medical Radionuclides

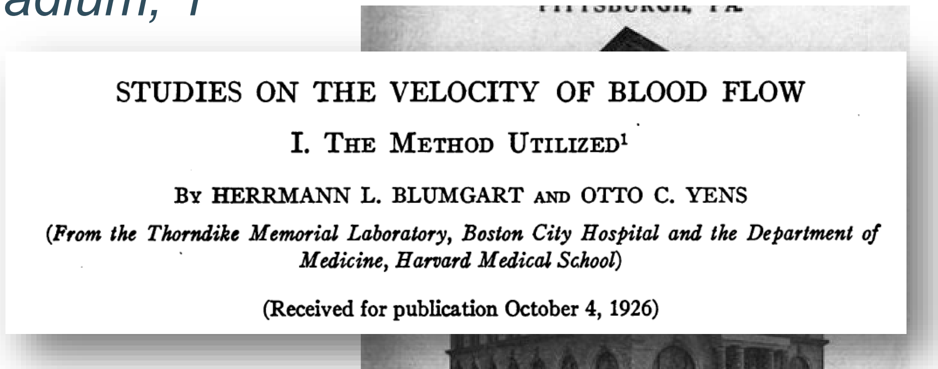
Nuclear Medicine

- Frederick Proescher – dir. of the “Research Lab for Experimental Treatment, Standard Chemical Co.” – first published “clinical” study

  “The intravenous injection of soluble radium salts in man”, Radium, 1 (1913), pp. 9-10

- Georg de Hevesy (1924) – ^{210}Pb and ^{210}Bi in animals
  - tracer principle – key concept for NM and theranostics
- Blumgart & Yens (1925) – ^{214}Bi (“radium C”) in humans
  - IV administration & arm-to-arm circulation time
  - birth of diagnostic nuclear medicine instrumentation
  - detection using Wilson cloud chamber
- the American Medical Association officially recognized nuclear medicine as a medical specialty in 1971
- this “new” discipline has evolved continuously, ever since





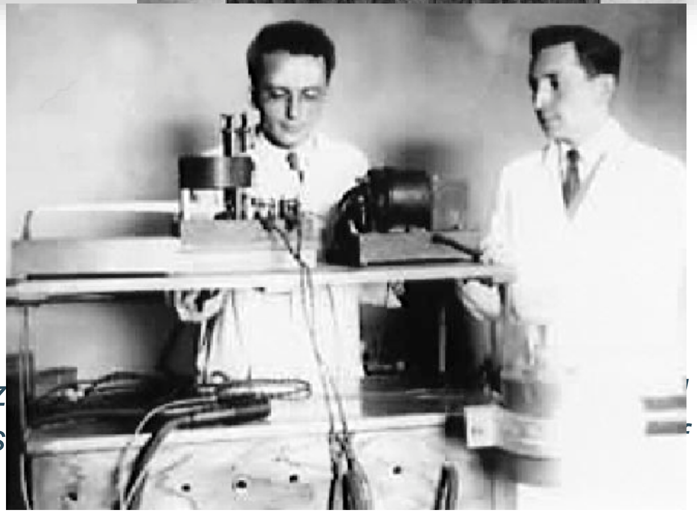
STUDIES ON THE VELOCITY OF BLOOD FLOW

I. The Method Utilized[1]

By HERRMANN L. BLUMGART and OTTO C. YENS

(From the Thorndike Memorial Laboratory, Boston City Hospital and the Department of Medicine, Harvard Medical School)

(Received for publication October 4, 1926)



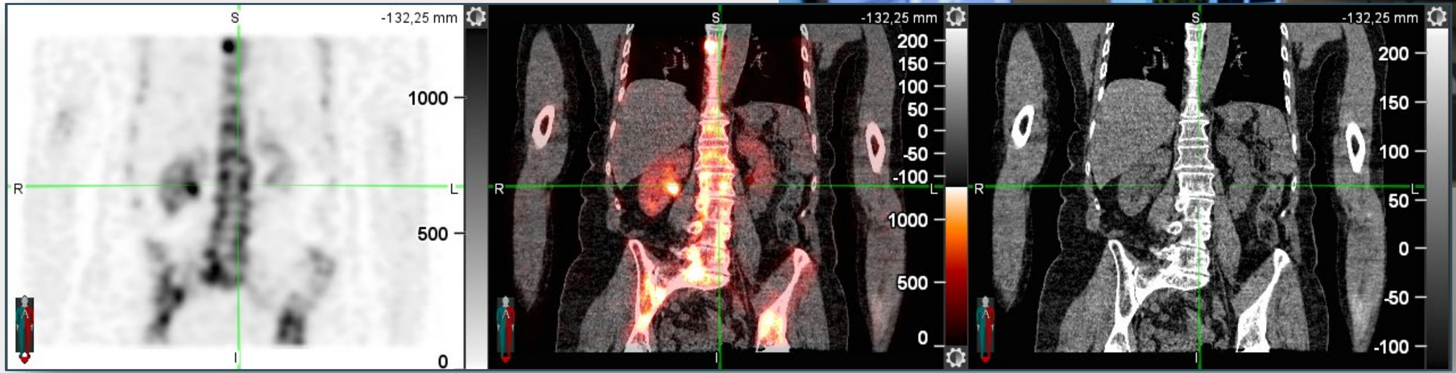
Rentetz
In-hous

Blumgart, Yens. J Clin Invest. 1926;4:1–13.

Nuclear Medicine

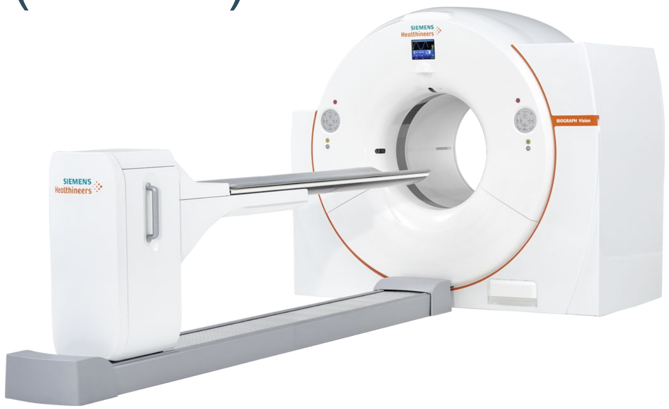
- medical specialty that makes use of radiopharmaceuticals for the diagnosis and staging of disease, for monitoring of a disease process, and for radionuclide therapy (RNT)
- used in basic sciences such as biology, drug discovery and in preclinical medicine.

- clinical aspects
- radiopharmaceutical
- instrumentation



Nuclear Medicine (NM) Instrumentation

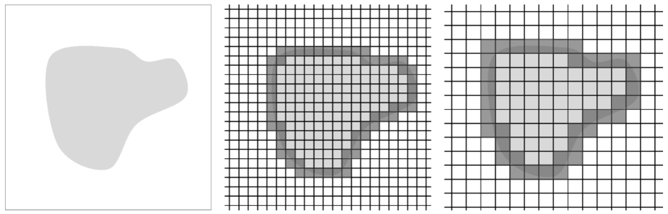
- gamma camera & single photon emission computed tomography (SPECT)
- positron emission tomography (PET)
- radionuclide calibrator or activity meter
- gamma counter / spectrometer
- intra-operative gamma & beta probe
- hybrid technology: computed tomography (CT) and magnetic resonance imaging (MRI)



NM instrumentation

- scale, precise laboratory balance
  - mass (g)
- size, stadiometer, VOI, …
  - length (m), area, volume, …
- clock
  - time (s)
- glucometer
  - blood sugar level (mg/dl)
- other instrumentation
  - respiratory gating, ECG, …
  - infusion pump, …
- software & hardware (MDR)

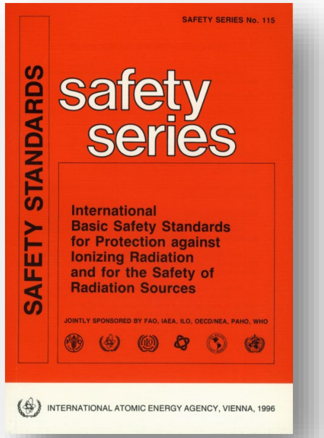





Gear, J.I., et al. Eur J Nucl Med Mol Imaging 45, 2456–2474 (2018).

Quality Control (QC) and Quality Assurance (QA)

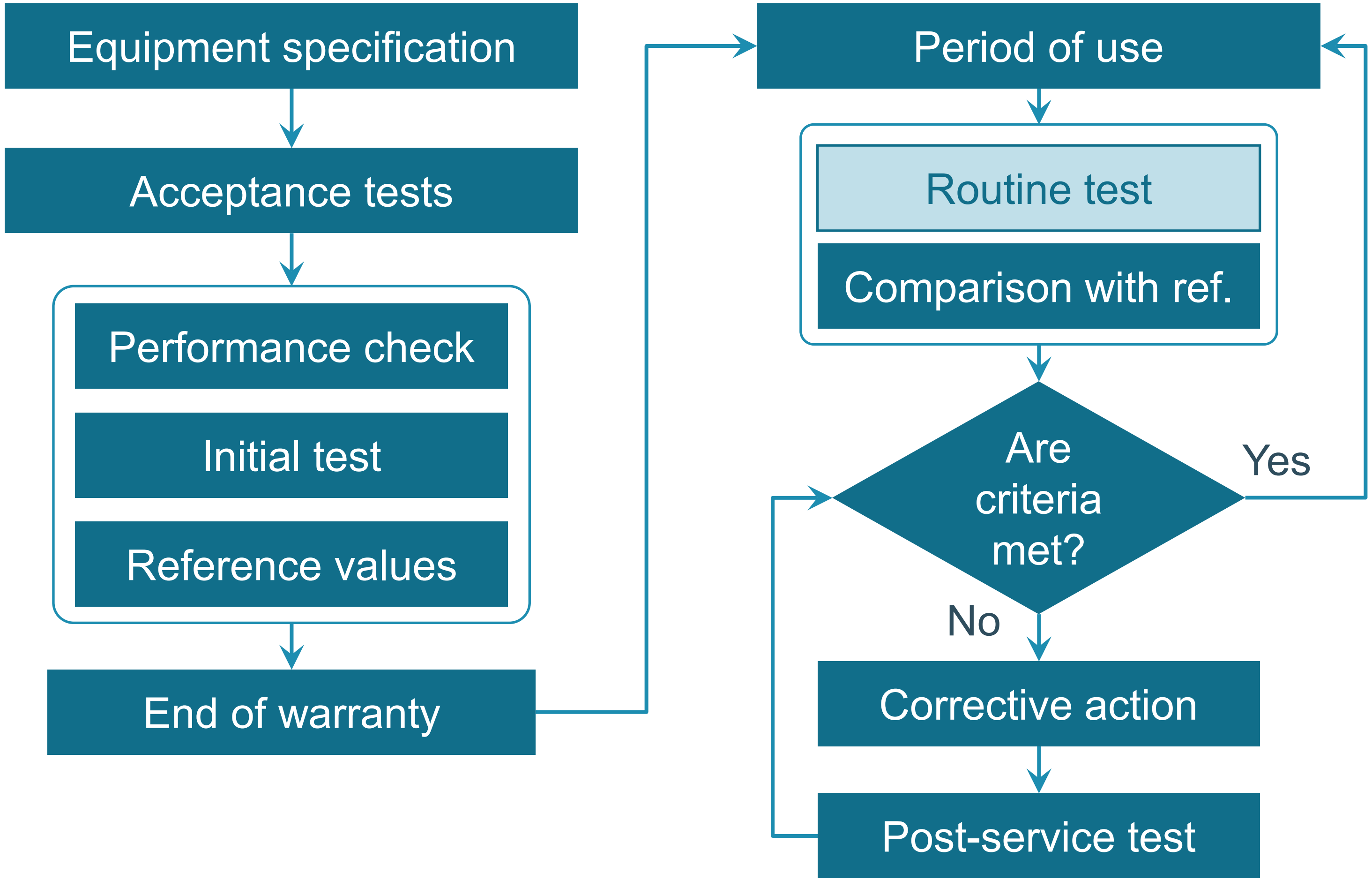
- with the intention to optimize the radiation protection, administration of activity, data acquisition, image quality, data processing, or radionuclidetherapy
- by observing and assessing systems and procedures, lowering risks, improving quality
  - instrumentation, equipment
    - gamma camera, SPECT, PET, radionuclide calibrator, gamma counter
  - actions, procedures and techniques
    - administration of radioactivity, data acquisition, data (image) processing, data storage & archiving, …
    - radioactive waste procedure, decontamination, …
- purpose of the observation, verification, or "control" is
  - to reach a certain recommendation, standard, criterion, objective, …
  - comparing the observation (measurement) with a threshold
  - comparing the results with a reference value or earlier values (e.g. acceptance)
- QA is focused on providing confidence that quality requirements are fulfilled



"In essence, QA is nothing more than thoroughly organized meticulousness of work."

QA & QC in Nuclear Medicine

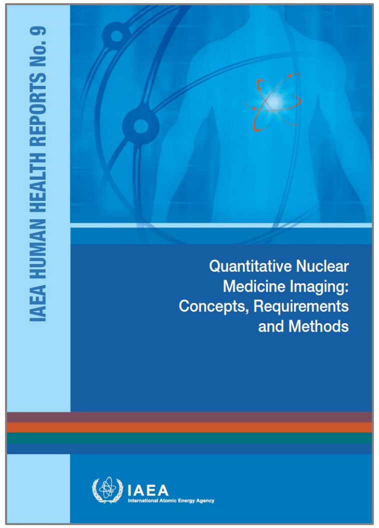
- evaluation and routine testing in medical imaging
- IEC-1223-1 (1993)
- equipment lifecycle
- performance measurements & reference values
- periodicity of routine testing
- acceptability criteria (AC)
- QC ≡ conformity of the AC
- role of medical physics expert
- quality management



Quality Control Recommendations

IPEM Institute of Physics and Engineering in Medicine

27 EU P Prismap



AAPM REPORT NO. 177

Acceptance Testing and Annual Physics Survey Recommendations for Gamma Camera, SPECT, and SPECT/CT Systems

The Report of AAPM Task Group 177

February 2019

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AAPM REPORT NO. 181

The Selection, Use, Calibration, and Quality Assurance of Radionuclide Calibrators Used in Nuclear Medicine

Report of AAPM Task Group 181

June 2012

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EANM Physics Committee

EFOMP

AMERICAN ASSOCIATION of PHYSICISTS IN MEDICINE

Eur J Nucl Med Mol Imaging (2010) 37:672–681
DOI 10.1007/s00259-009-1348-x

GUIDELINES

Acceptance testing for nuclear medicine instrumentation

Ellinor Busemann Sokole · Anna Płachcínska · Alan Britten ·
on behalf of the EANM Physics Committee

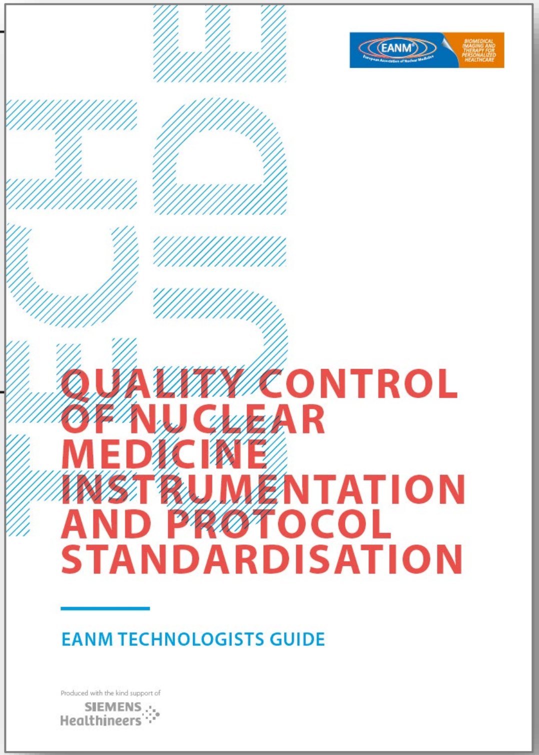
Eur J Nucl Med Mol Imaging (2010) 37:662–671
DOI 10.1007/s00259-009-1347-y

GUIDELINES

Routine quality control recommendations for nuclear medicine instrumentation

On behalf of the EANM Physics Committee:
Ellinor Busemann Sokole · Anna Płachcínska · Alan Britten
With contribution from the EANM Working Group on Nuclear Medicine Instrumentation Quality Control:
Maria Lyra Georgosopoulou · Wendy Tindale · Rigobert Klett

EANM EUROPEAN ASSOCIATION OF NUCLEAR MEDICINE



IAEA International Atomic Energy Agency

EANM Technologists committee

Table 1 Routine QC tests for a gamma camera: planar, whole-body, SPECT and SPECT/CT. *Equipment type*: scintillation Anger gamma camera

Test	Purpose	Frequency	Comments
GC1. Physical inspection	To check collimator and detector head mountings, and to check for any damage to the collimator	Daily	Inspect for mechanical and other defects that may compromise safety of patient or staff; if collimator damage is detected or suspected, immediately perform a high-count extrinsic uniformity test
GC2. Collimator touch pad and gantry emergency stop	To test that the touch pads and emergency stops are functioning	Daily	Both the collimator touch pads and gantry emergency stop must function if there is an unexpected collision with the patient or an obstacle during motion; the touch pads must be checked each time the collimators are changed
GC3. Energy window setting for ^{99m}Tc	To check and centre the preset energy window on the ^{99m}Tc photopeak	Daily	The test is intended to check the correct ^{99m}Tc energy window
GC4. Energy window setting – other radionuclides to be used	To test that preset energy windows are properly centred for the energies of other clinically used radionuclides	Daily when used	Frequency of the test should be adapted to the particular camera and frequency of use of the radionuclides
GC5. Background count rate	To detect radioactive contamination/excess electronic noise	Daily	The background count rate should be stable under constant measuring conditions
GC6. Intrinsic/extrinsic uniformity and sensitivity	To test the response to a spatially uniform flux of ^{99m}Tc (or ^{57}Co)	Daily	Visually inspect either an intrinsic or extrinsic (whichever is most convenient) low count

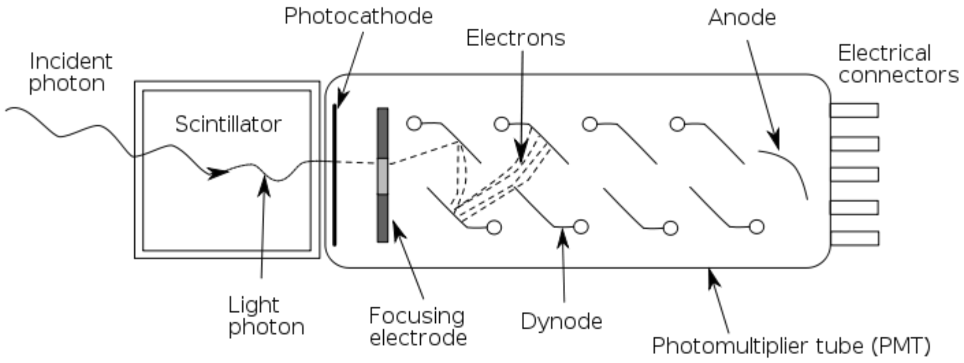
Eur J Nucl Med Mol Imaging (2010) 37:662–671
DOI 10.1007/s00259-009-1347-y

Quality assurance & control (1.x)

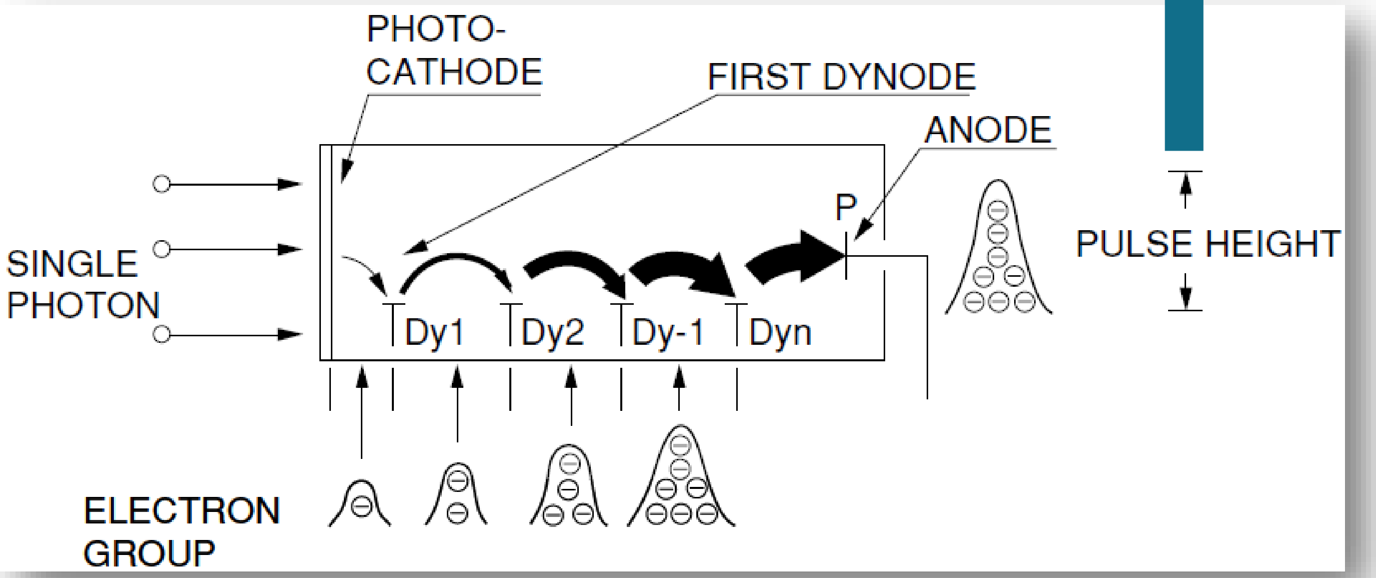
- general
  - time references, hardware & software integrity, data exchange, …
- gamma & SPECT camera
  - planar & tomographic uniformity, energy, centre-of-rotation, planar & volumetric sensitivity, image quality & signal recovery, …

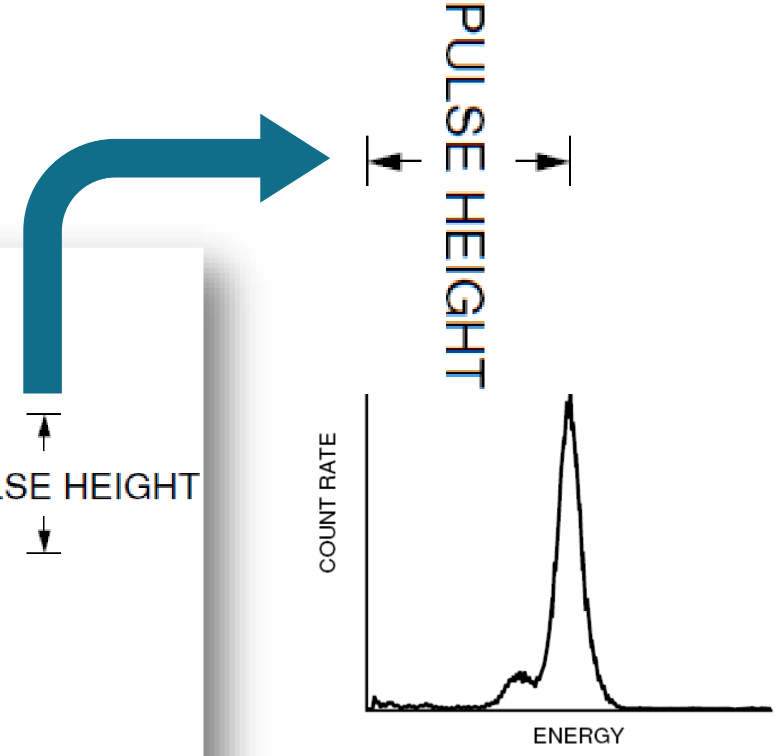
- PET camera
  - detector & tomographic uniformity, quantification, image quality, …
- hybrid technology
  - multi-modal alignment, influences for corrections (attenuation, scatter, …), …
- activity meter
  - background, zero, accuracy, constancy, reproducibility, repeatability, stability, linearity, …
- gamma counter
  - background, efficiency, constancy, reproducibility, energy & resolution, linearity, …

Photon Energy Determination



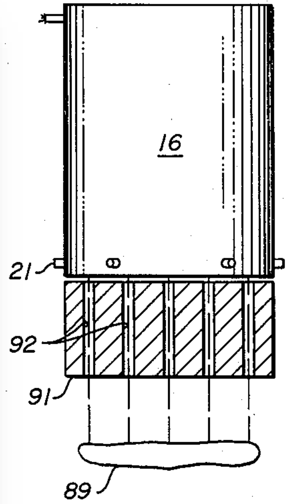
- detector type - gamma camera
- scintillation detection: weak spot → PMT
  - # scintillation photons / gamma keV
  - # photo-electrons
  - electron multiplication – dynodes
  - high-voltage, electronic noise





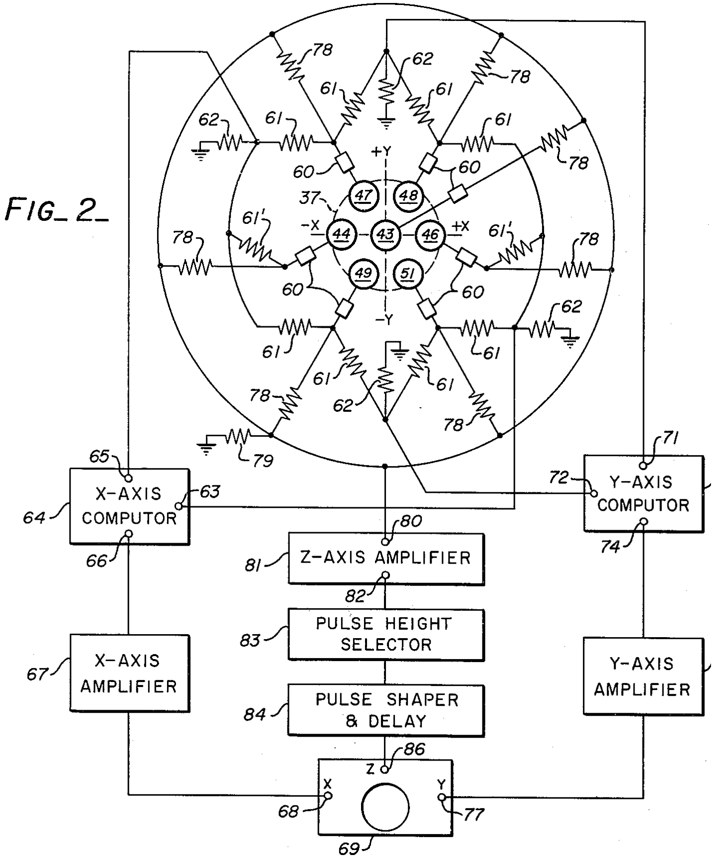
Radiation Image Device (1958)

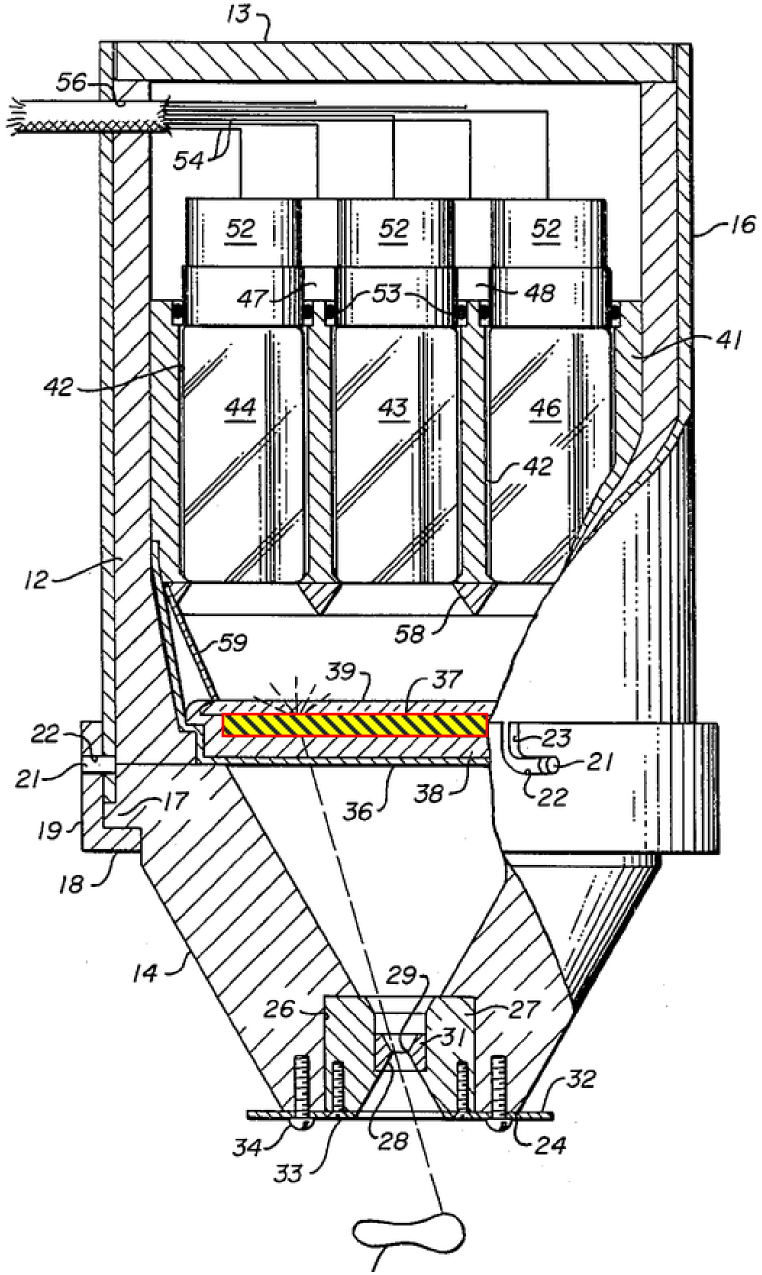
- Hal O. Anger (1920-2005)
  - invention of the gamma camera, basis for SPECT
  - anger “positional” logic: X and Y signal
  - photon energy: Z signal



“alternative” detector configuration

FIG_2_

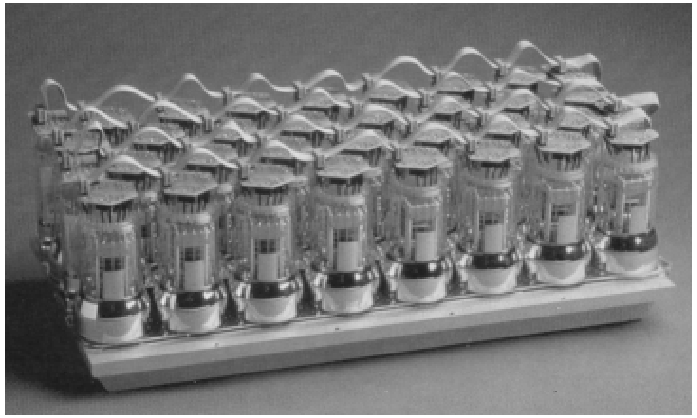


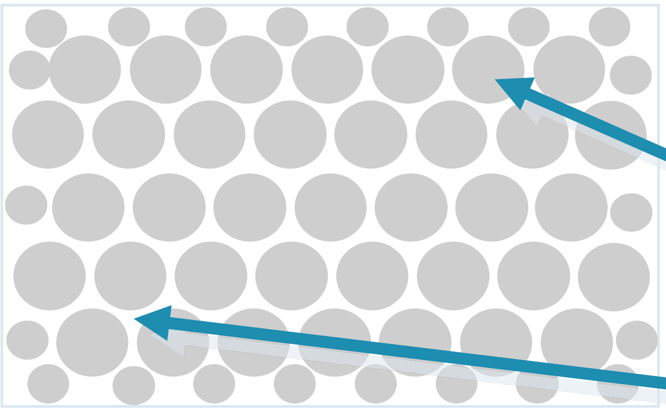


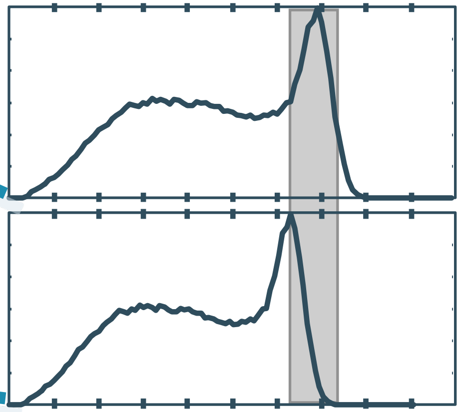
J Nucl Med Technol, Dec 1, 2005, 33(4): 250-253 – See also US patent US3011057 A

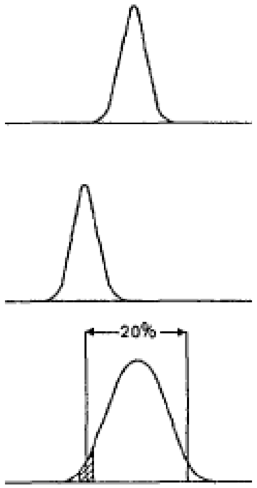
QC of gamma camera photon energy settings

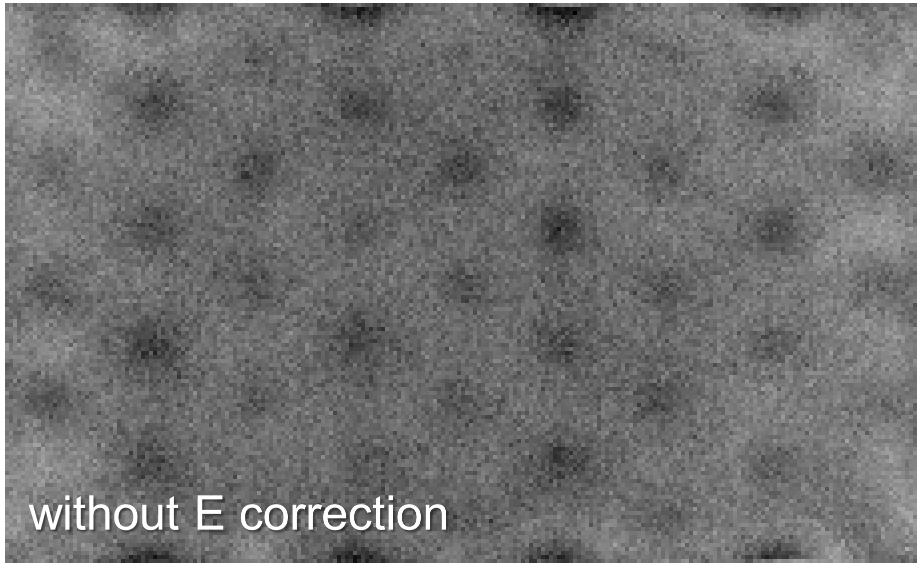
- global E-setup
  - “peaking”
- local E-setup
  - “tuning”

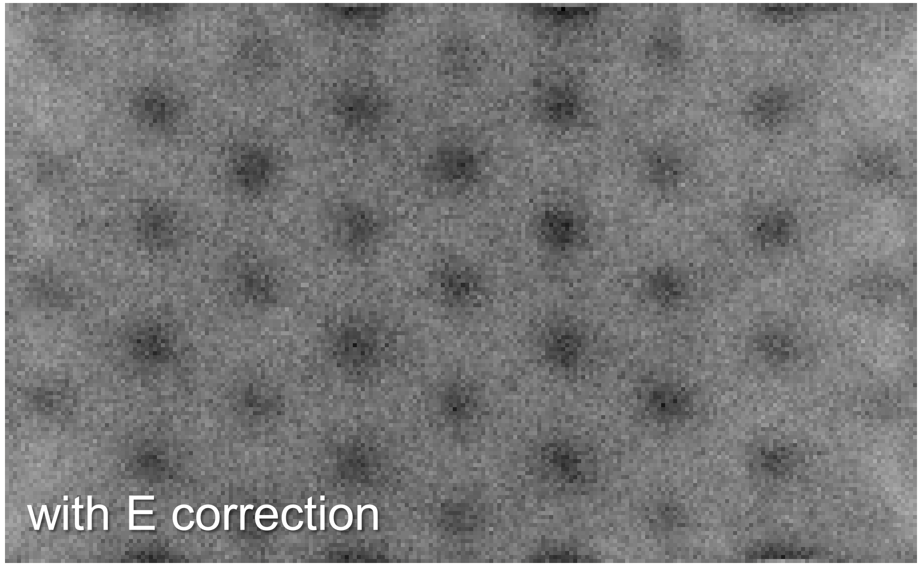






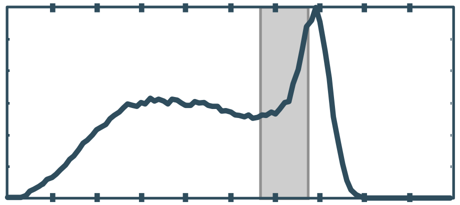




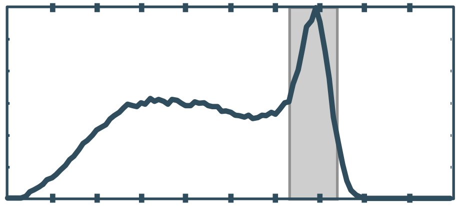


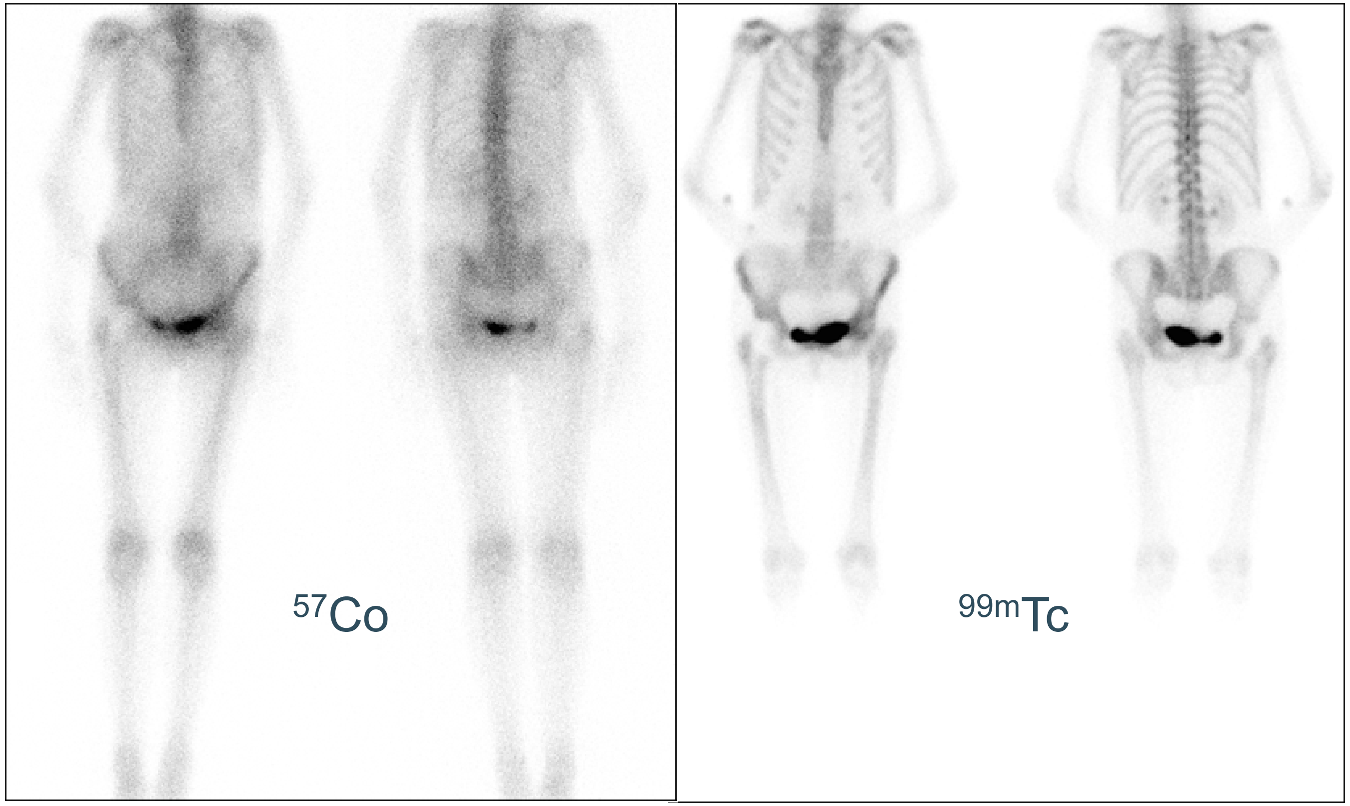
QC of gamma camera photon energy settings

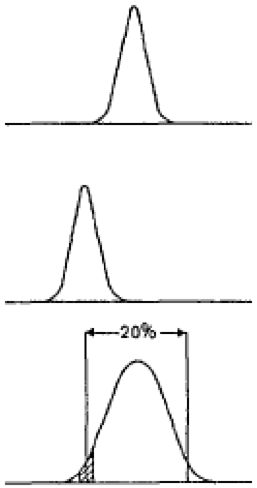
- QC of the energy settings is important (peak position & window width)
- needs daily verification, at least before the start of its clinical use
- e.g. bone scintigraphy
  - ^{57}Co – 122 keV



  - ^{99m}Tc – 140 keV

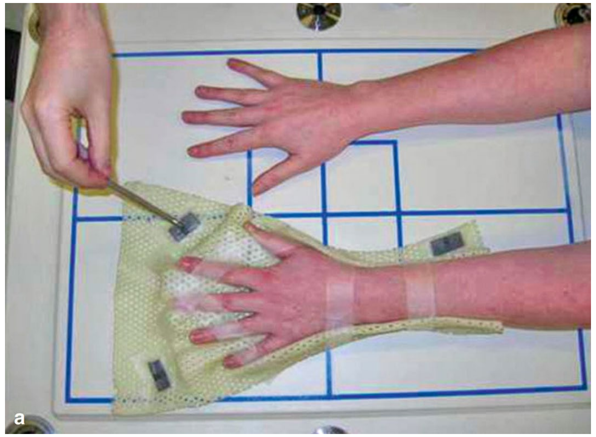


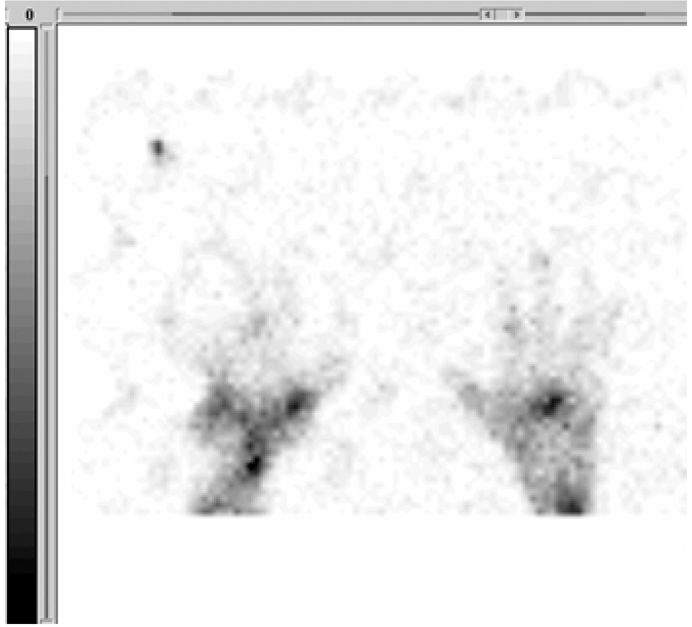


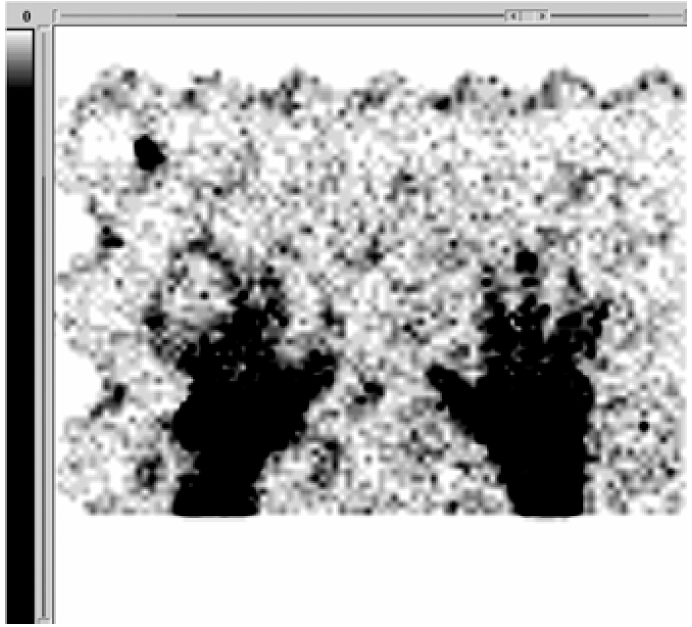


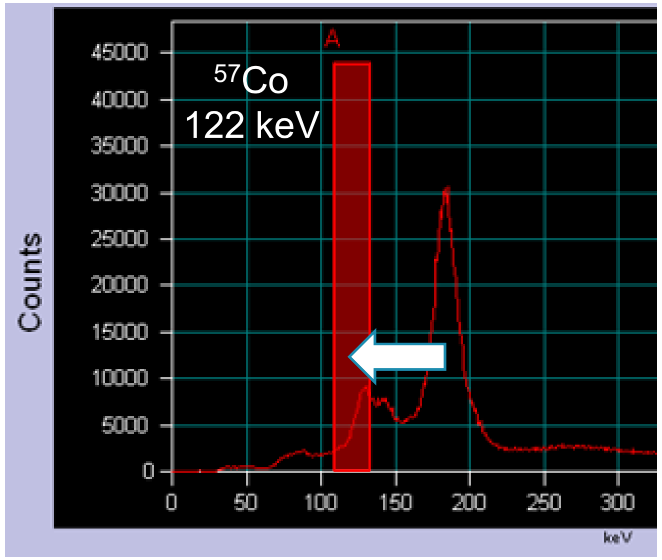
Importance of energy setting verification

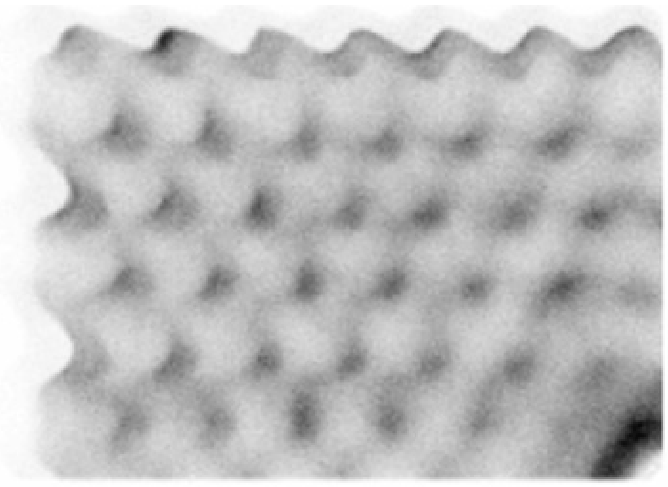
- dynamic phase of a bone scintigraphy study
- positioning of the hands onto the detector
- first investigation of the day
- acquisition starts with administration
- committed dose – no clinical benefit
- QC energy
- ^{57}Co-flood
- energy shift







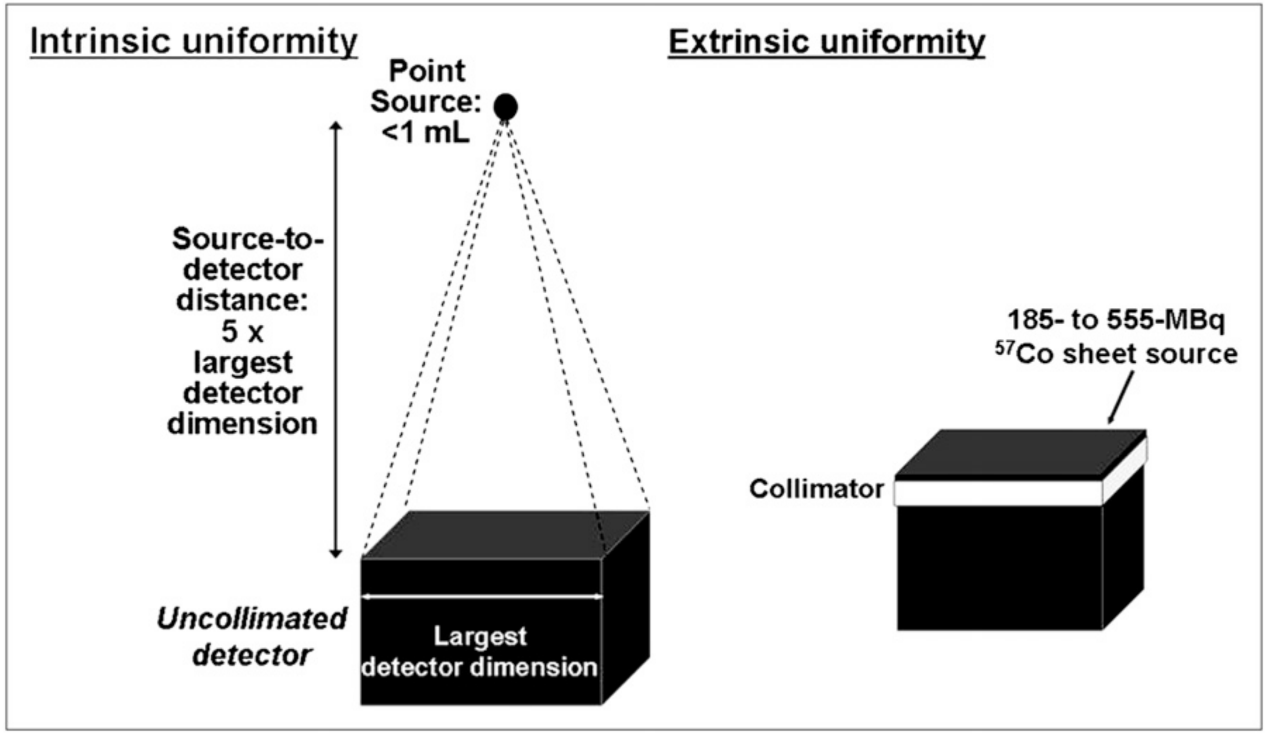


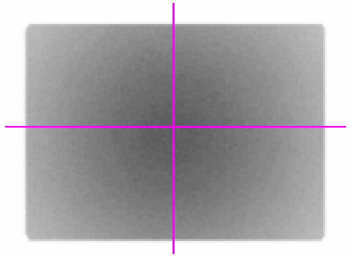


Radionuclide and Hybrid Bone Imaging (2012)
Fogelman et al., Springer (978-3-642-02400-9)

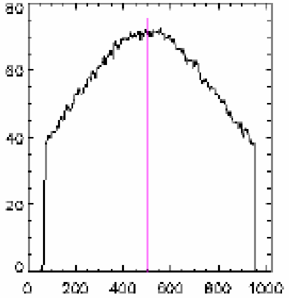
Detector uniformity

- aim: detector response to a uniform exposure, should give a uniform response
- extrinsic verification
  - ^{57}Co sheet source (or ^{99m}Tc flood)
  - verifies the "whole" system, incl. collimator
- intrinsic verification
  - ^{99m}Tc point source (or another isotope)
  - far away
  - close by
    - dome effect
- quality metrics
  - integral uniformity
  - differential uniformity

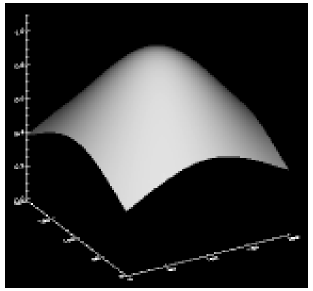




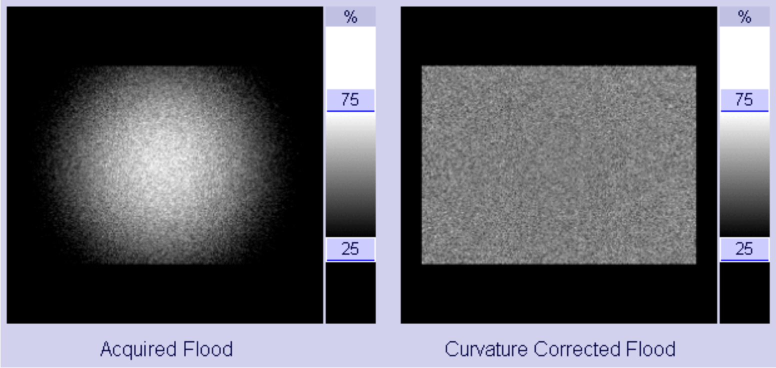
meting



profiel doorheen meting



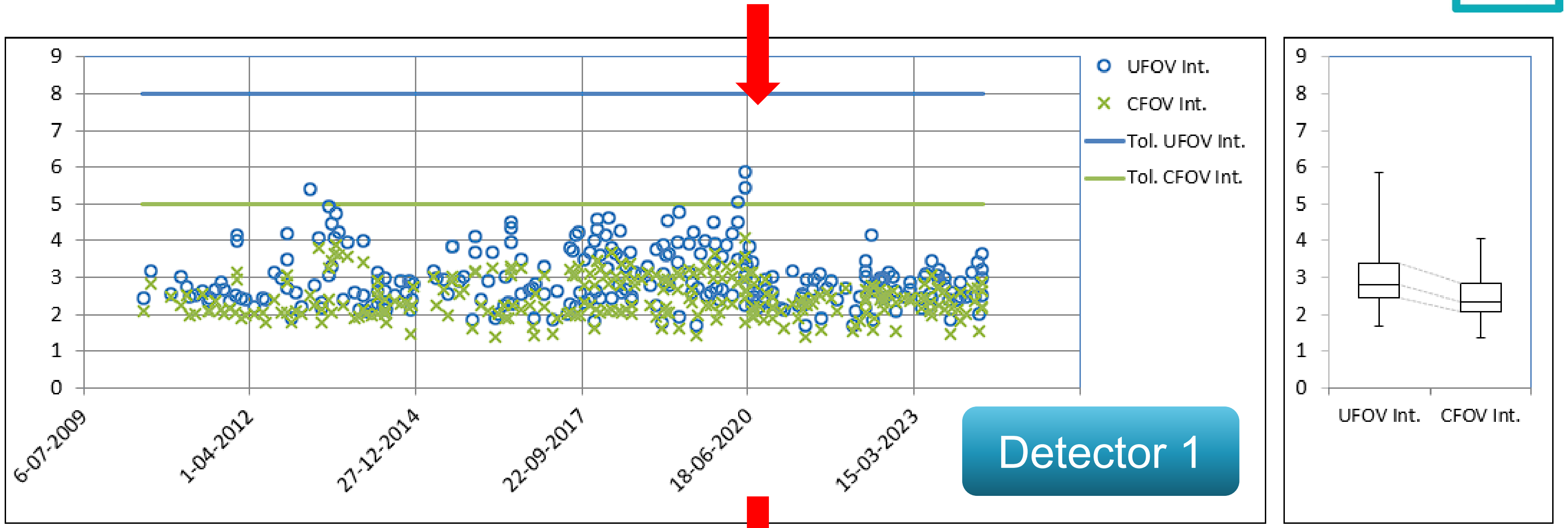
theoretisch intensiteitsoppervlak

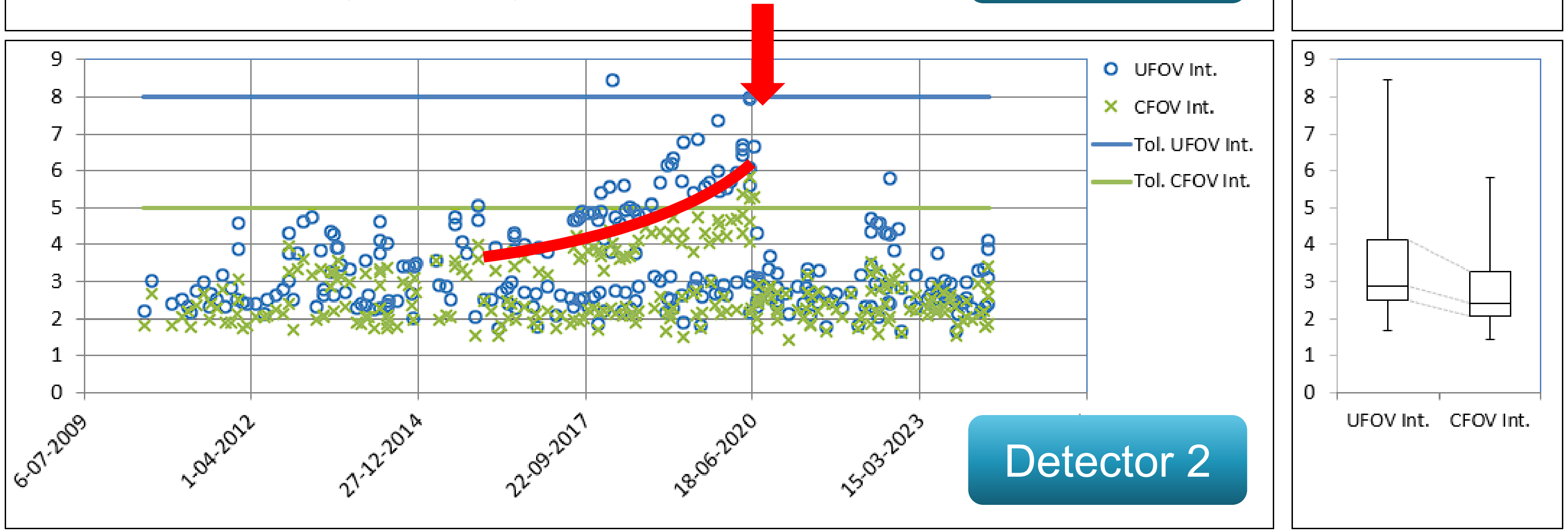


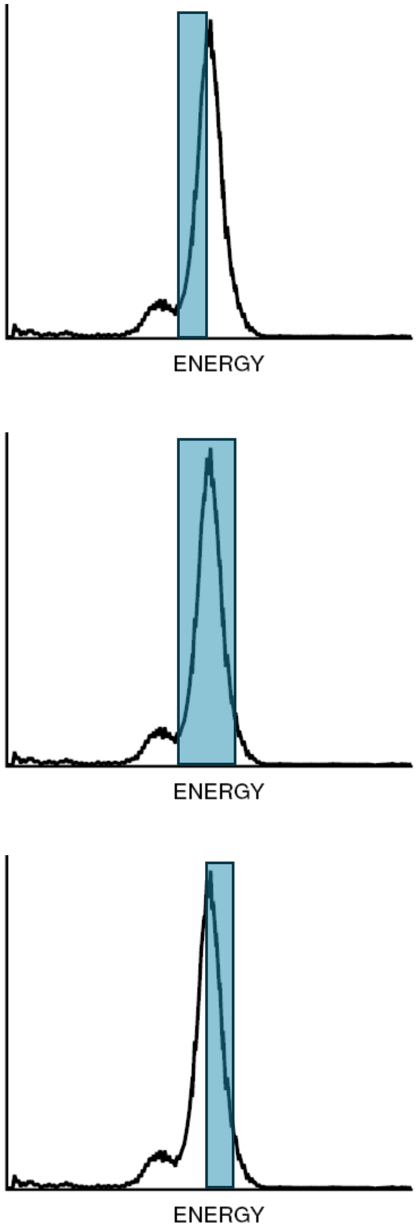
$$100\left(\frac{\text{Max} - \text{Min}}{\text{Max} + \text{Min}}\right)$$

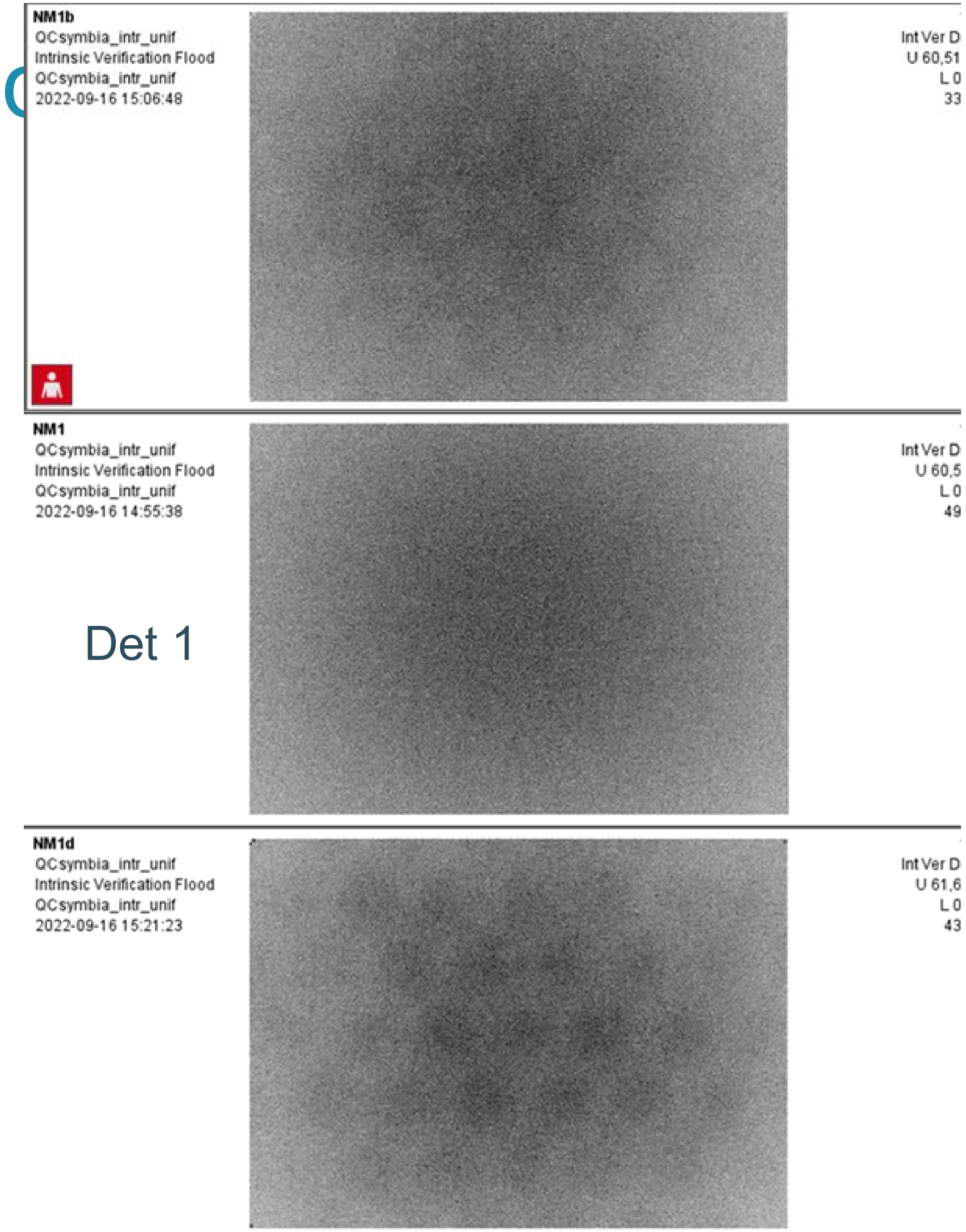
Trend analysis of detector performance – uniformity

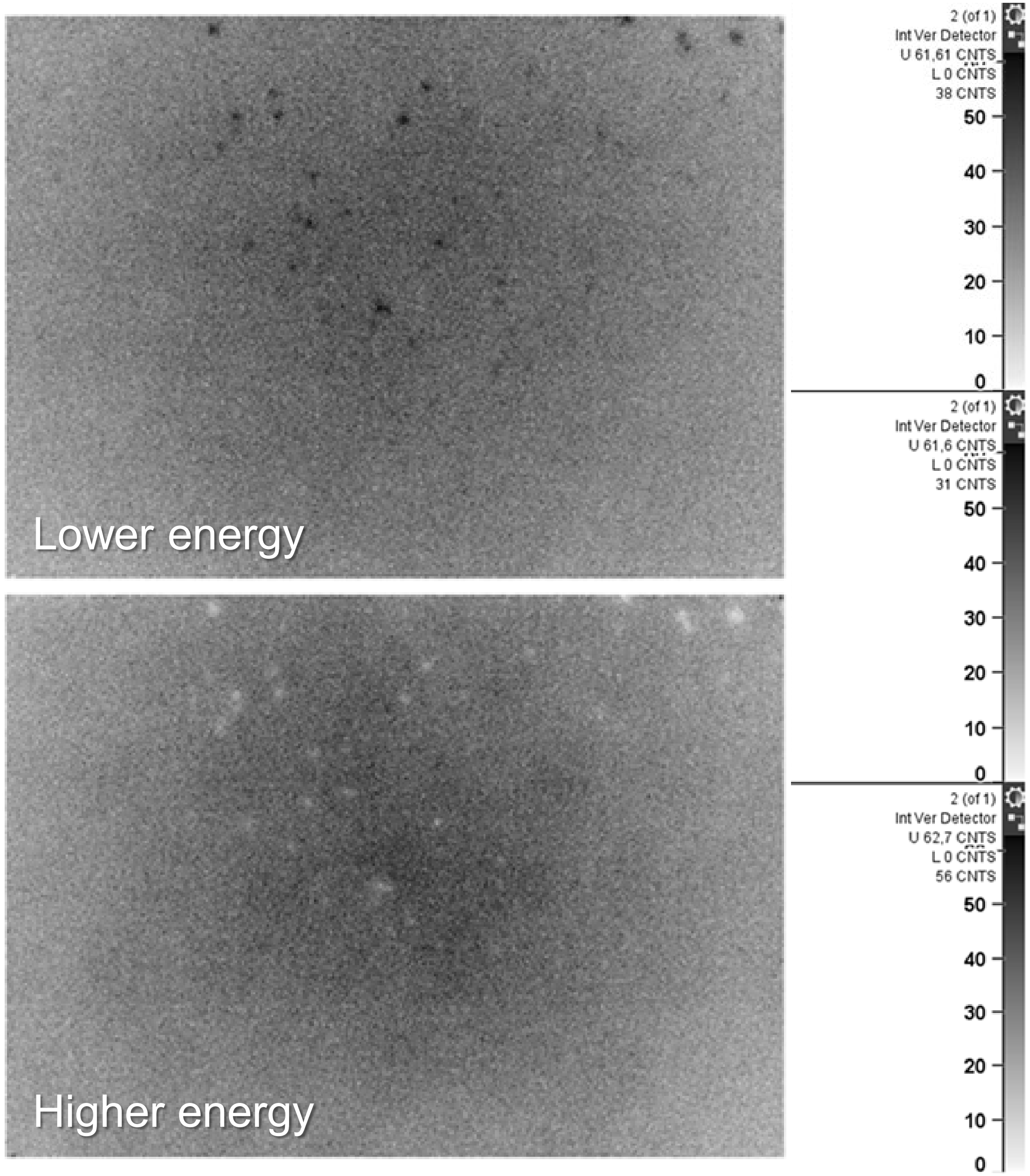
- typical values
- subtle deviations
- environmental reasons
  - temperature
  - humidity
- component drift
  - electronics
  - voltage supply
  - …
- comparison between
  - systems
  - system parts



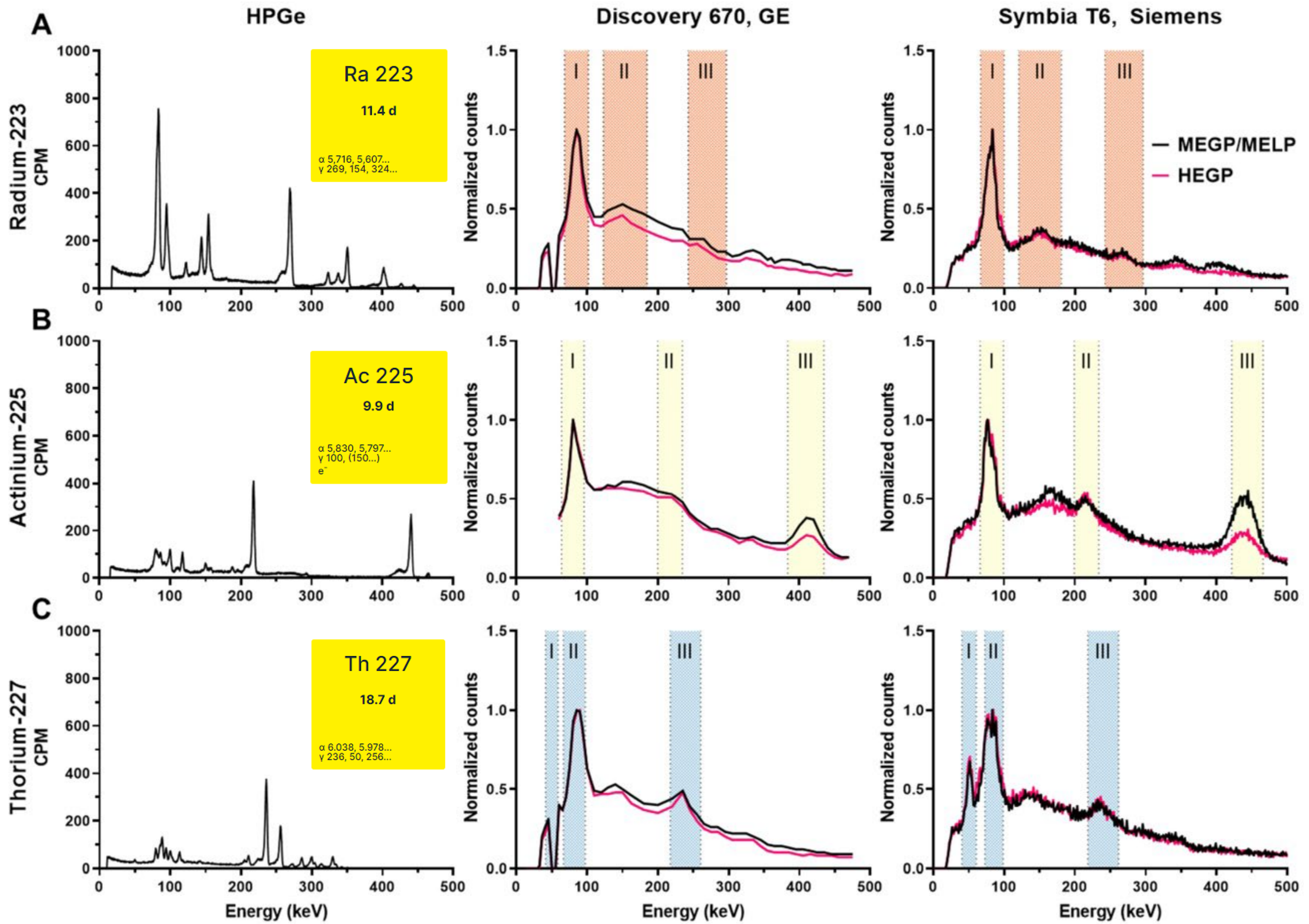



ENERGY
ENERGY
ENERGY

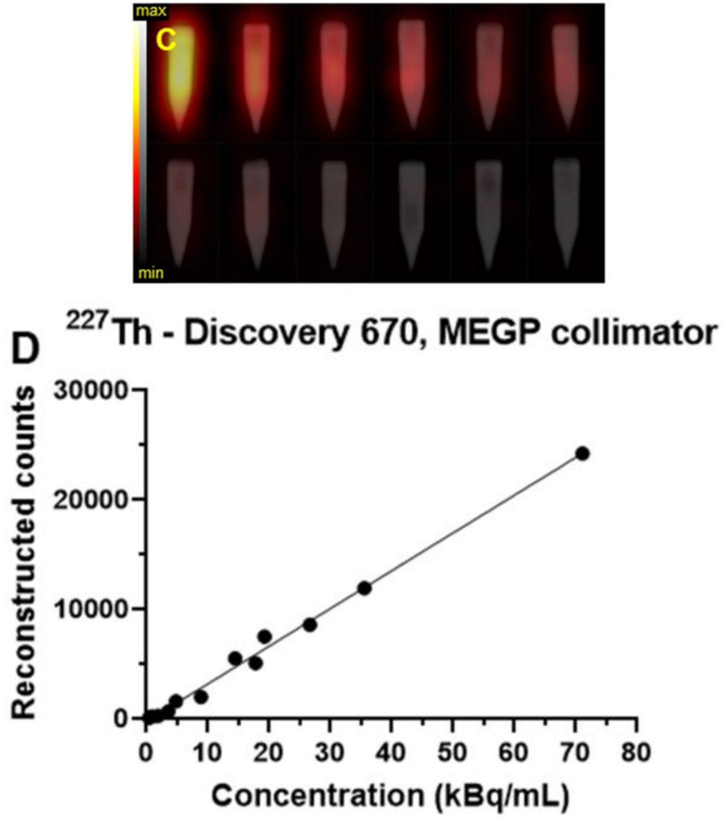

NM1b
QCsymbia_intr_unif
Intrinsic Verification Flood
QCsymbia_intr_unif
2022-09-16 15:06:48
Int Ver D
U 60,51
L 0
33
NM1
QCsymbia_intr_unif
Intrinsic Verification Flood
QCsymbia_intr_unif
2022-09-16 14:55:38
Int Ver D
U 60,5
L 0
49
Det 1
NM1d
QCsymbia_intr_unif
Intrinsic Verification Flood
QCsymbia_intr_unif
2022-09-16 15:21:23
Int Ver D
U 61,6
L 0
43


Lower energy
Higher energy
2 (of 1)
Int Ver Detector
U 61,61 CNTS
L 0 CNTS
38 CNTS
50
40
30
20
10
0
2 (of 1)
Int Ver Detector
U 61,6 CNTS
L 0 CNTS
31 CNTS
50
40
30
20
10
0
2 (of 1)
Int Ver Detector
U 62,7 CNTS
L 0 CNTS
56 CNTS
50
40
30
20
10
0

Energy settings for novel radionuclides (alpha emitters)



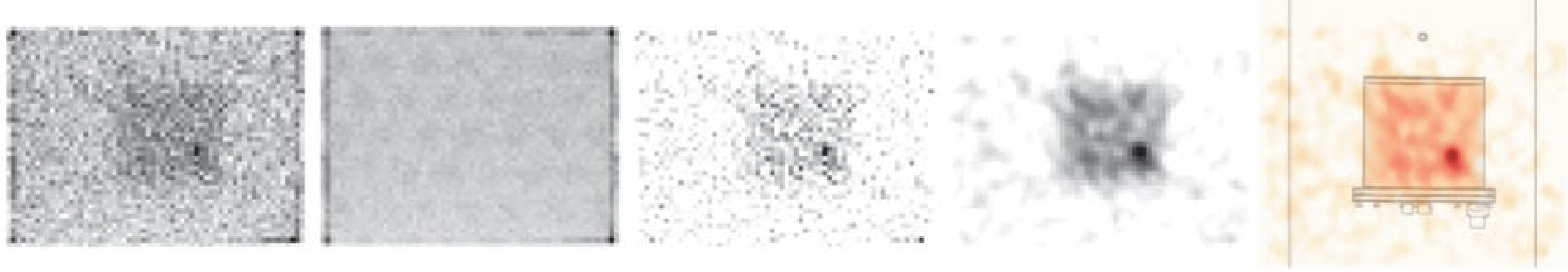
- system calibration and clinical protocol development
- limit-of-detection analysis

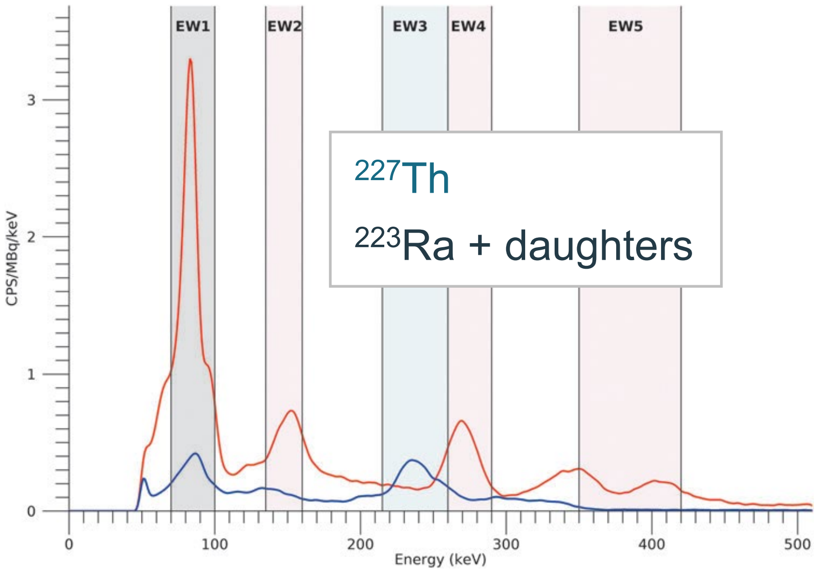


Benabdallah *et al.*, Theranostics, 2021, 11(20):9721-9737

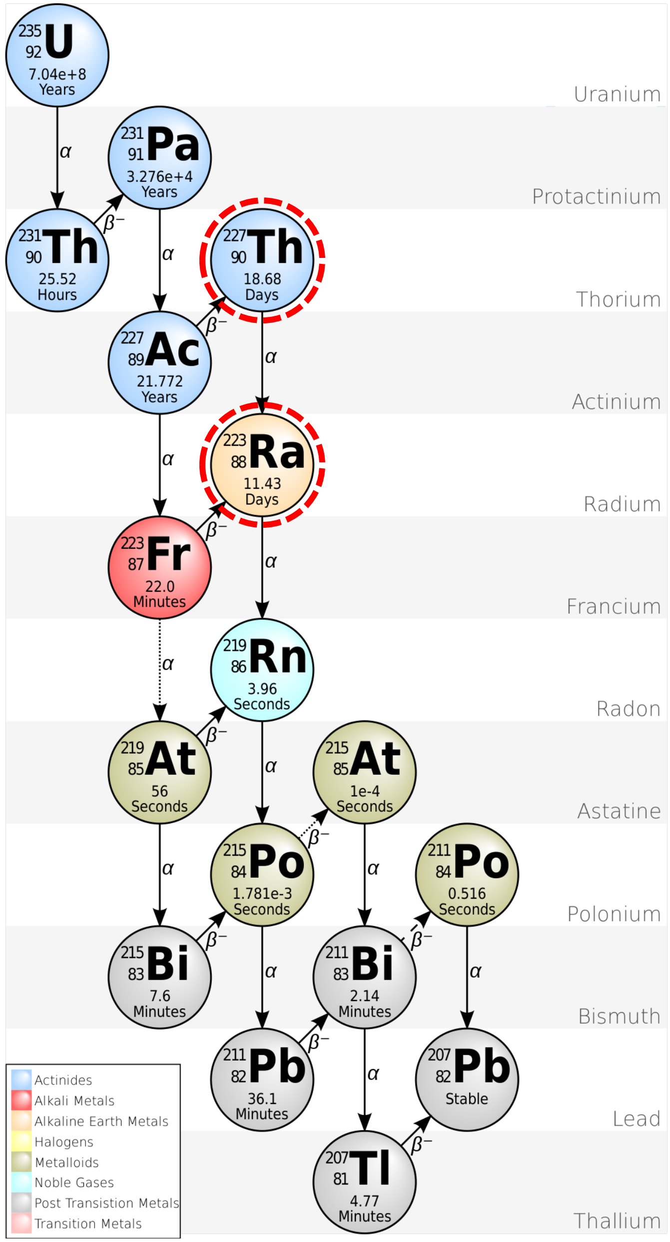
Establishment of clinical imaging protocols

- gamma-camera imaging of Th-227 / Ra-223
- requires good background correction (using a 10 hour acq!)



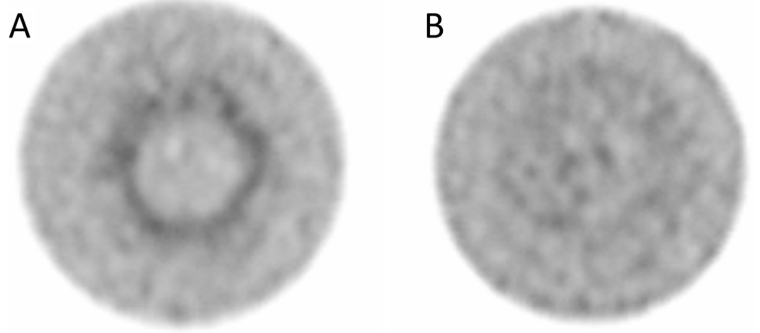


EW3 (215-260 keV) | EW5 (350-420 keV) | Sum-EW1,3,4,5

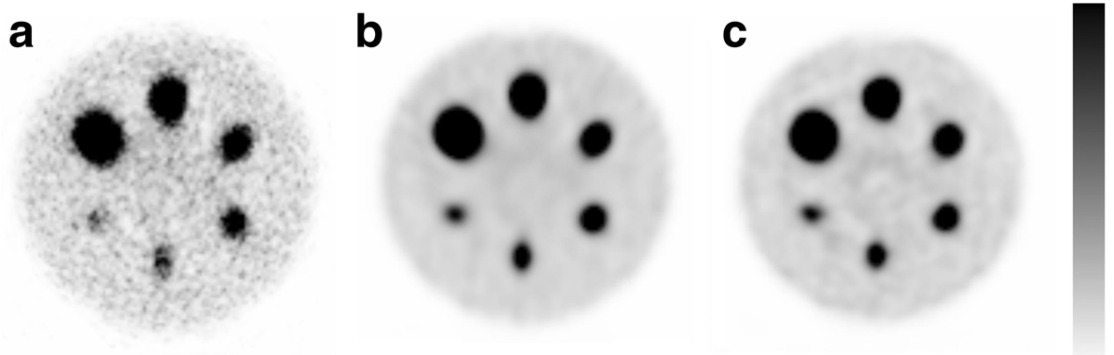


Establishment of clinical imaging protocols

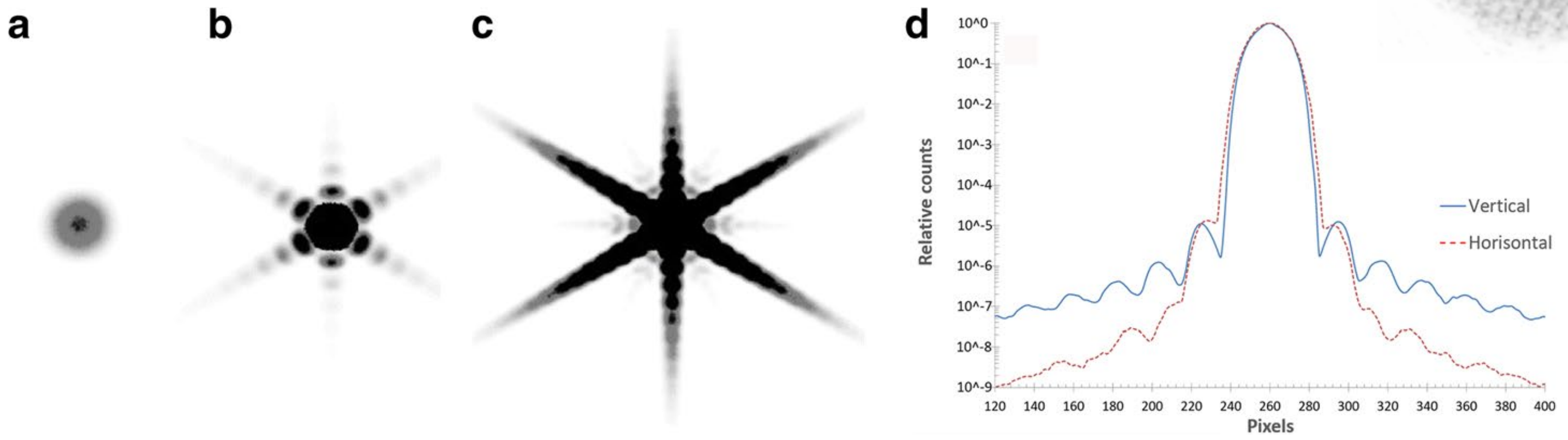
- SPECT/CT is feasible for Tb-161
  - complex energy spectrum
  - extrinsic uniformity correction is recommended
  - Monte-Carlo based iterative reconstruction techniques
- currently beyond available commercial solutions
- computational burden / collimator modelling
- fast GPU-based MC improves Lu-177 imaging



Marin *et al.* *EJNMMI Physics* (2020) 7:45
https://doi.org/10.1186/s40658-020-00314-x



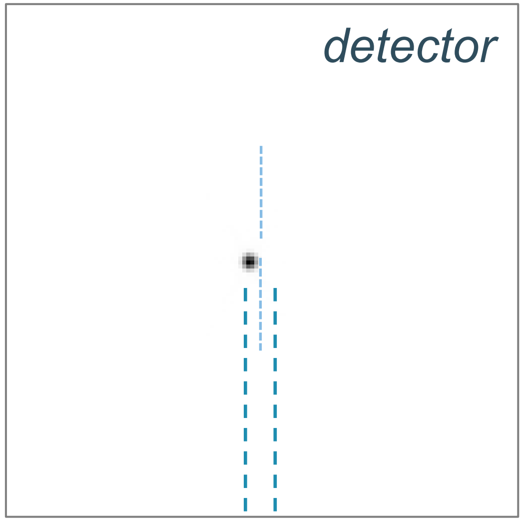
Rydén *et al.* *EJNMMI Physics* (2018) 5:1
DOI 10.1186/s40658-017-0201-8

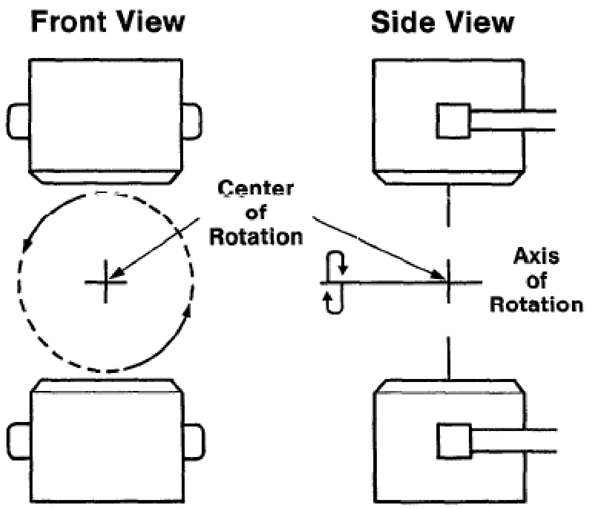


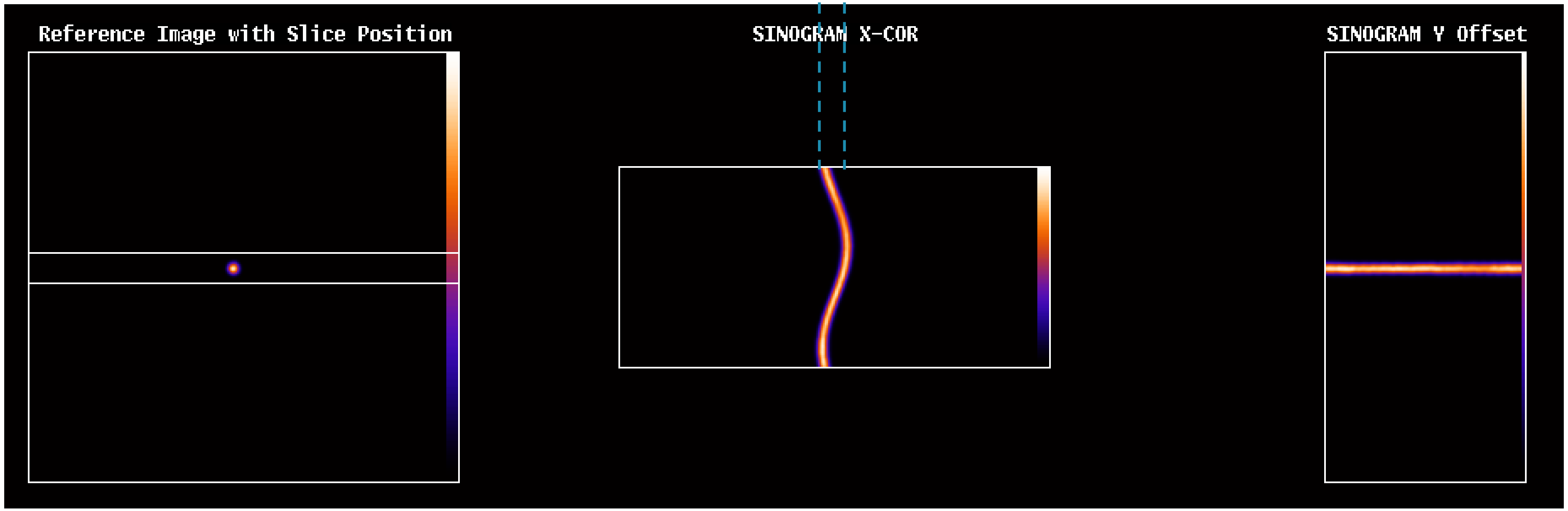
- current clinical QC does not cover advanced image quality analysis

SPECT – center-of-rotation (COR)

- mechanical (physical) COR should be identical to the electronic (image) COR
- analysis of a SPECT acquisition of a point source
- revolving over 180°, 360°

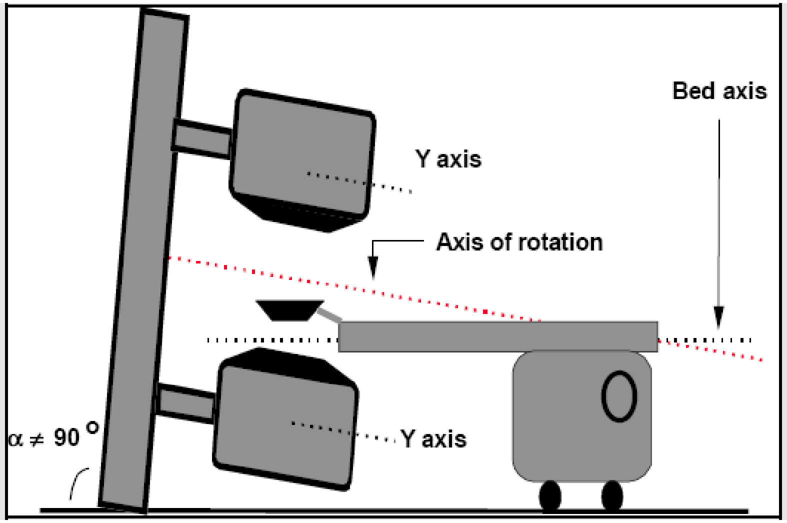


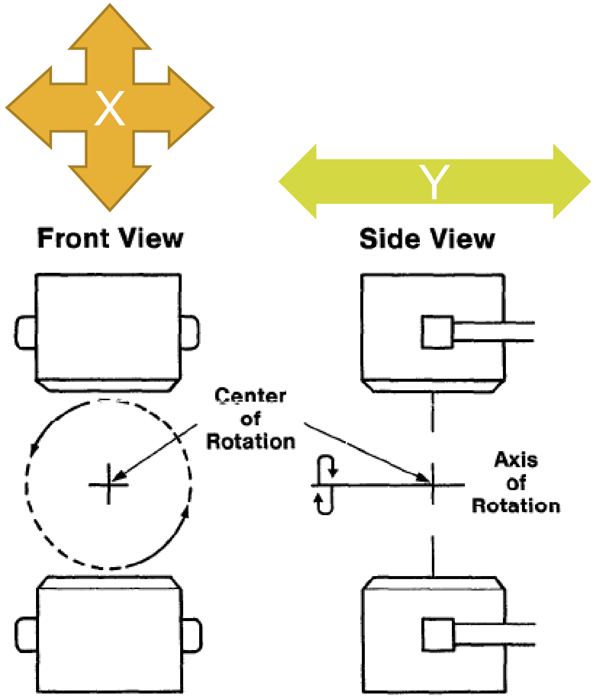




SPECT – center-of-rotation (COR)

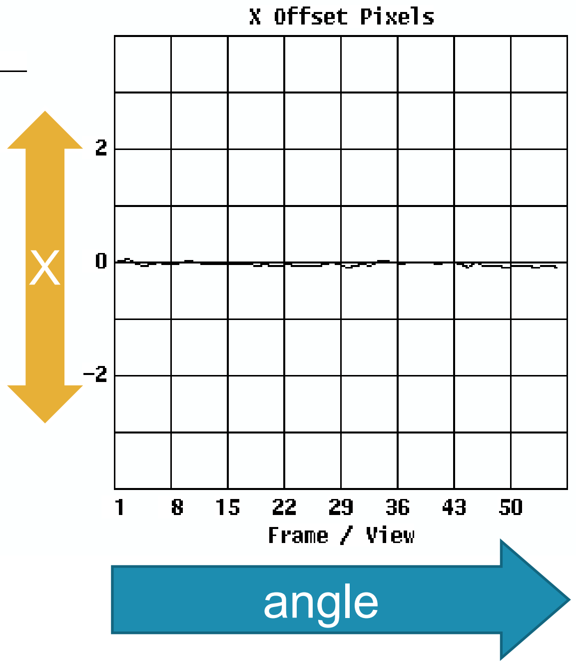
- there should be no offset in the regression of a sine function
- criterion (regulator):
  - the offset should be below 0.5 pixel size in clinical acquisition mode (e.g. 128 matrix ≈ 4.8 mm pixel, hence COR < 2.2 mm)

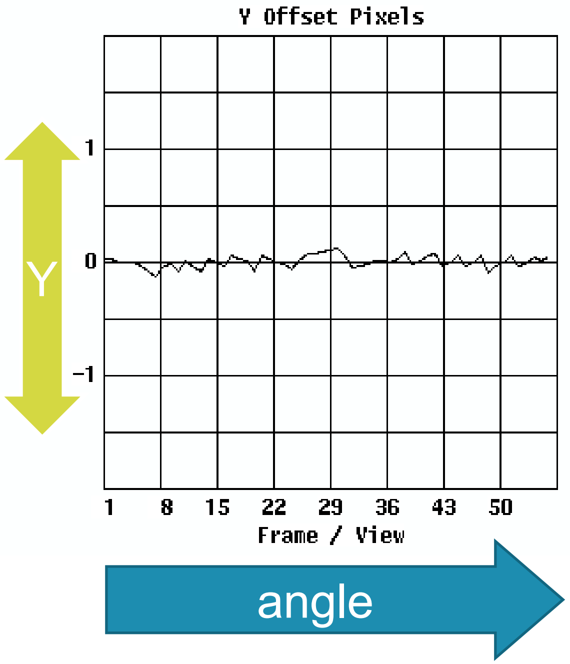




RESULT CENTER OF ROTATION CHECK

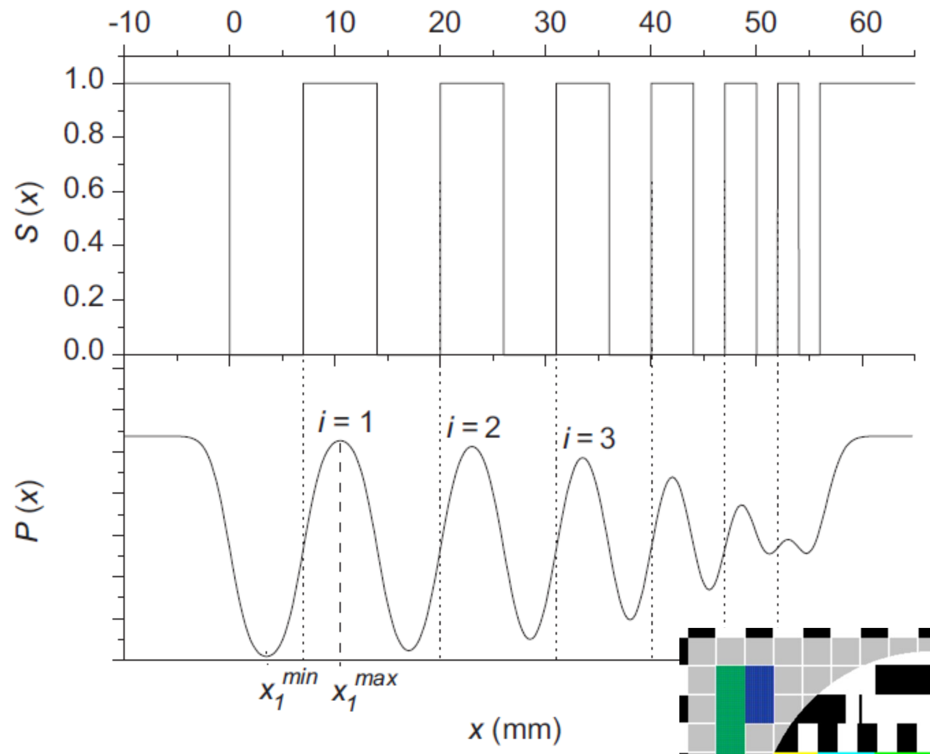
COR offset	:	-0.049	in Pixels
COR offset	:	-0.233	in mm
ChiSquare	:	0.065	from the fitting
SD Y Offset	:	0.065	in pixels
Views	:	60	
Matrix	:	128*128	
Time/Frame	:	3.3 sec	
Pixel Size	:	4.795 mm	



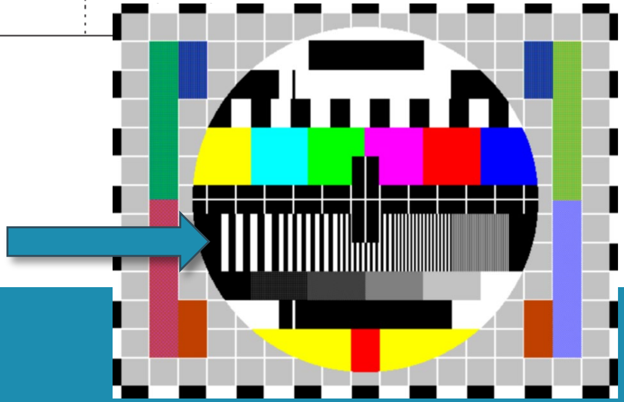


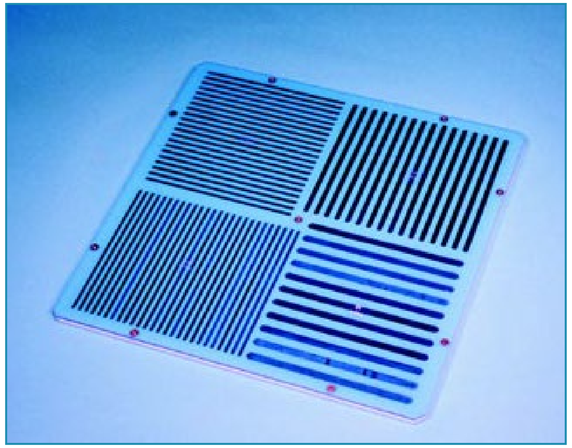
Gamma camera planar spatial resolution

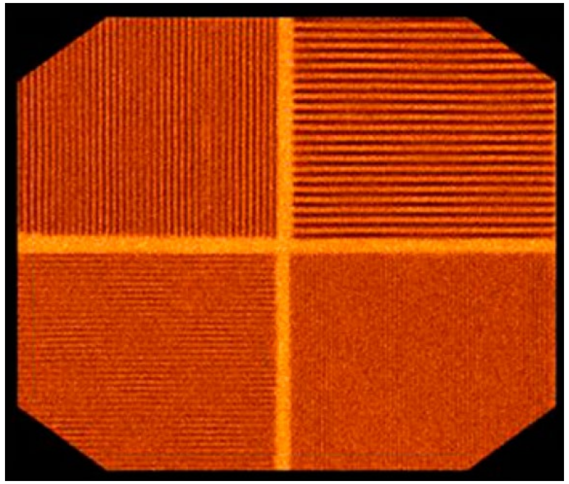
- Modulation Transfer Function (MTF) – spatial frequency response of an imaging system

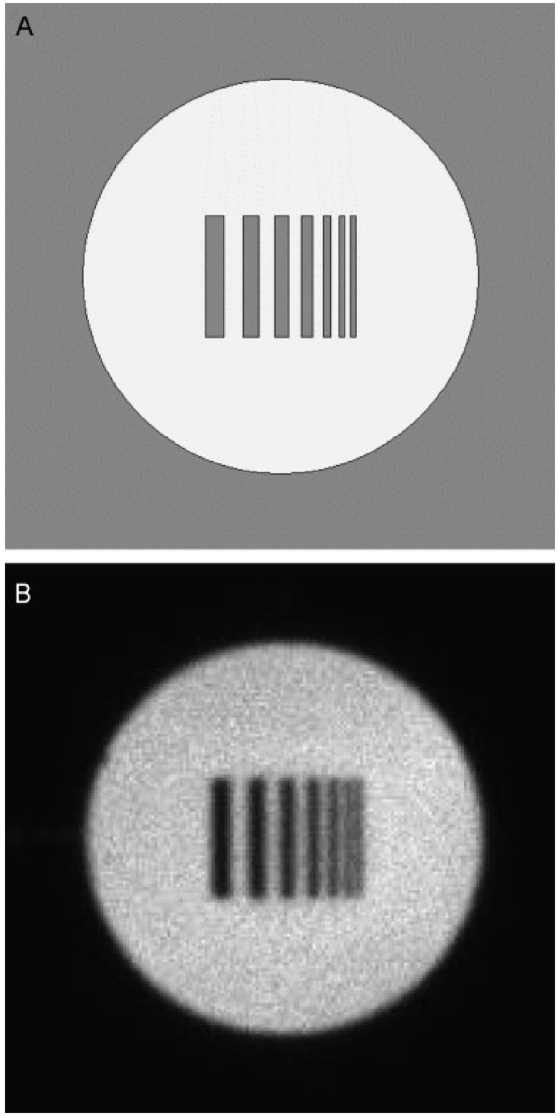


J. Santos, et al., Appl Radiat Isot, 66:1 (2008), pp. 44–49



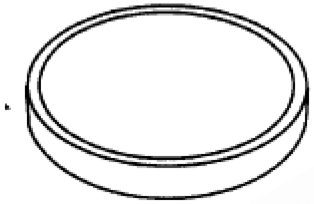


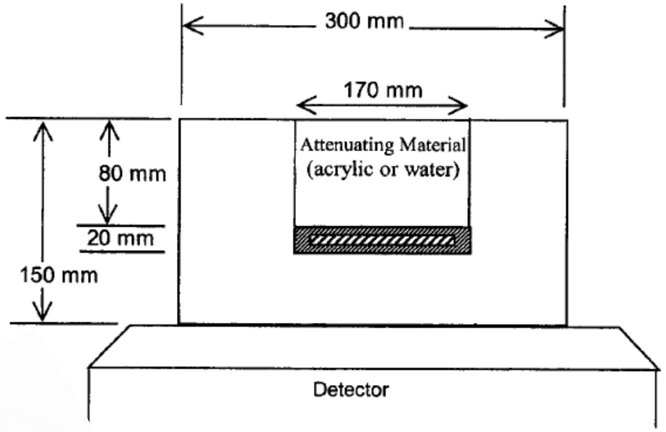


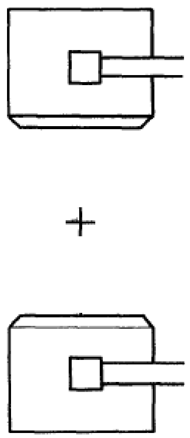


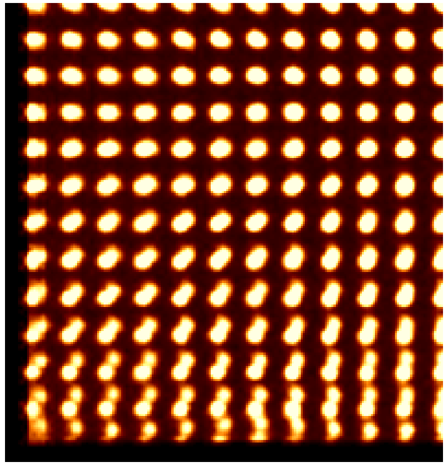
More advanced quality control

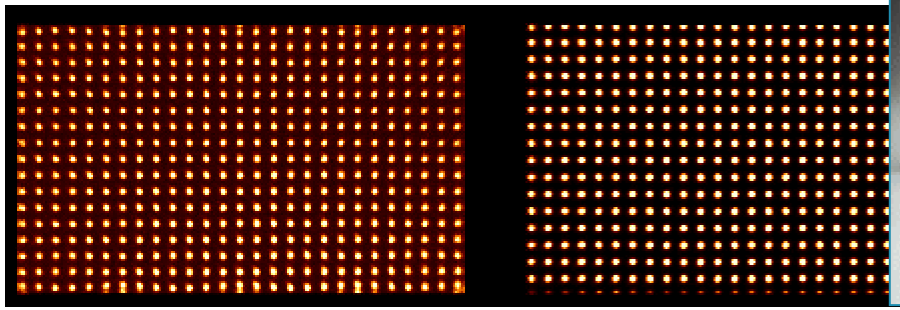
- geometry, linearity, alignment, pixel size, sensitivity
- SPECT uniformity, image quality
- overall system performance test

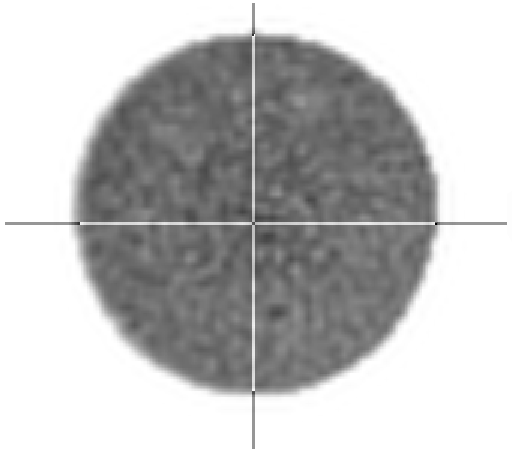


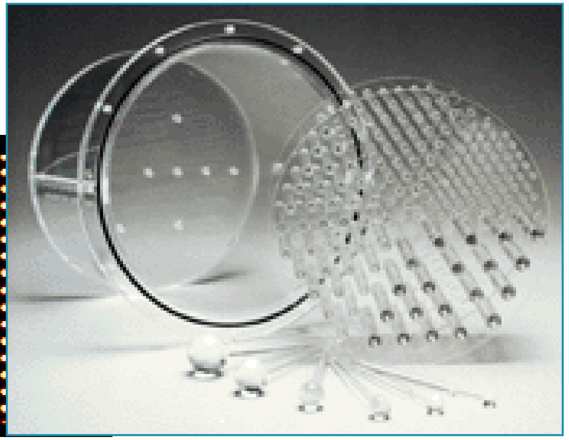


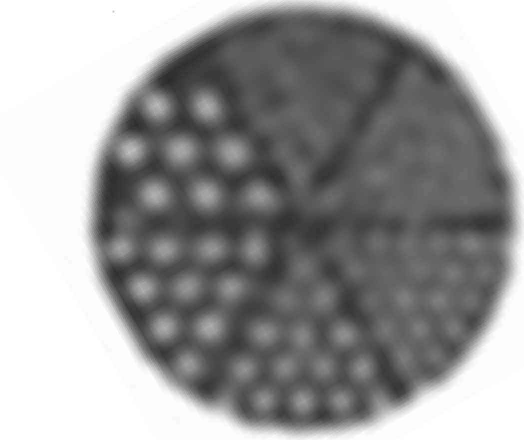


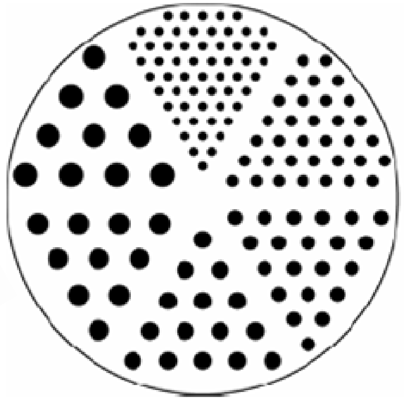


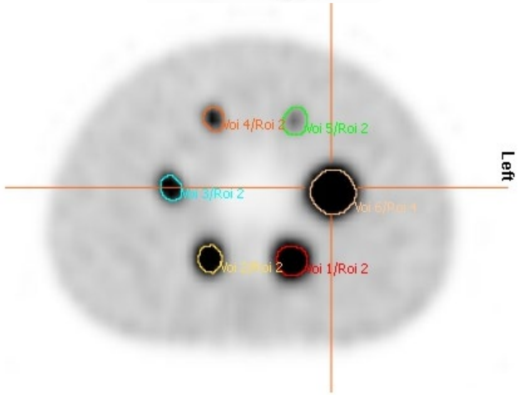


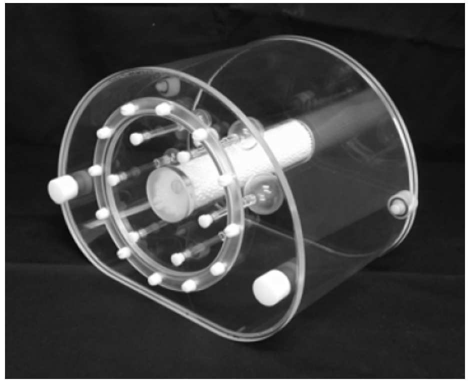








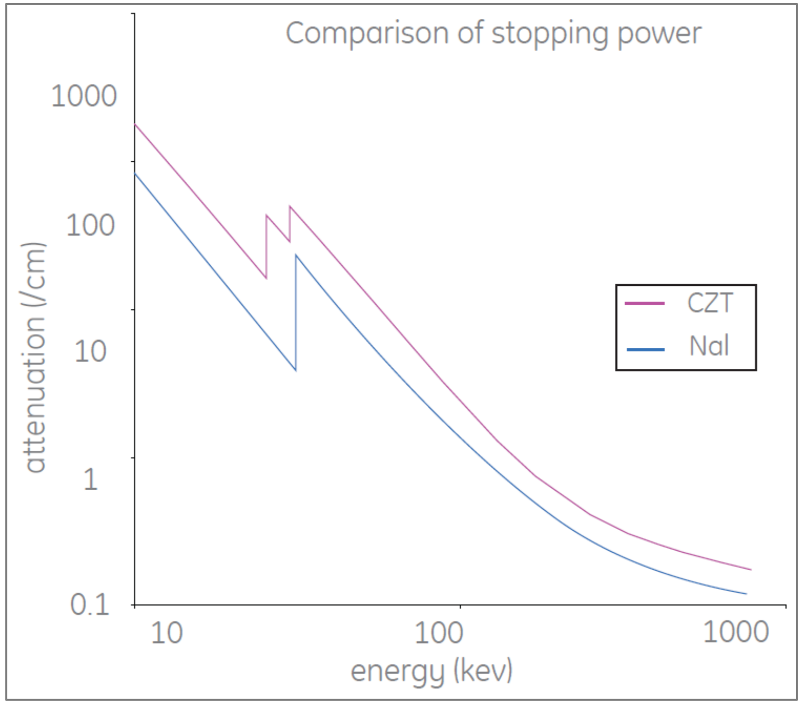


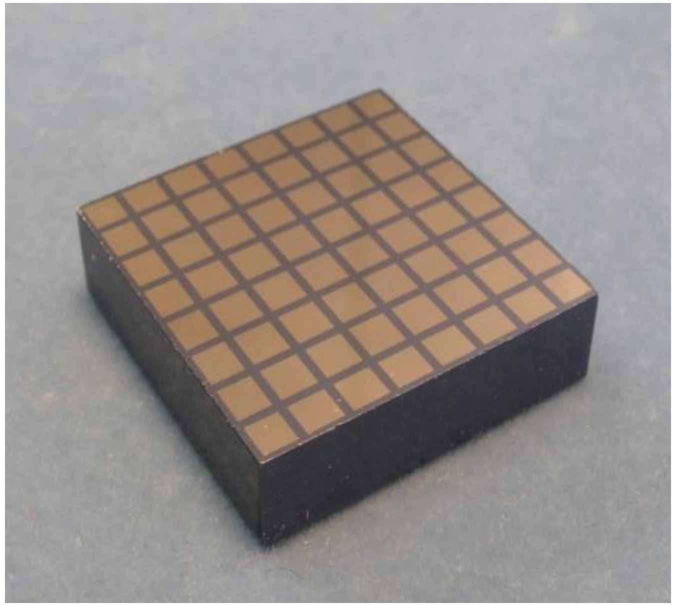


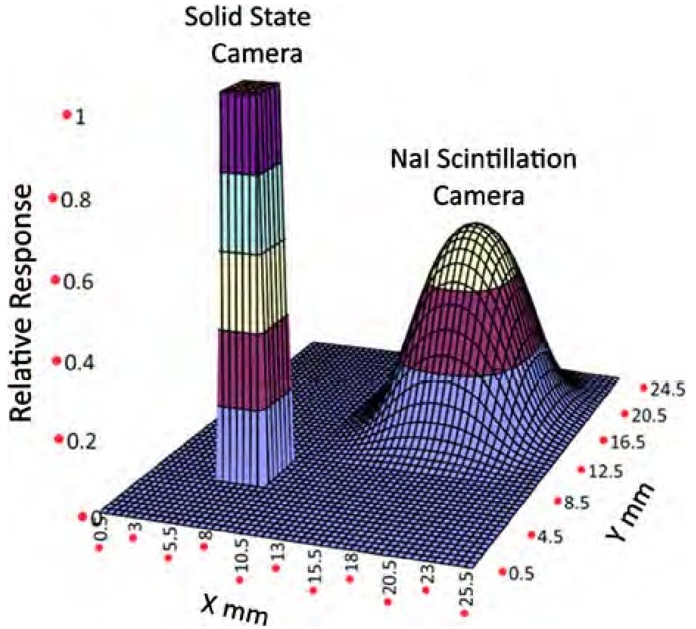
Novel detector technology – CdZnTe or CZT

- $Cd_{1-x}Zn_xTe$ – usually x < 0.2
- compact "pixelated" detector tile
- better energy resolution ~ 6%

	NaI(Tl)	CZT
density (g/cm^3)	3.67	5.81
μ (cm^2/g) @ 150 keV	0.566	0.544
Z_{eff}	51	50
crystal thickness (mm)	9	5
intrinsic efficiency (%)	85	80



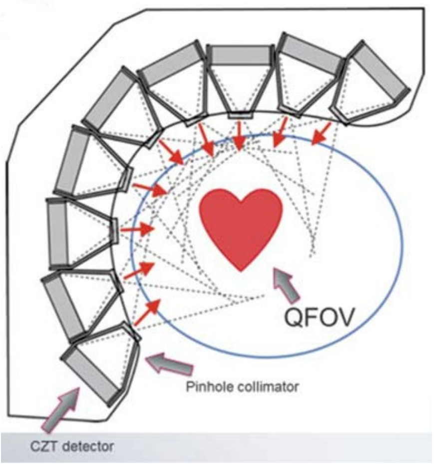




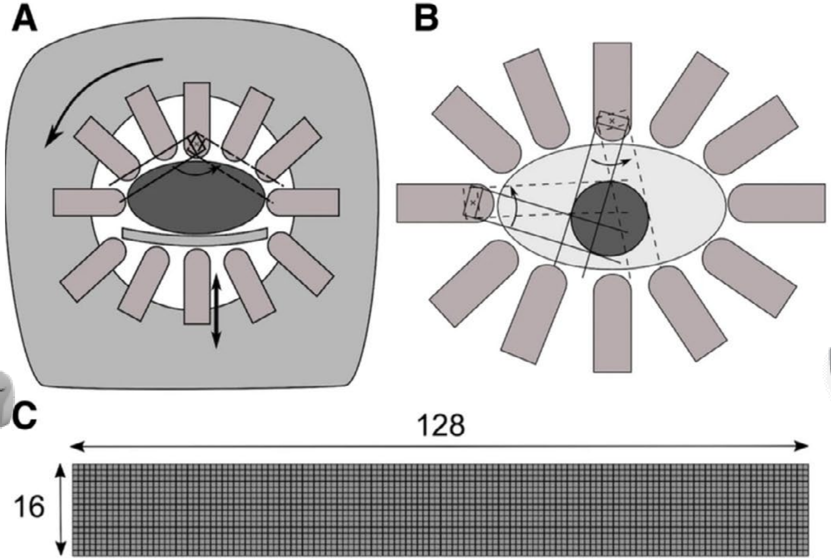
A. Bolotnikov, Brookhaven National Laboratory, NY, 2012

New gantry design and detector geometry

- multiple CZT tiles together
- novel gantry designs
- swivelling CZT detector
- 360° dynamic SPECT
- new QC strategies required



GE HealthCare

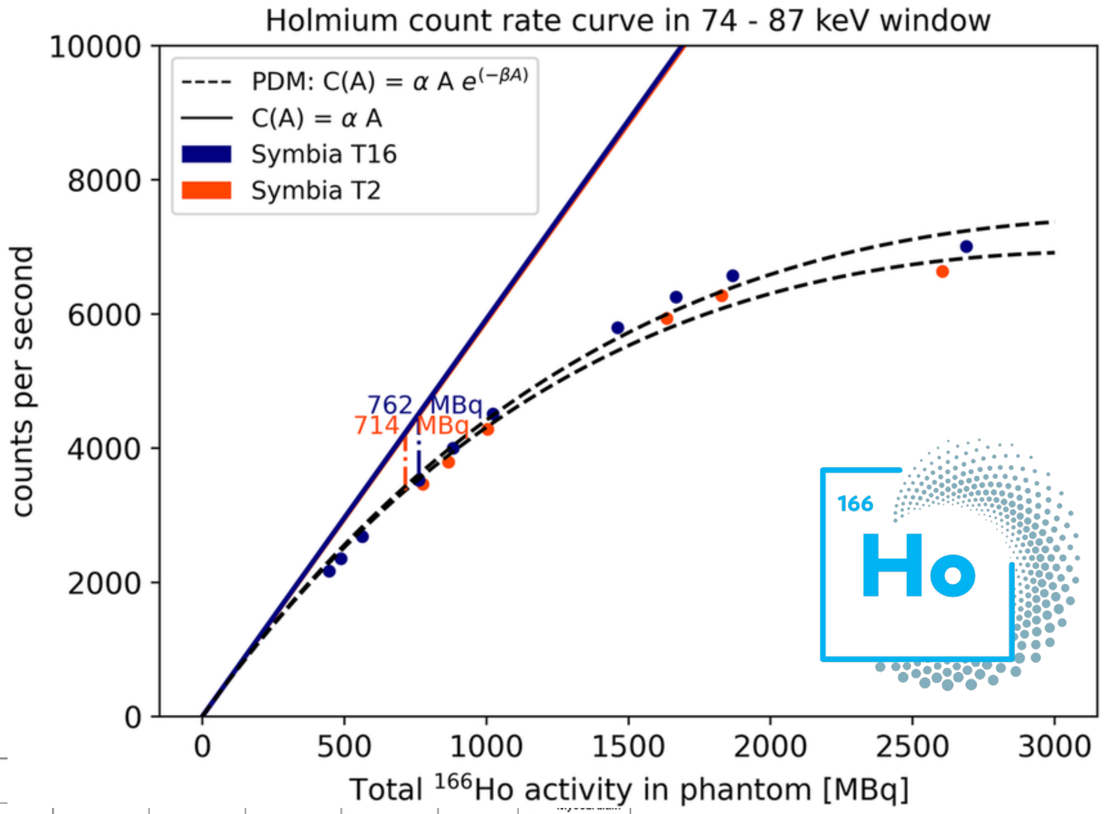


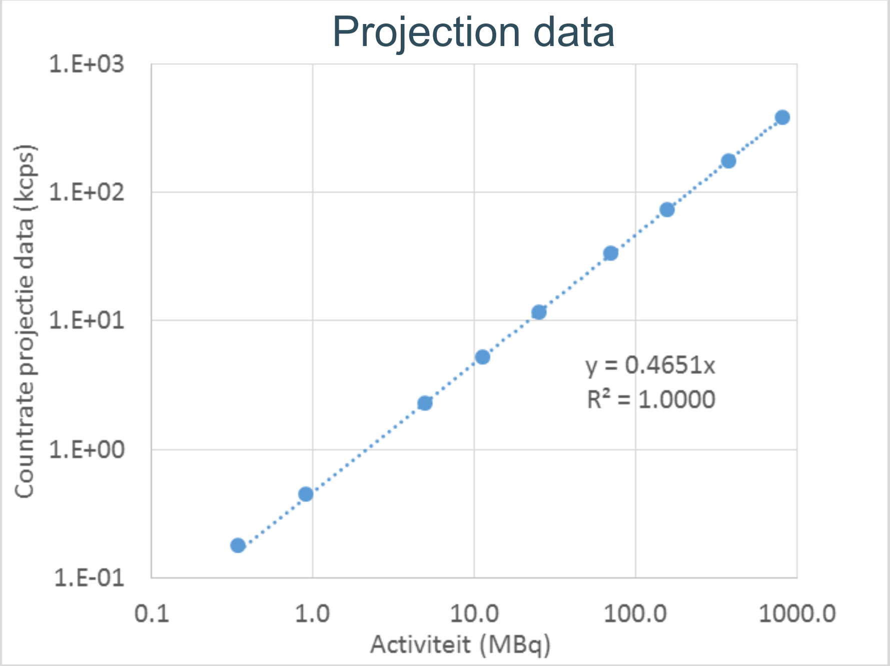
SPECTRUM DYNAMICS MEDICAL

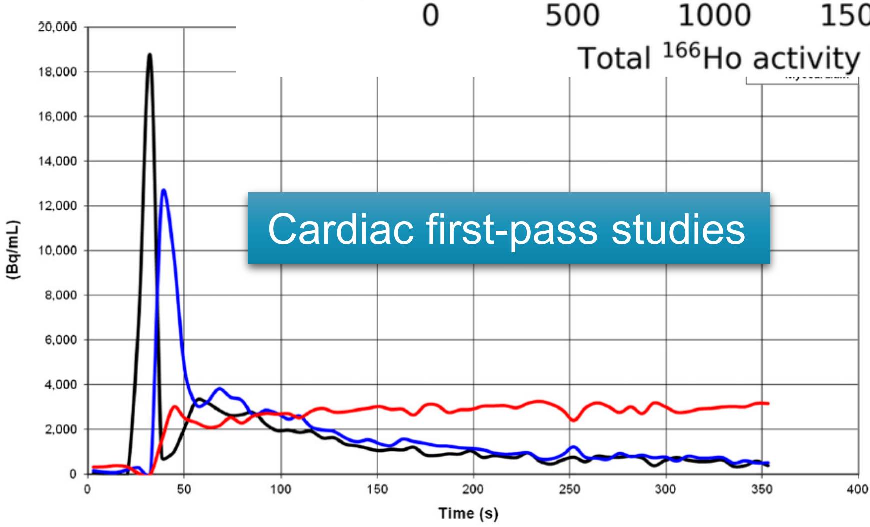
Ritt, Semin Nucl Med, 2022, 52:276-285

Count rate performance

- detector dead time – count loss
- particularly important for NaI(Tl) detector
- high energy photons (^{166}Ho-SIRT)
- CZT almost no count loss (e.g. therapy)





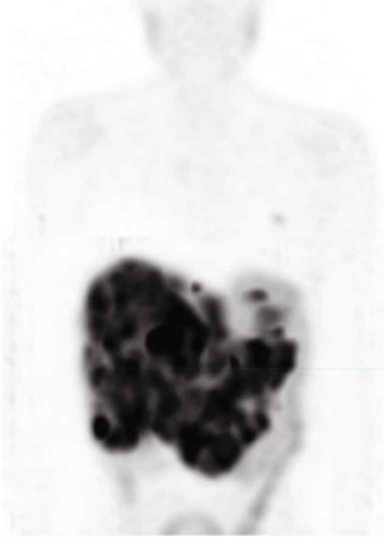


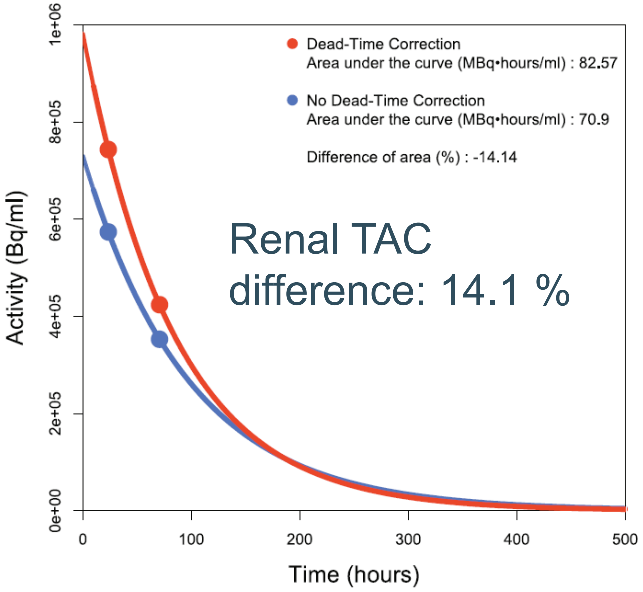
Stella, M., *et al.* EJNMMI Phys 8, 22 (2021)
doi.org/10.1186/s40658-021-00372-9

Dead-time correction for NaI(Tl) based SPECT cameras

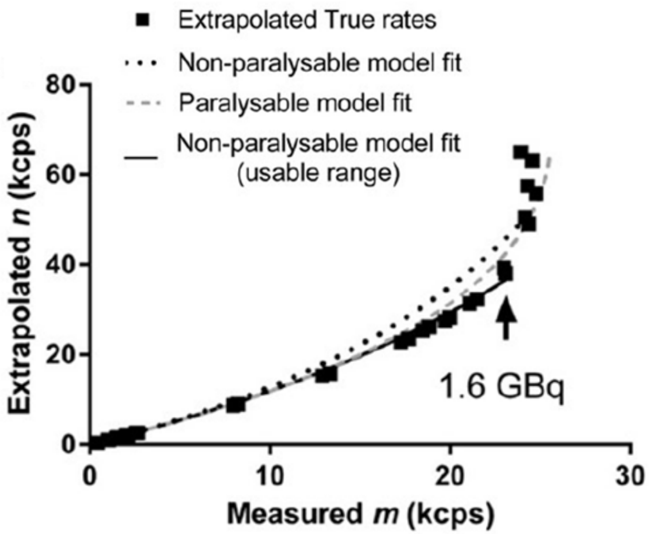
- investigation of system behaviour might take some time, and bring extra costs like e.g. making available large amounts of activity (not required to be a radiopharmaceutical)
- underestimation of activity in extensive disease without dead-time correction
- with new CZT technology, dead-time might become a substantially lesser problem

^{177}Lu-PRRT

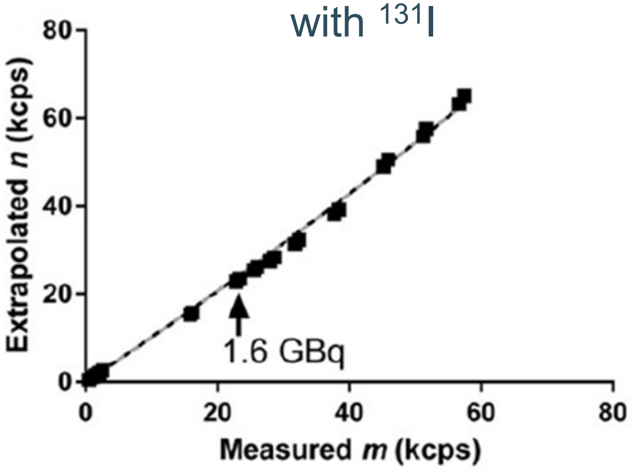




Desy *et al.* *EJNMMI Physics* (2020) 7:32
https://doi.org/10.1186/s40658-020-00303-0



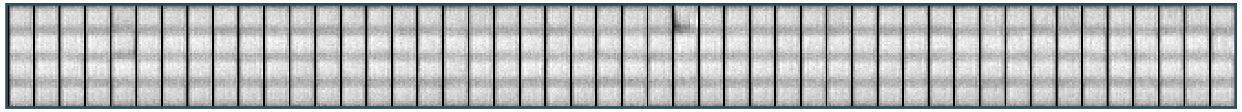
"Fast-mode imaging" with ^{131}I



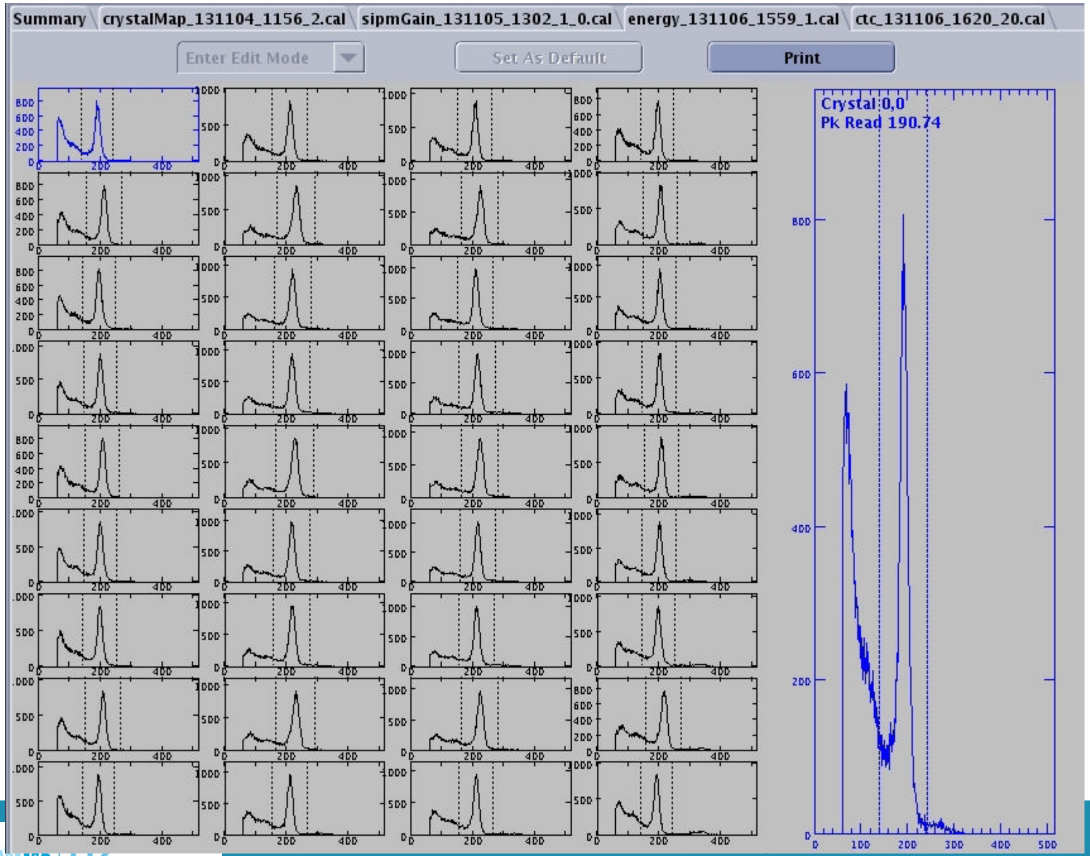
Rebecca A Gregory *et al* 2019 *Phys. Med. Biol.* **64** 245013

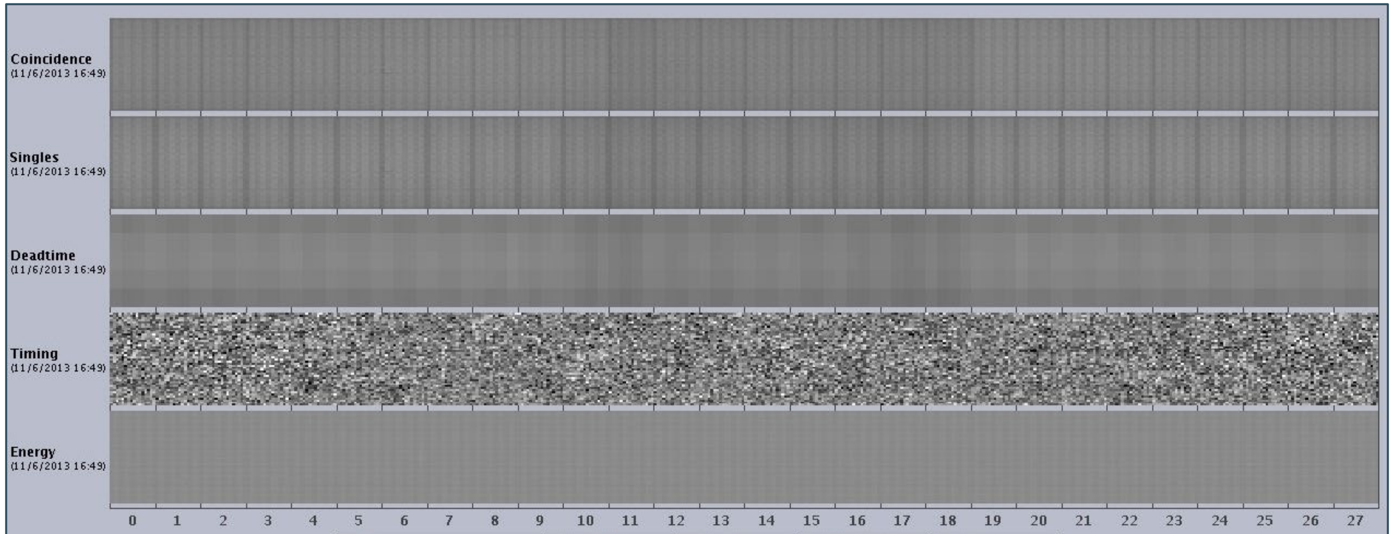
PET – assessing detector response

- energy analysis & uniformity
- sinogram/projection



- daily QC – typically incorporated in an automated startup procedure

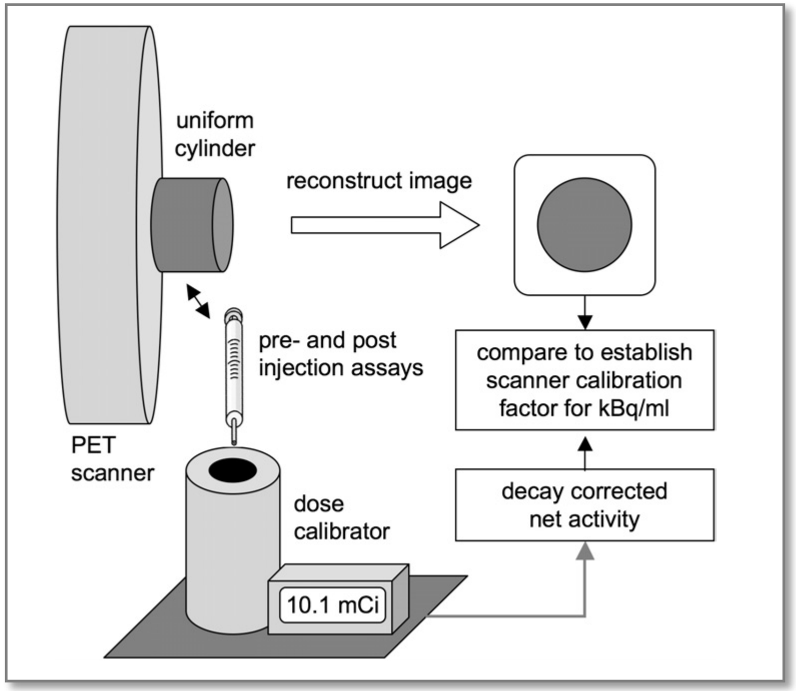




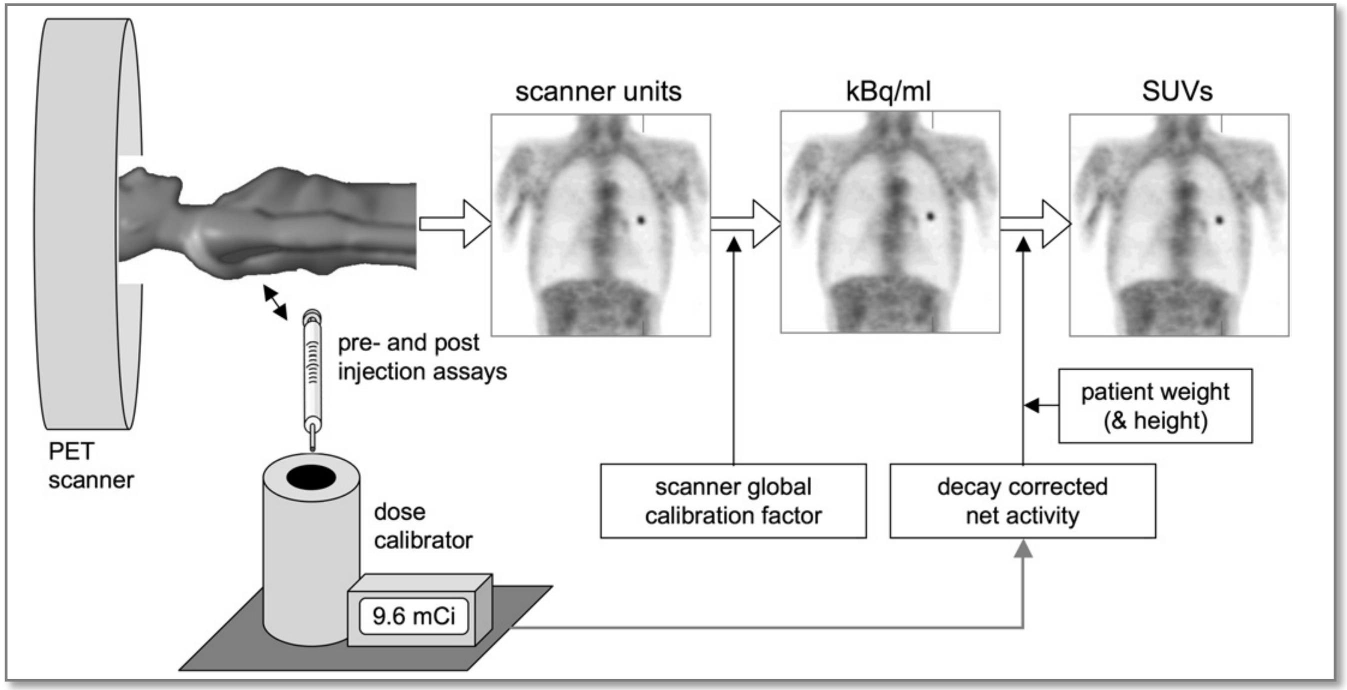
Item	Low Limit	High Limit	Current Reading	R/Y/G
PET Coincidence Mean	38725.75	43669.46	41236.83	Green
PET Coincidence Variance	3346.03	3773.18	3566.09	Green
PET Singles Mean	141973.91	160098.23	151087.16	Green
PET Singles Variance	377.33	425.50	401.48	Green
PET Deadtime Mean	0.00002	0.04749	0.01750	Green
PET Timing Mean	-0.09685	0.02315	-0.03312	Green
PET Energy Shift	-8.00	8.00	0.05	Green

Coincidence Rate	Singles Rate	Block Busy	Timing Changes	Gain Changes	Temperature Status	Module ID Mismatch	Source Phantom Life
No Data is Out of Limits	No Data is Out of Limits	No Data is Out of Limits	No Data is Out of Limits	No Data is Out of Limits	No Data is Out of Limits	All Module ID Match	Source Life Is 824 days
Green	Green	Green	Green	Green	Green	Green	Green

PET radionuclide calibrator cross-calibration



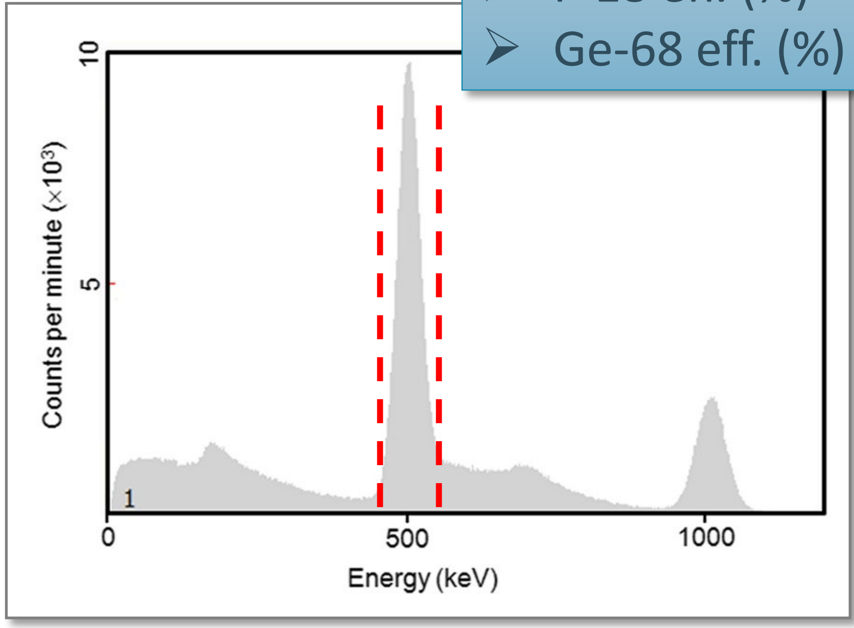
- uniform cylinder with ^{18}F solution
- radionuclide calibrator (RC) measure (Bq)
- known cylinder volume (ml)
- known Bq/ml → measured cpm/voxel
- cross-calibration factor determined



- same RC used for patient administration
- measured cpm/voxel
- converted to Bq/ml, SUV, …

Internal calibration using gamma counter

- problem for radionuclides with short $T_{1/2}$
  - ^{11}C, ^{13}N, ^{15}O, ^{68}Ga, …
- positron emitters -> narrow *E* window
  - correction factor for positron branching ratio



> ➢ F-18 eff. (%) = 34.2 cps/positron
> ➢ Ge-68 eff. (%) = 33.2 cps/positron

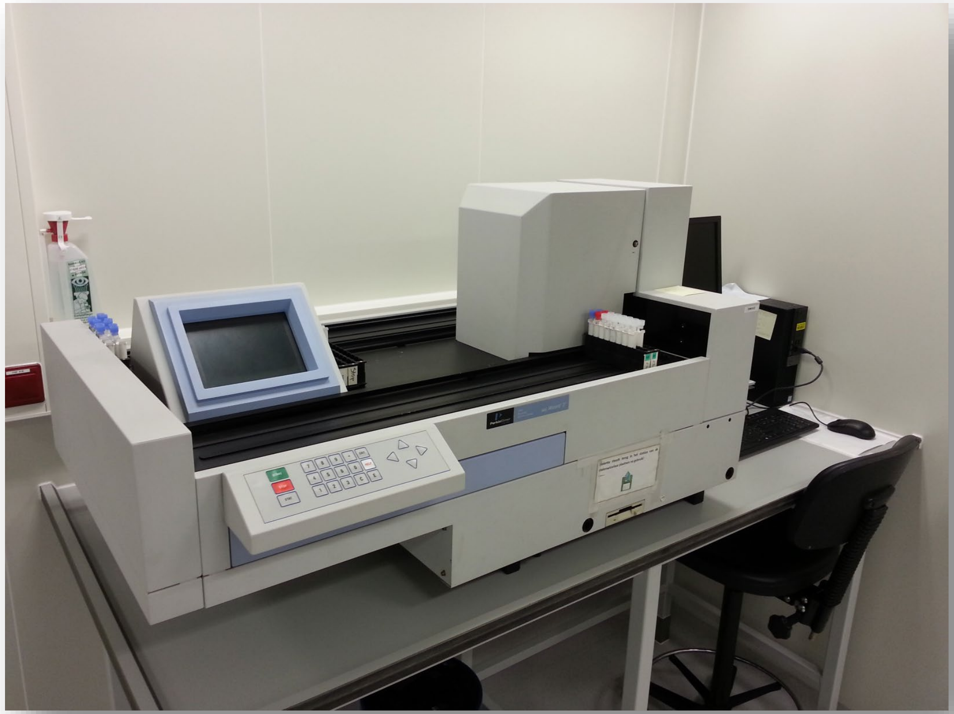


Table 1 Experimental measurements of gamma counter efficiency (mean ± SD) for ^{18}F and $^{68}Ge/^{68}Ga$

Isotope	Efficiency (%)	Positron fraction	Efficiency (%)/positron fraction
^{18}F	34.4 ± 0.18	0.97	35.5 ± 0.18
$^{68}Ge/^{68}Ga$	30.1 ± 0.07	0.89	33.8 ± 0.07

Both isotopes were measured using a 409- to 613-keV energy window.

Lodge et al., EJNMMI Physics (2015) 2:11

Quality assurance – gamma counter efficiency

- ^{68}Ge reference sources
- mean eff. (%) = 33.5 ± 0.4 cps/pos

Eckert & Ziegler
Isotope Products

Medical Imaging Laboratory
24937 Avenue Tibbitts Valencia, California 91355
Tel 661·309·1010 Fax 661·257·8303
Industrial Gauging and Medical Imaging Laboratory
1800 North Keystone Street Burbank, California 91504
Tel 661·309·1010 Fax 661·257·8303

CELEBRATING 50 YEARS Eckert & Ziegler Isotope Products 1967 · 2017

**CERTIFICATE OF CALIBRATION
GAMMA STANDARD SOURCE**

Radionuclide:	Ge-68	Customer:	IDB HOLLAND BV
Half-life:	270.8 ± 0.3 days	P.O. No.:	04040/19JAN
Catalog No.:	GF-0318-220N	Reference Date:	2017-02-01 12:00 PST
Source No.:	1924-30-2	Contained Radioactivity: (Ge-68 only)	225.7 nCi 8351 Bq

Physical Description:
- A. Capsule type: T (12 mm diameter x 75 mm length)
- B. Nature of active deposit: Dispersed in epoxy matrix
- C. Active diameter/volume: Approximately 0.71mL (0.7124 grams; balance filled with inactive epoxy)
- D. Backing: Plastic
- E. Cover: Plastic

Radioimpurities:

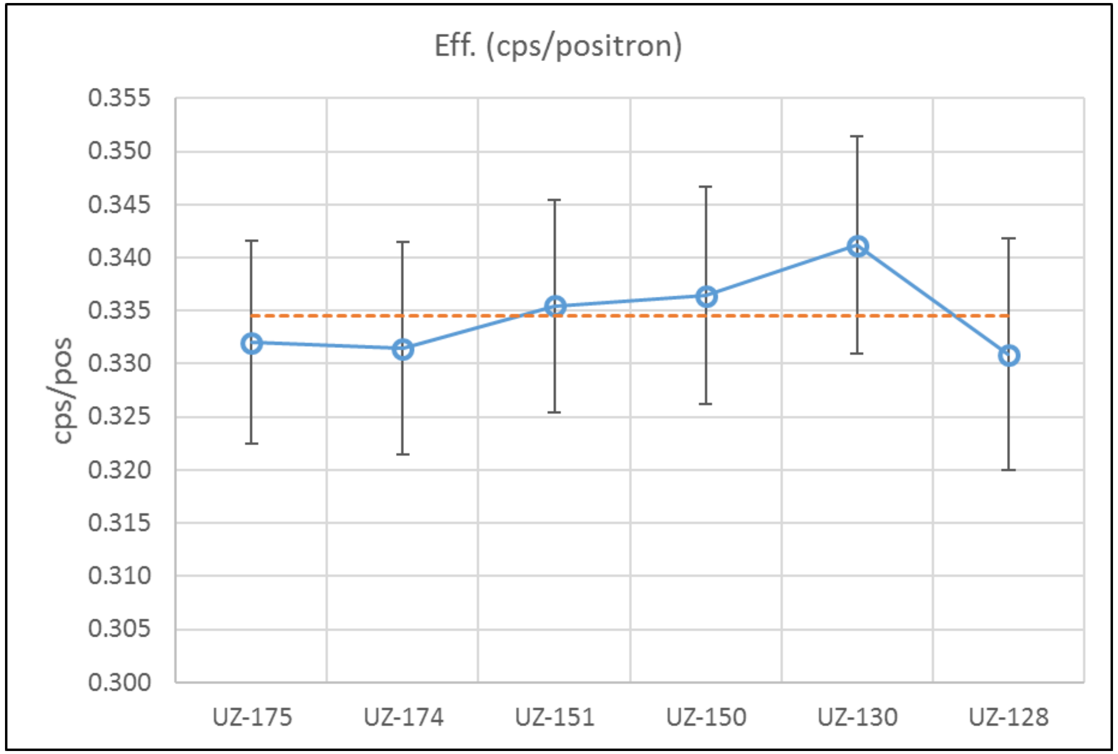
None detected (Ga-68 daughter in equilibrium)

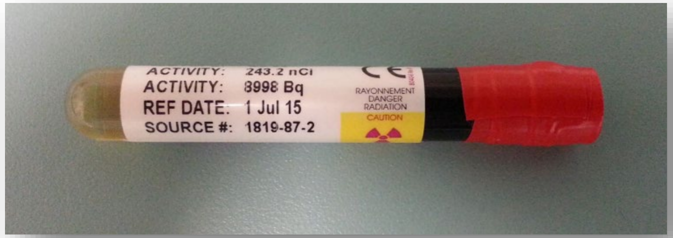
Method of Calibration:

This source was prepared from a weighed aliquot of solution whose activity in µCi/g was determined using a pressurized well type ionization chamber.

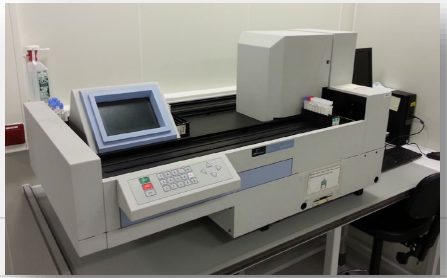
Uncertainty of Measurement:
- A. Type A (random) uncertainty: ± 0.0 %
- B. Type B (systematic) uncertainty: ± 3.0 %
- C. Uncertainty in aliquot weighing: ± 0.0 %
- D. Total uncertainty at the 99% confidence level: ± 3.0 %

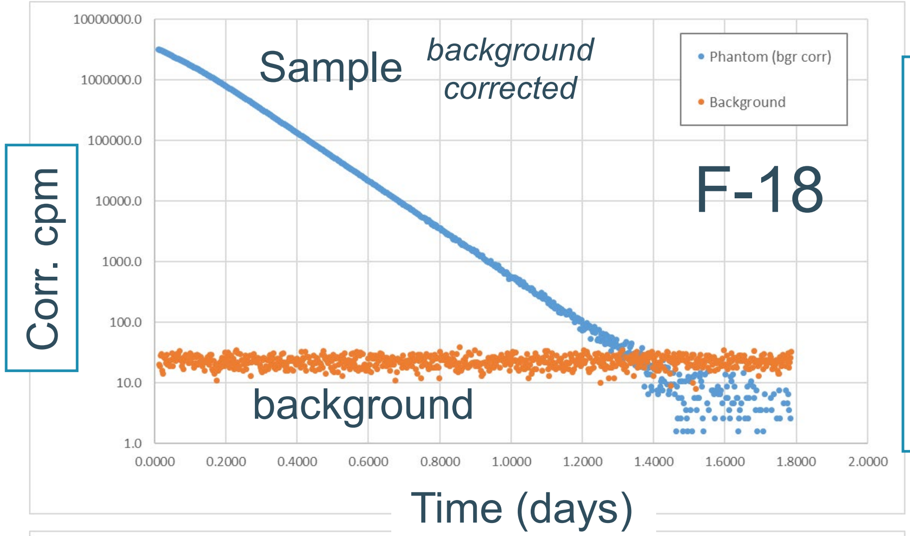
Notes:
- See reverse side for leak test(s) performed on this source.
- This document uses the date convention YYYY-MM-DD in accordance with ISO 8601.
- EZIP participates in a NIST measurement assurance program to establish and maintain implicit traceability

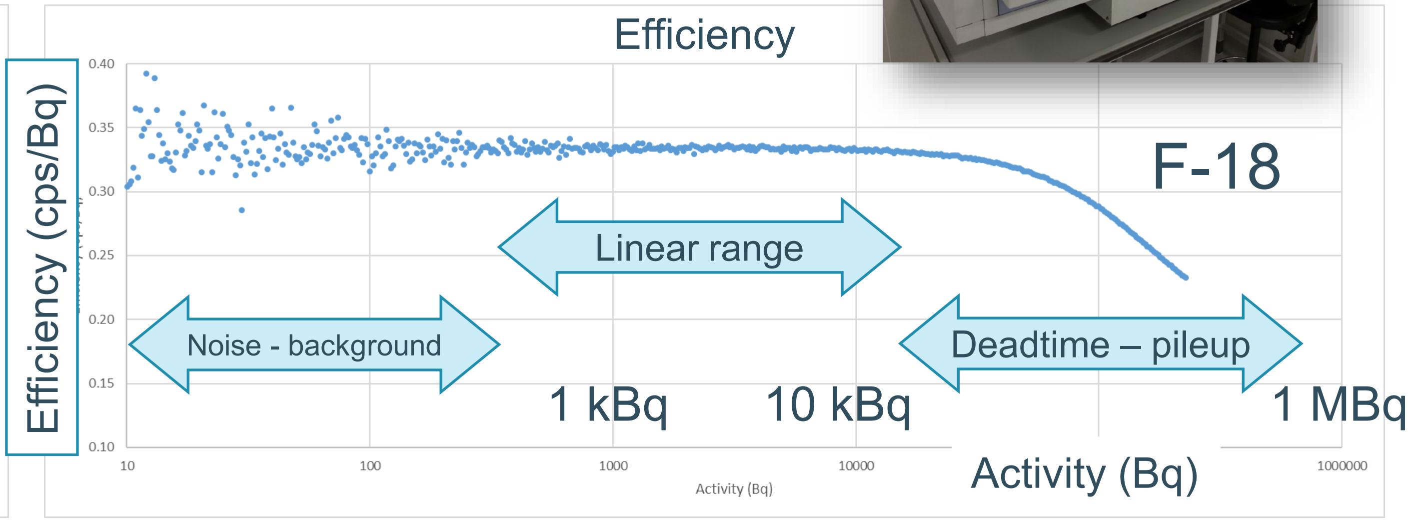


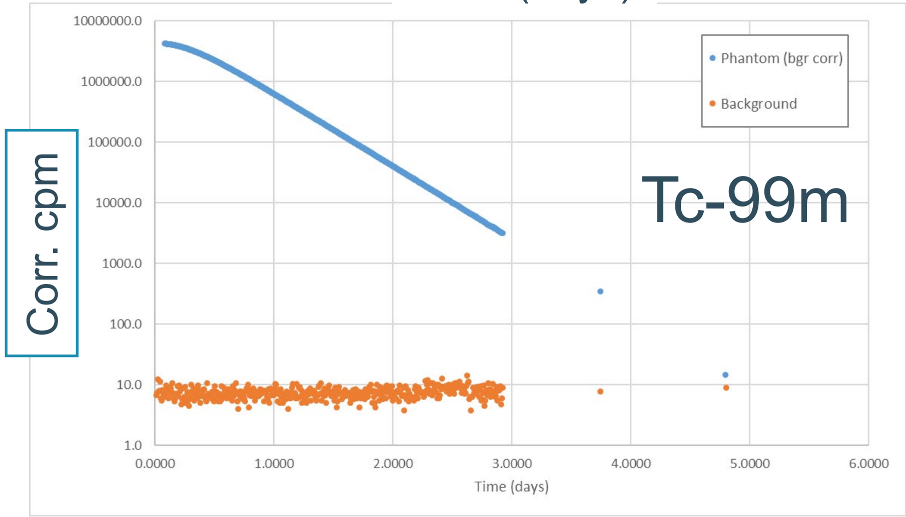


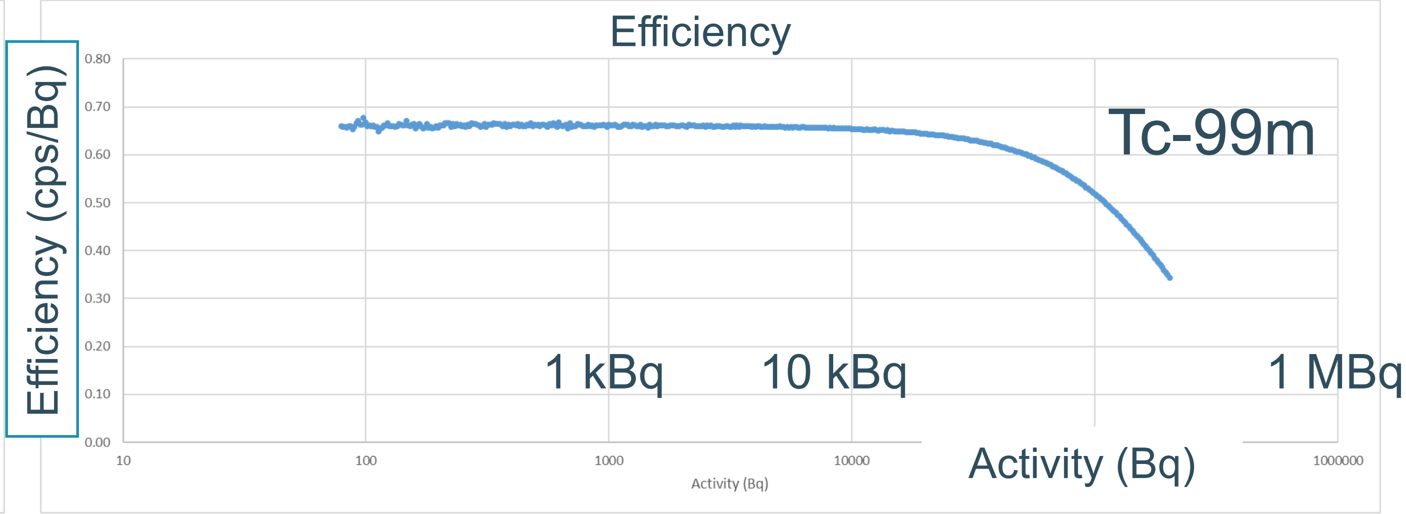
Linearity analysis – gamma counter





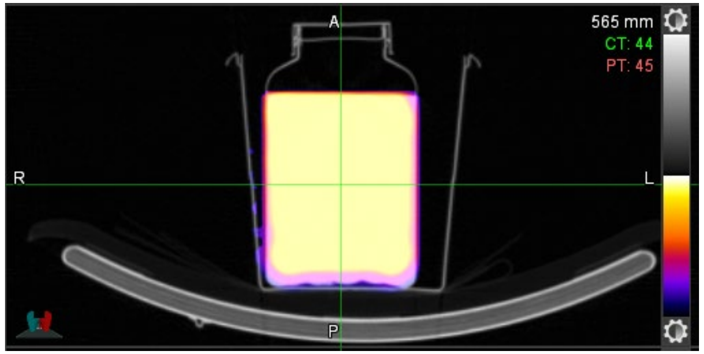




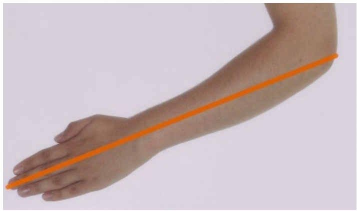


Nuclear Medicine Equipment Standards

- a quantified and traceable measure using an NM instrument
  - numerical value – relative or absolute measure
  - physical quantity – (SI) unit of measurement
- nuclear medicine (NM) instruments
  - radionuclide calibrator or activity meter (Bq)
  - gamma counter samples (Bq/ml)
  - SPECT phantom (cps/voxel)
  - quantitative PET/CT or SPECT/CT (Bq/ml)
- calibration step
  - conversion between units
- verification and follow-up
  - QA & QC, incl. Q-management



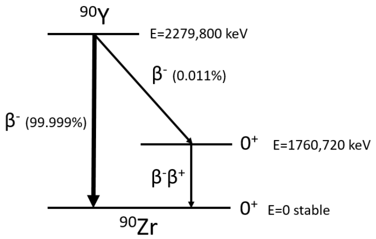
Standardization and QC

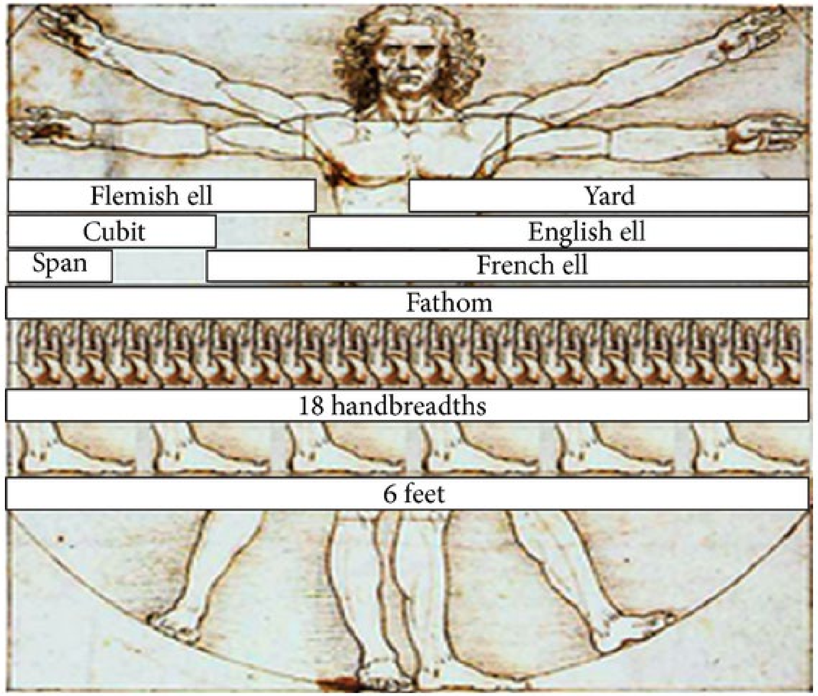


Mark H. Stone, "The Cubit: A History and Measurement Commentary", *Journal of Anthropology*, vol. 2014, 489757, 11 pp, 2014

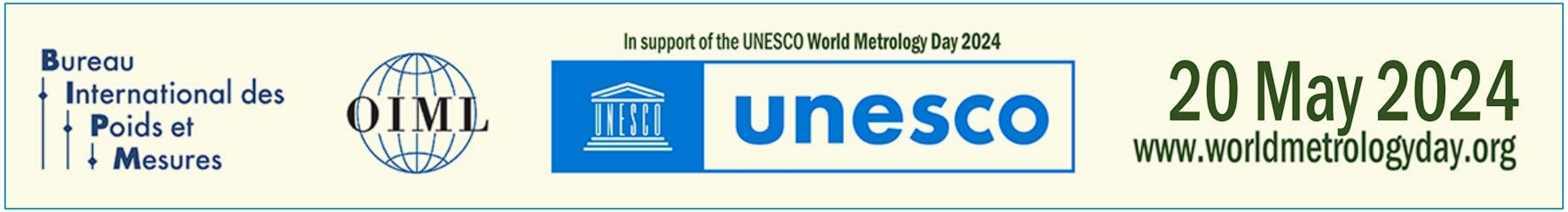
- the challenge of standardization is not new
  - ell (ulna) – cubit (forearm)
- nuclear data, half-life, e.g. branching ratio for positron emission of ^{90}Y in PET acquisition software
  - device A : 3<u>2</u> $\times 10^{-6}$
  - device B : 3<u>4</u> $\times 10^{-6}$

Branching ratio
Bq ←→ e^+



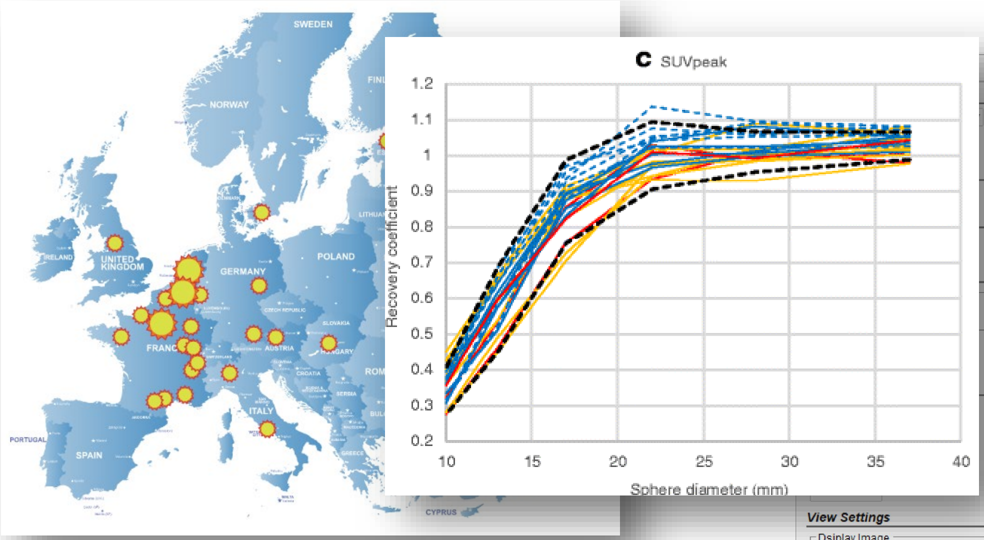


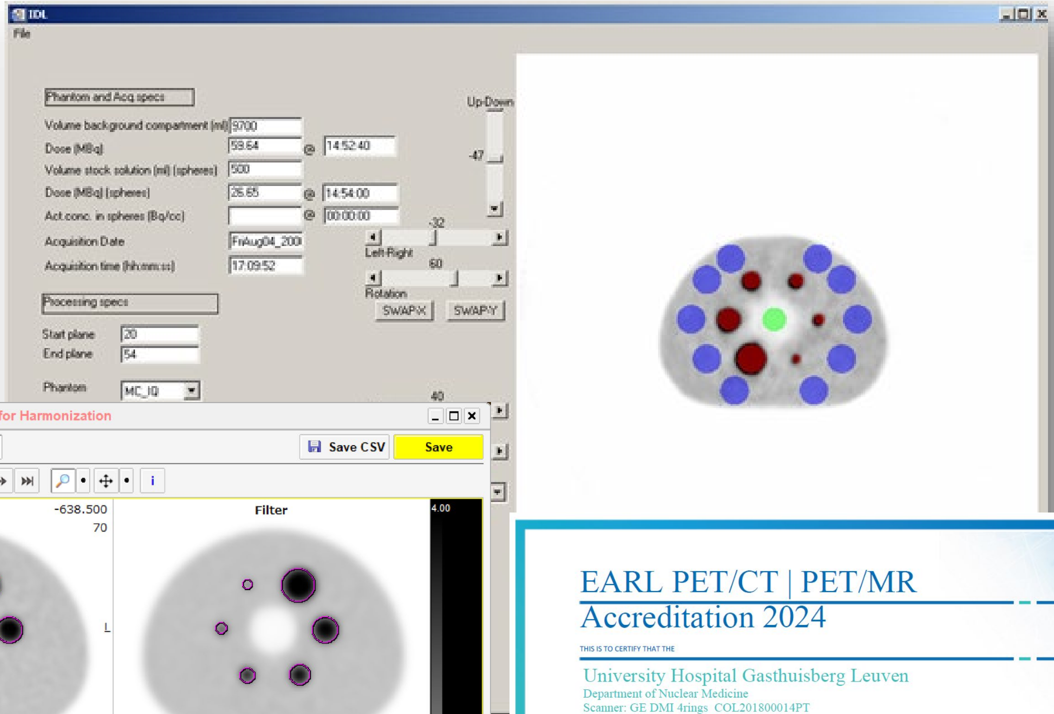
- imaging standards (DICOM, ISO-12052, …)
  - time references & decay correction
- it looks like … there's much more need for standardization, even <u>before</u> calibration / verification (QC)

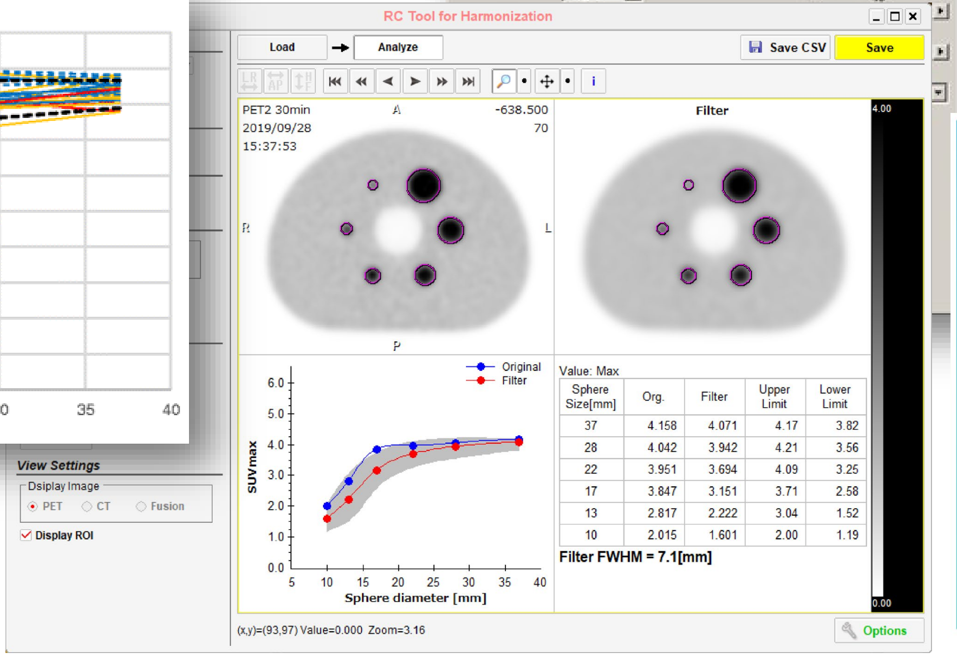


Standardization in PET and SPECT

- international effort → accreditation of PET
- SUV & image quality verification
- harmonization for multicenter trials



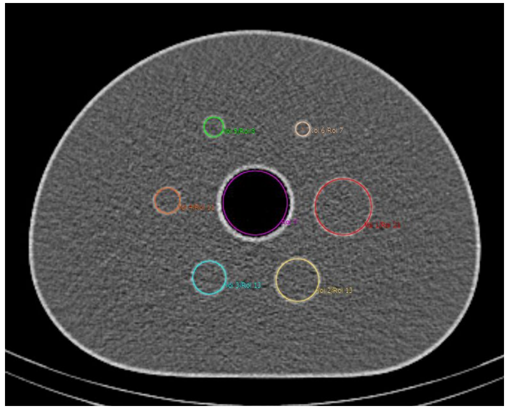


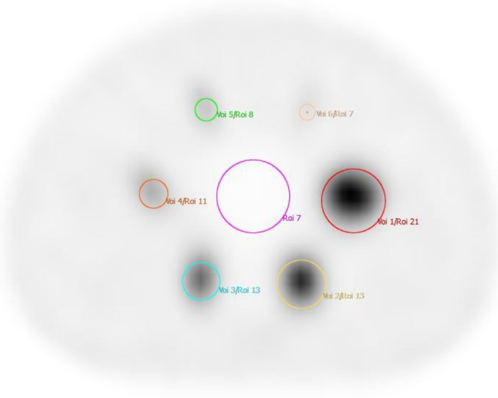


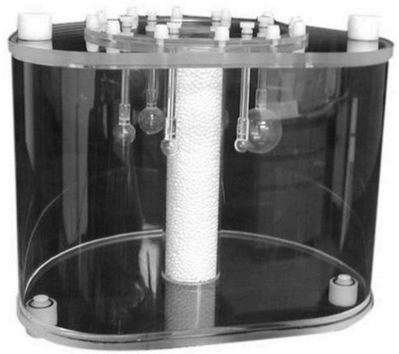
Daisaki, H. *et al.*, *Sci Rep* **11**, 8517 (2021)
Kaalep, A. *et al.*, *EJNMMI* **45**, 1344–1361 (2018)

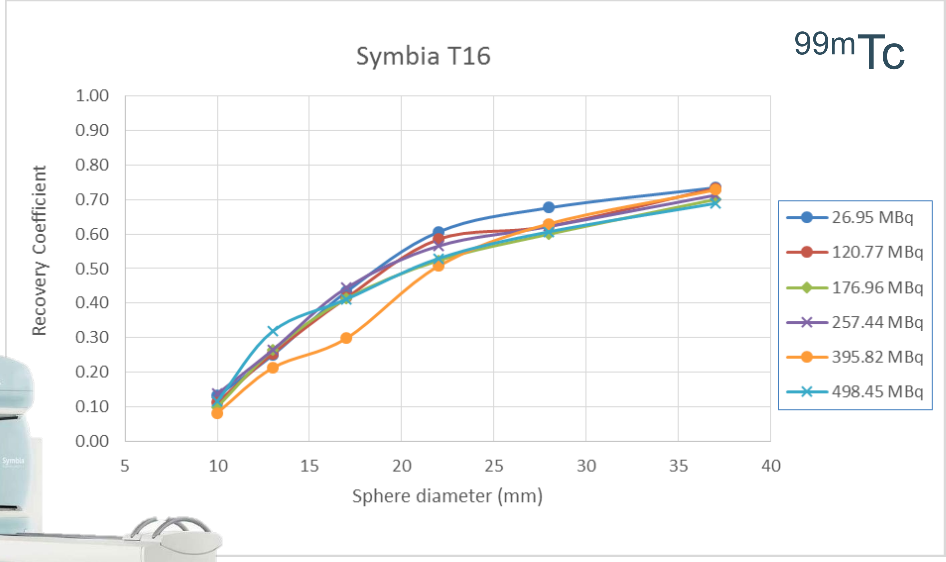
Image Quality for 2 clinical SPECT-CT systems

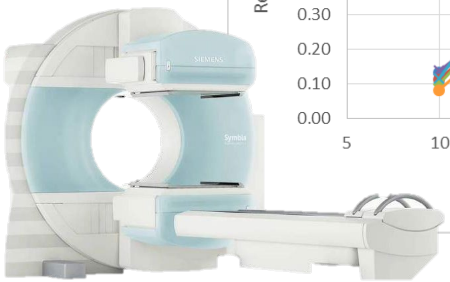
- variety of activity concentrations
- quantitative capabilities of SPECT/CT
- reproducibility and accuracy
- performance of the imaging system
- accreditation for ^{177}Lu-SPECT in prep

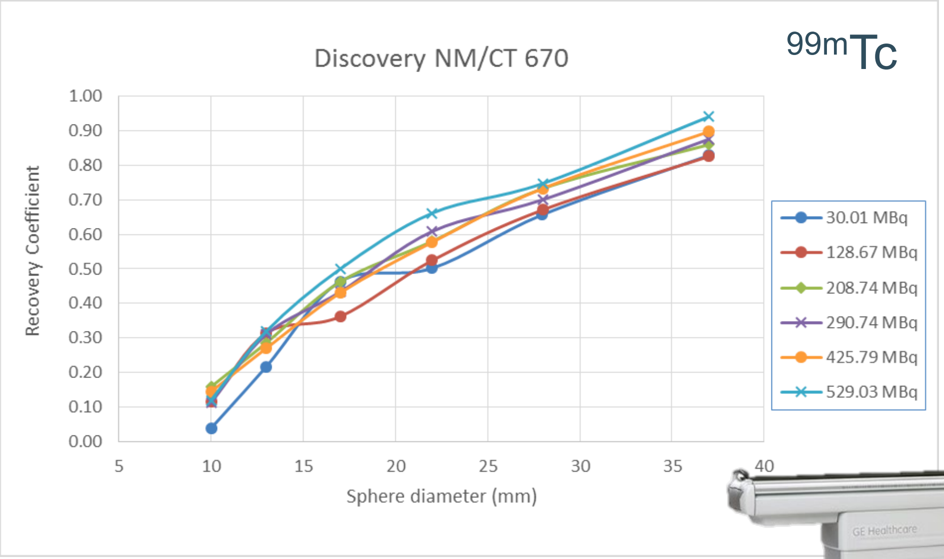












MSc. thesis Burak Yalvac (2016)

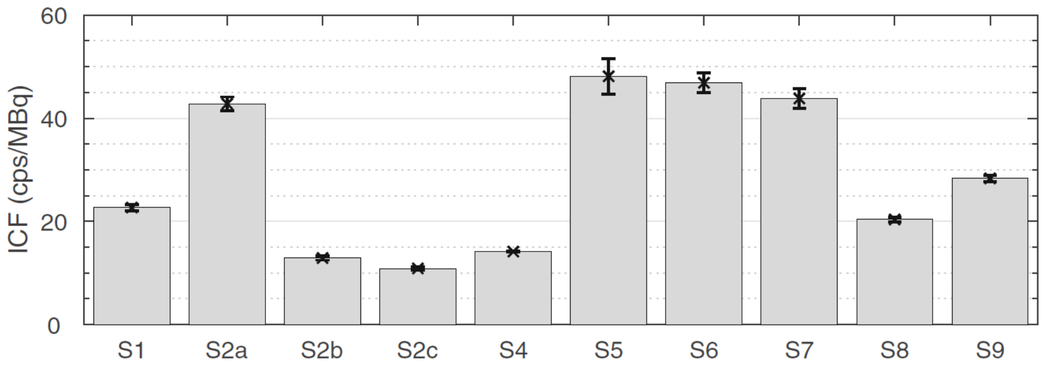
Feasibility of harmonization: intercomparison exercises

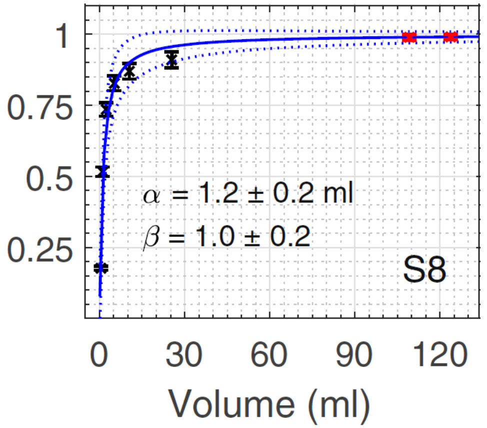
A multicentre and multi-national evaluation of the accuracy of quantitative Lu-177 SPECT/CT imaging performed within the MRTDosimetry project

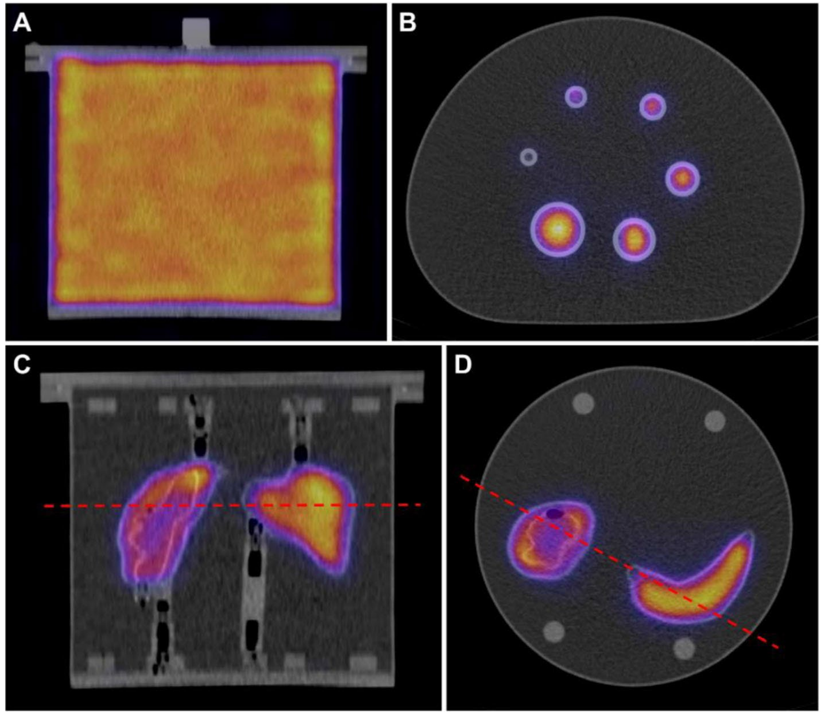
MRT DOSIMETRY
Metrology for clinical implementation of dosimetry in molecular radiotherapy

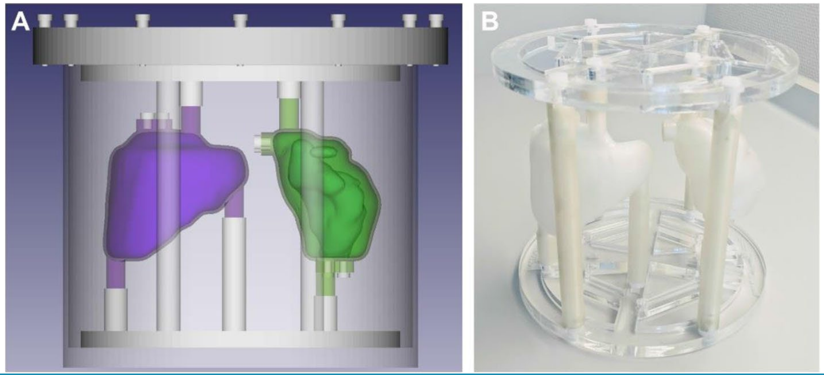
Tran-Gia *et al. EJNMMI Physics* (2021) 8:55
https://doi.org/10.1186/s40658-021-00397-0

- setup-specific image calibration factors (ICF) and recovery curves (RC) of a variety of SPECT/CT systems for quantitative imaging



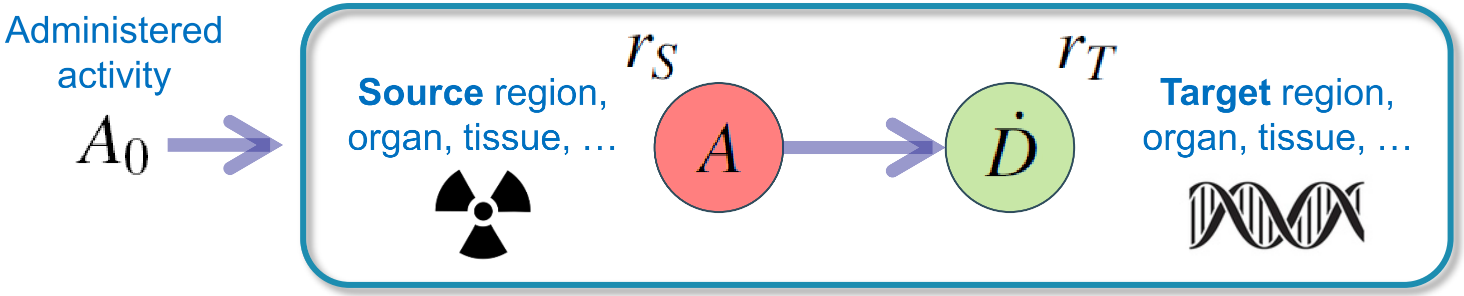






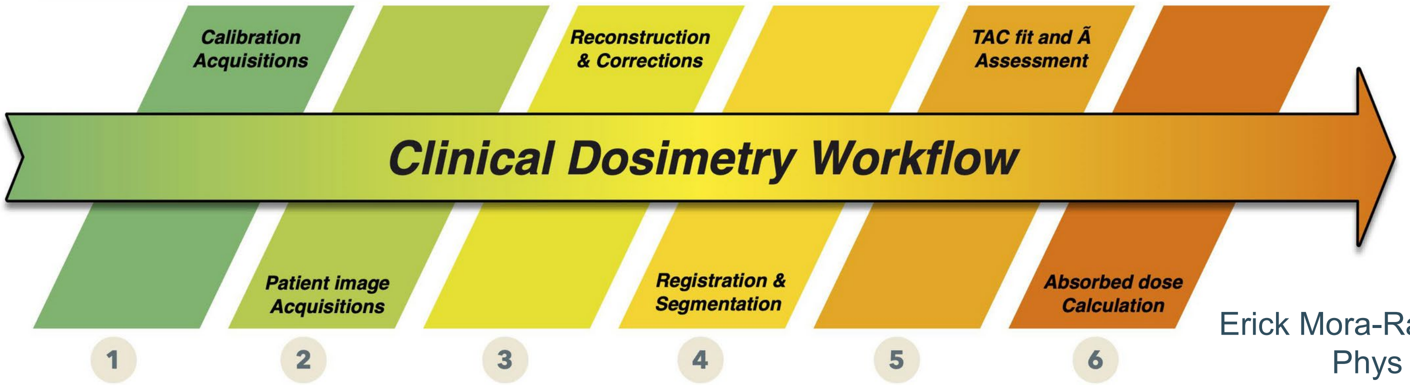
QC for dosimetry and therapy planning

- <u>General aim</u>: the absorbed dose to target region(s)

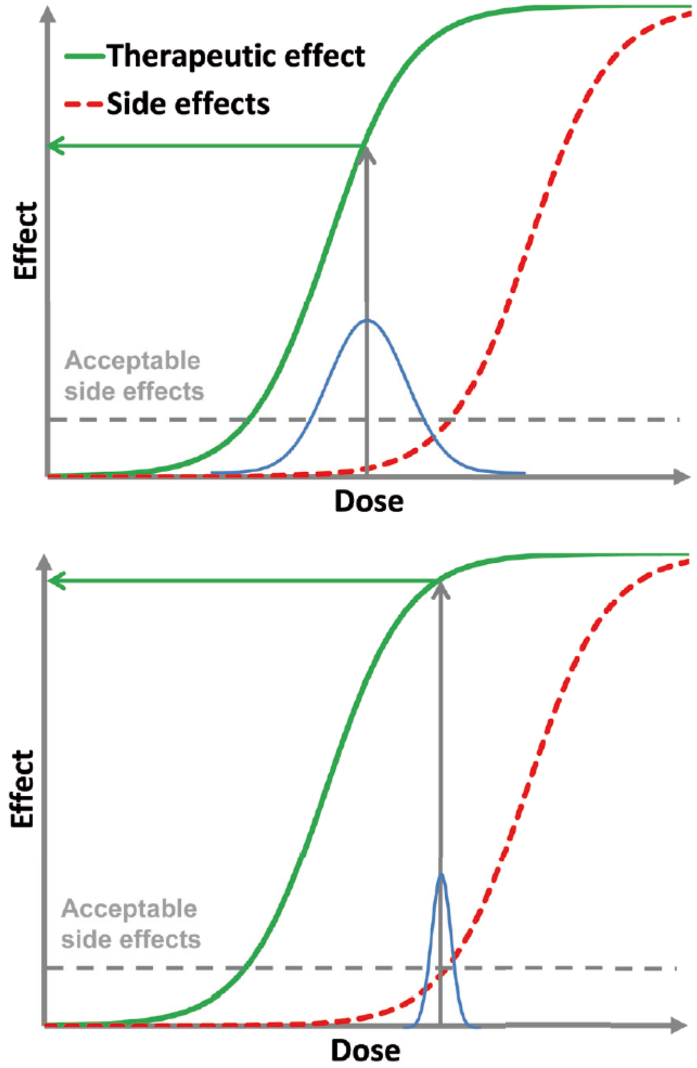


$$\dot{D}(t) \propto A(t)$$

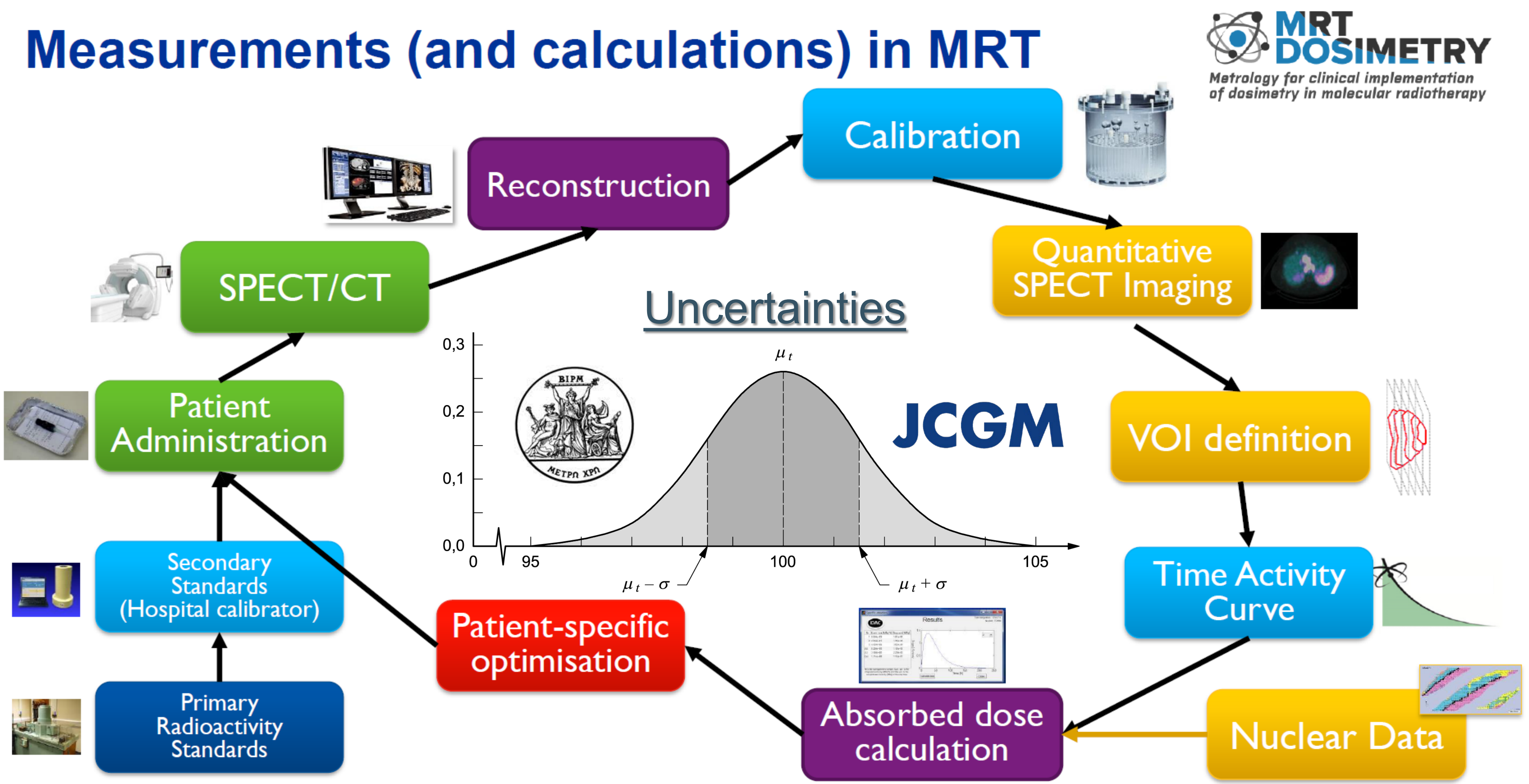
$$D(r_T) = \int_0^{T_D} \dot{D}(r_T, t)\,dt$$



Erick Mora-Ramirez *et al.*, Med Phys 47 (9), Sept 2020



Measurements (and calculations) in MRT



National Physical Laboratory - 20th May 2019

EMPIR EURAMET

The EMPIR initiative is co-funded by the European Union's Horizon 2020 research and innovation programme and the EMPIR Participating States

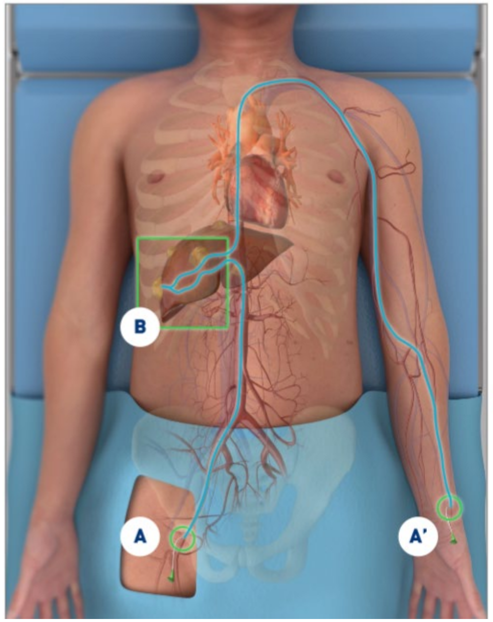
Selective Internal Radiation Therapy (SIRT)

- primary liver tumors: HCC, ICC
- liver predominant metastatic disease: mCRC, breast, NET
- SIRT portfolio @ UZ Leuven
  - ^{90}Y – SIR-Spheres – Sirtex Medical Europe GmbH
  - ^{90}Y – TheraSphere – Boston Scientific Benelux NV
  - ^{166}Ho – QuiremSpheres – Quirem Medical, Terumo
- patient selection & work-up (CBCT, SPECT)
- pre- & post-SIRT procedures & analysis

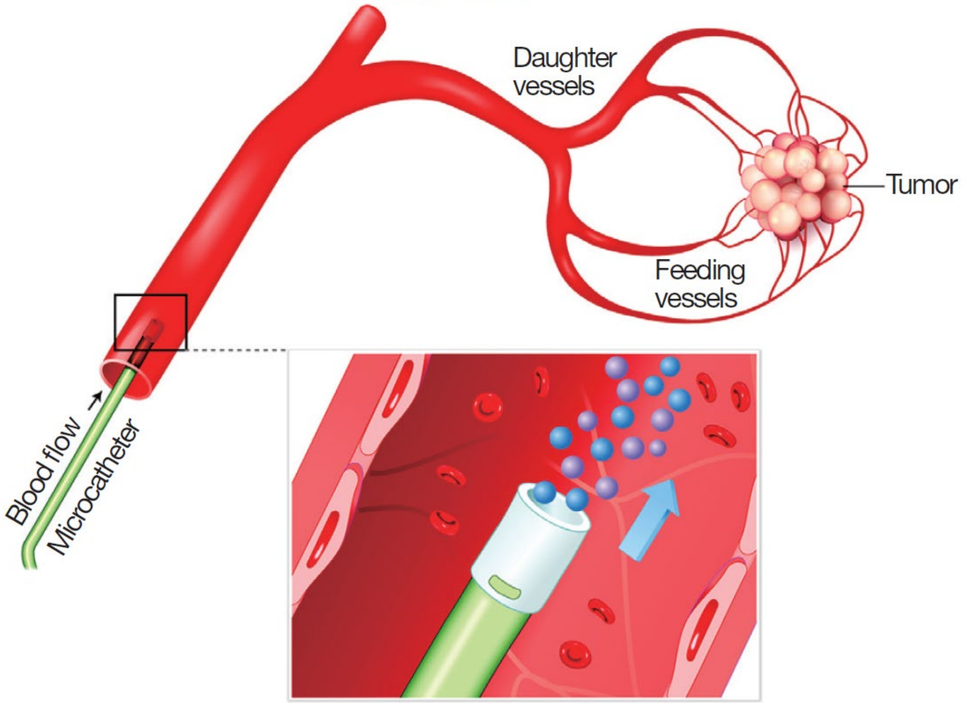
SIR-Spheres® Y-90 resin microspheres

QuiremSpheres®

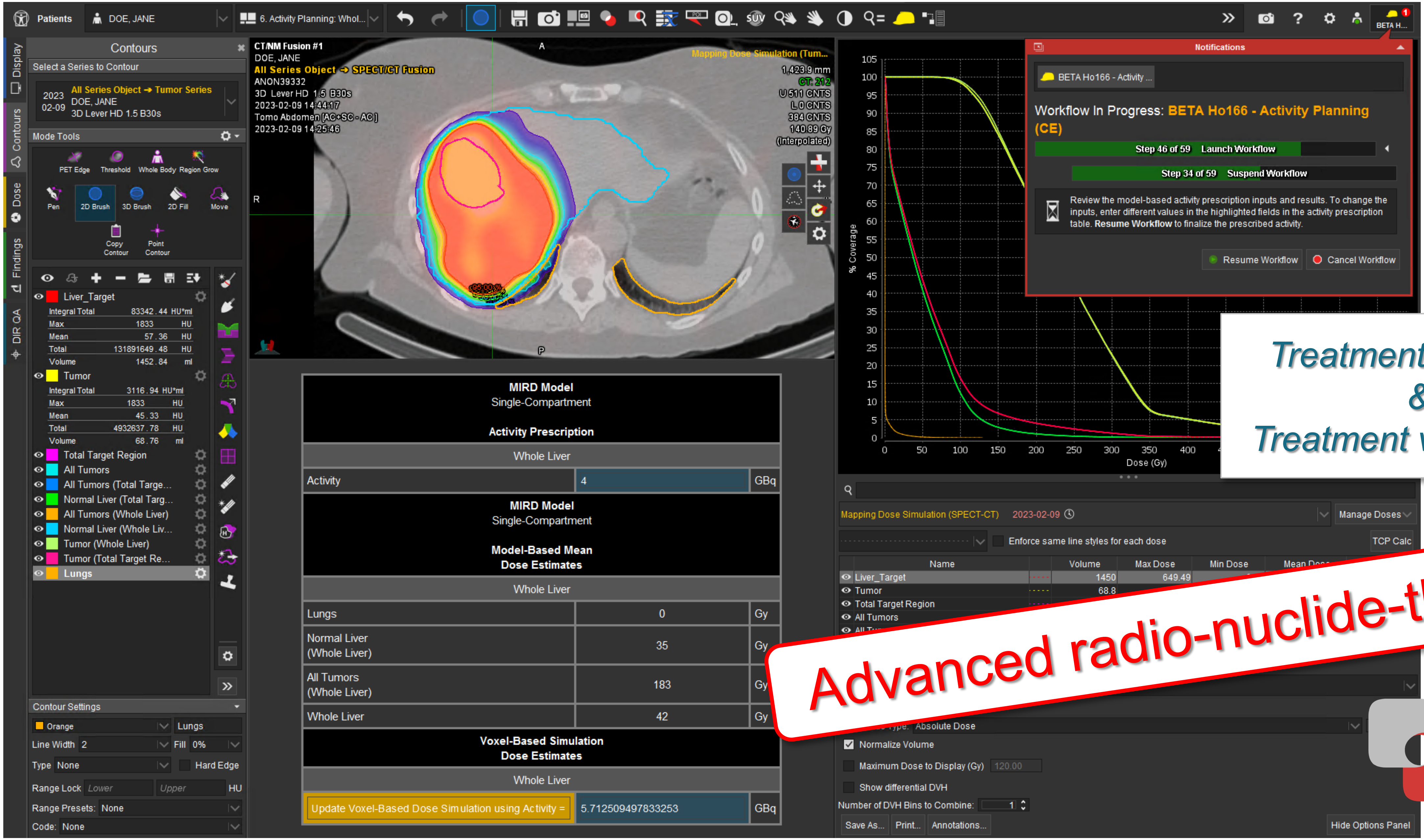
TheraSphere®



SIRTeX



Kennedy, J Gastrointest Oncol. 2014;5(3):178-189

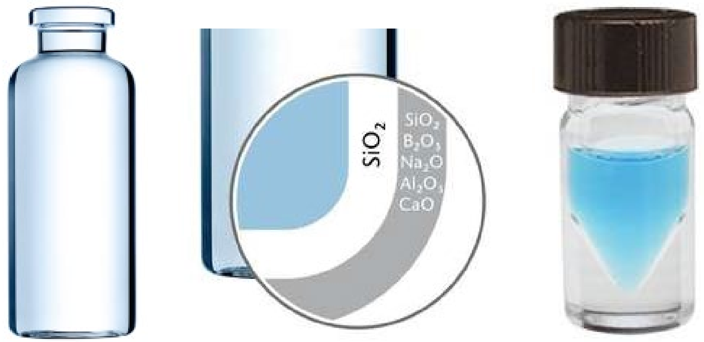


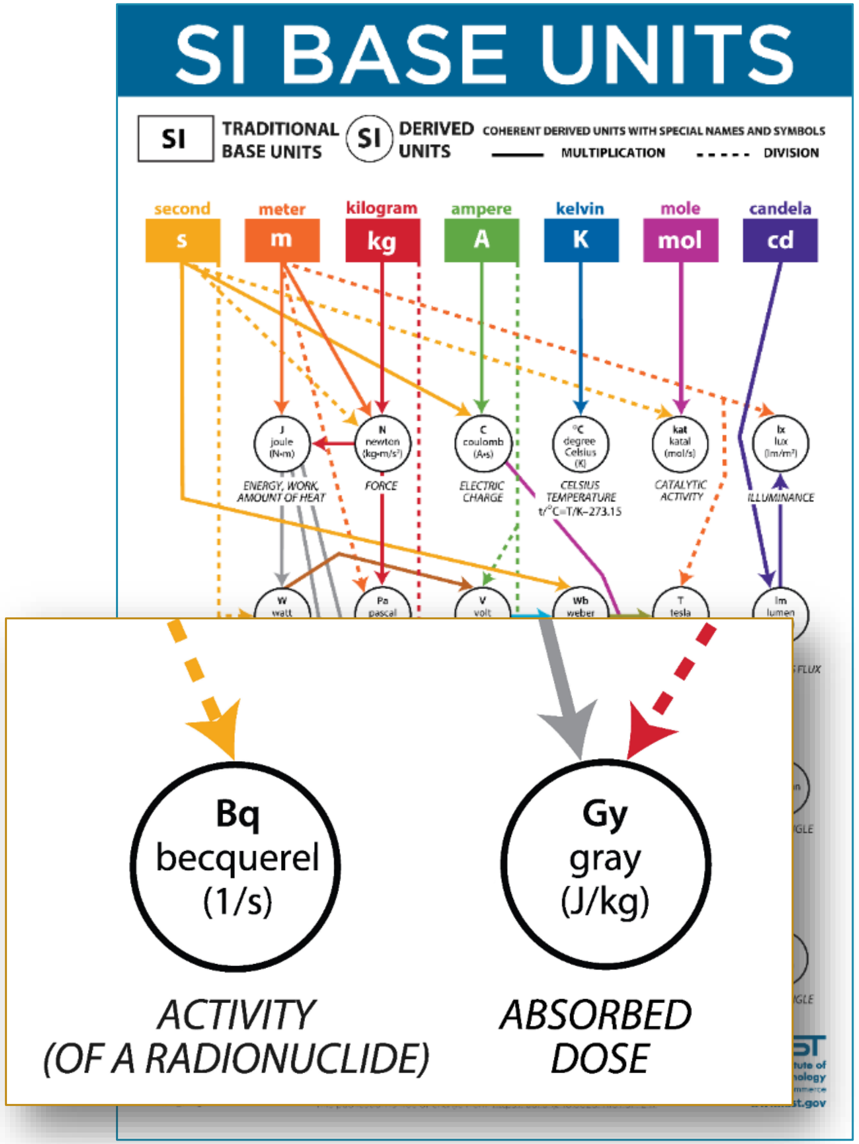
Treatment planning
&
Treatment verification

Advanced radio-nuclide-therapy

Standardization challenges in NM

- crossing the valley of death – translational research
  - global : regulatory – radioprotection – medicines agencies
  - local : health physics – radiopharmacy – clinical environment
- closing gaps between radiopharmacy and medical physics
  - use of standardised recipients : V-vial, 10R Type 1+ Schott vial, …
- approach manufacturers
- approach R-pharma suppliers
- approach EMA, FDA, …



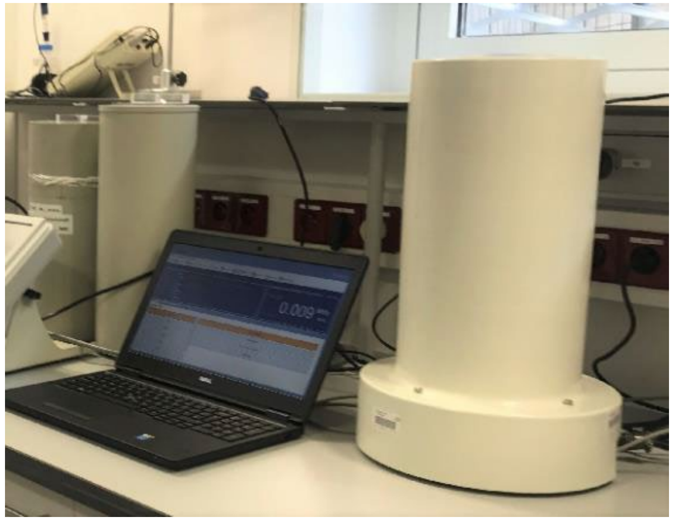


Special Publication (NIST SP) – 1247
https://doi.org/10.6028/NIST.SP.1247

NIST National Institute of Standards and Technology

Calibration challenges in NM

- the "calibration" problem is typically not intercepted by standard quality assurance measures in nuclear medicine (unfortunately)
- this can lead to significant inaccuracies with the determination of the activity [Bq] of a radiopharmaceutical
- more advanced quality control measures are therefore urgently required → medical physics experts & metrology experts
- theranostics: quantitative imaging for radionuclide therapy and personalized dosimetry are based on this



World Health Organization

IAEA

TRS-374 – Calibration of Dosimeters Used in Radiotherapy (IAEA, 1994)

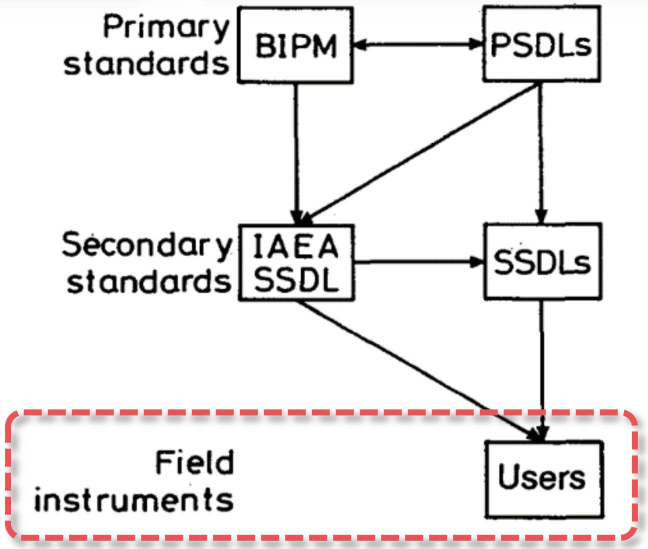


FIG. 1. The international measurement system.

Traceability of radionuclide calibrators

Physica Medica 45 (2018) 134–142

Contents lists available at ScienceDirect

Physica Medica

journal homepage: www.elsevier.com/locate/ejmp

ELSEVIER

Physica Medica
European Journal of Medical Physics

Original paper

Intercomparison of ^{99m}Tc, ^{18}F and ^{111}In activity measurements with radionuclide calibrators in Belgian hospitals

Check for updates

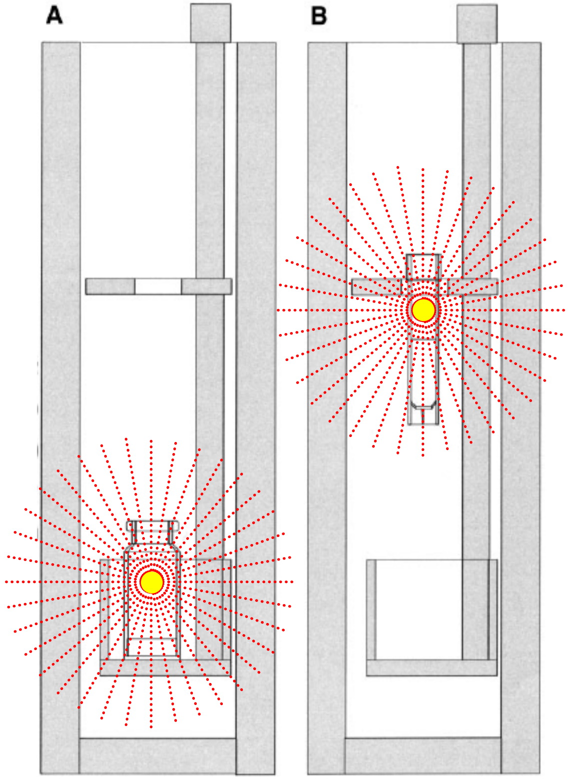
Clarita Saldarriaga Vargas[a,*], Sunay Rodríguez Pérez[a], Kristof Baete[b,c], Stefaan Pommé[d], Jan Paepen[d], Raf Van Ammel[d], Lara Struelens[a]

[a] Belgian Nuclear Research Centre (SCK·CEN), Boeretang 200, 2400 Mol, Belgium
[b] UZ Leuven, Department of Nuclear Medicine, Herestraat 49, 3000 Leuven, Belgium
[c] KU Leuven, Department of Imaging and Pathology, Herestraat 49, 3000 Leuven, Belgium
[d] European Commission, Joint Research Centre (JRC), Directorate for Nuclear Safety and Security, Retieseweg 111, 2440 Geel, Belgium

sck cen
Belgian Nuclear Research Centre

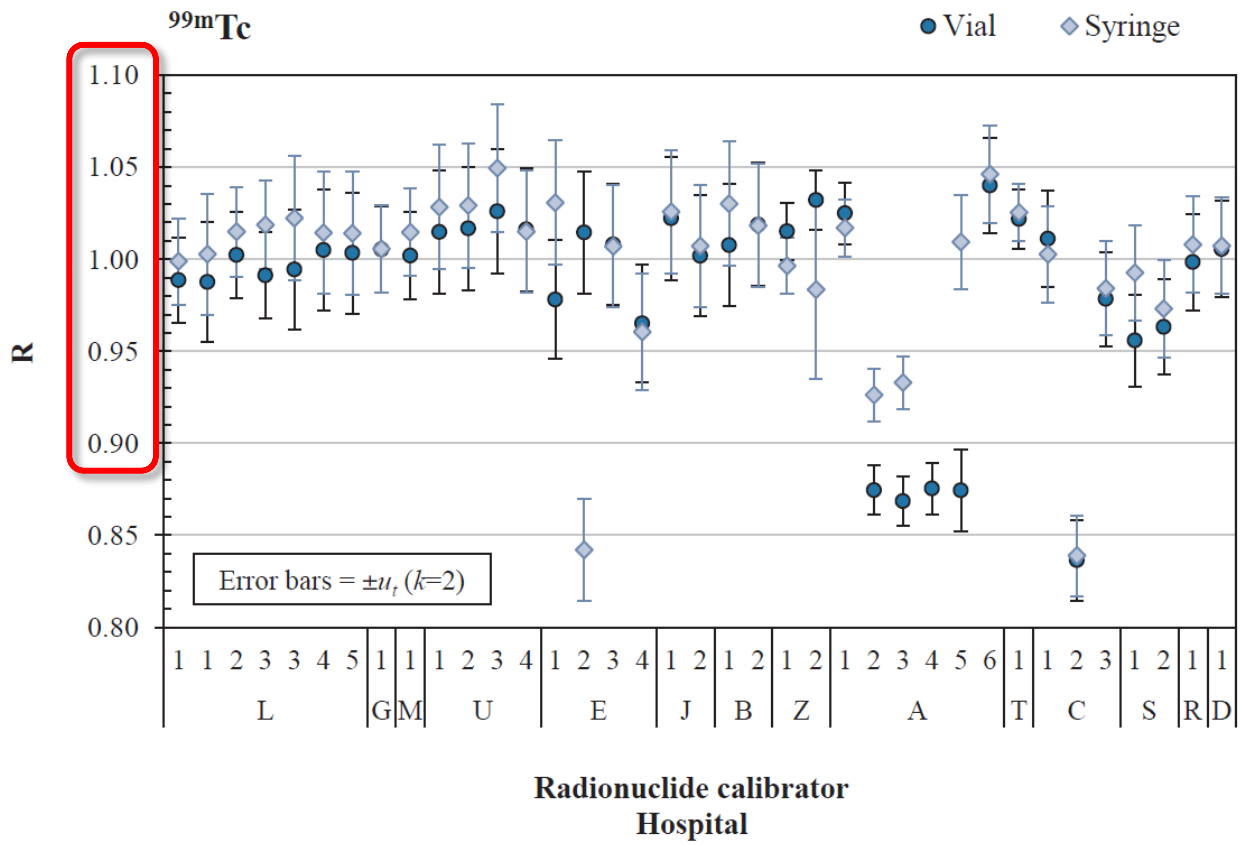
European Commission

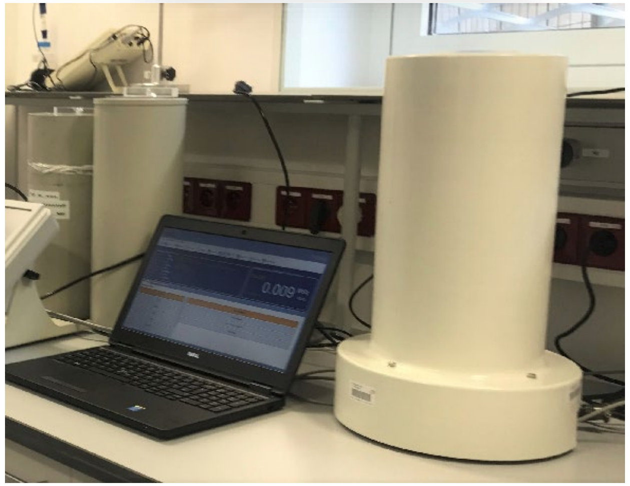
irmm
Institute for Reference Materials and Measurements



Traceability of radionuclide calibrators

- results for Tc-99m
- use of Fidelis – secondary standard radionuclide calibrator





southern scientific

Saldarriaga Vargas C, et al.
Phys Med. 2018;45:134-142.

Traceability of radionuclide calibrators

- results for In-111 – *"The Good, the Bad and the Ugly"*

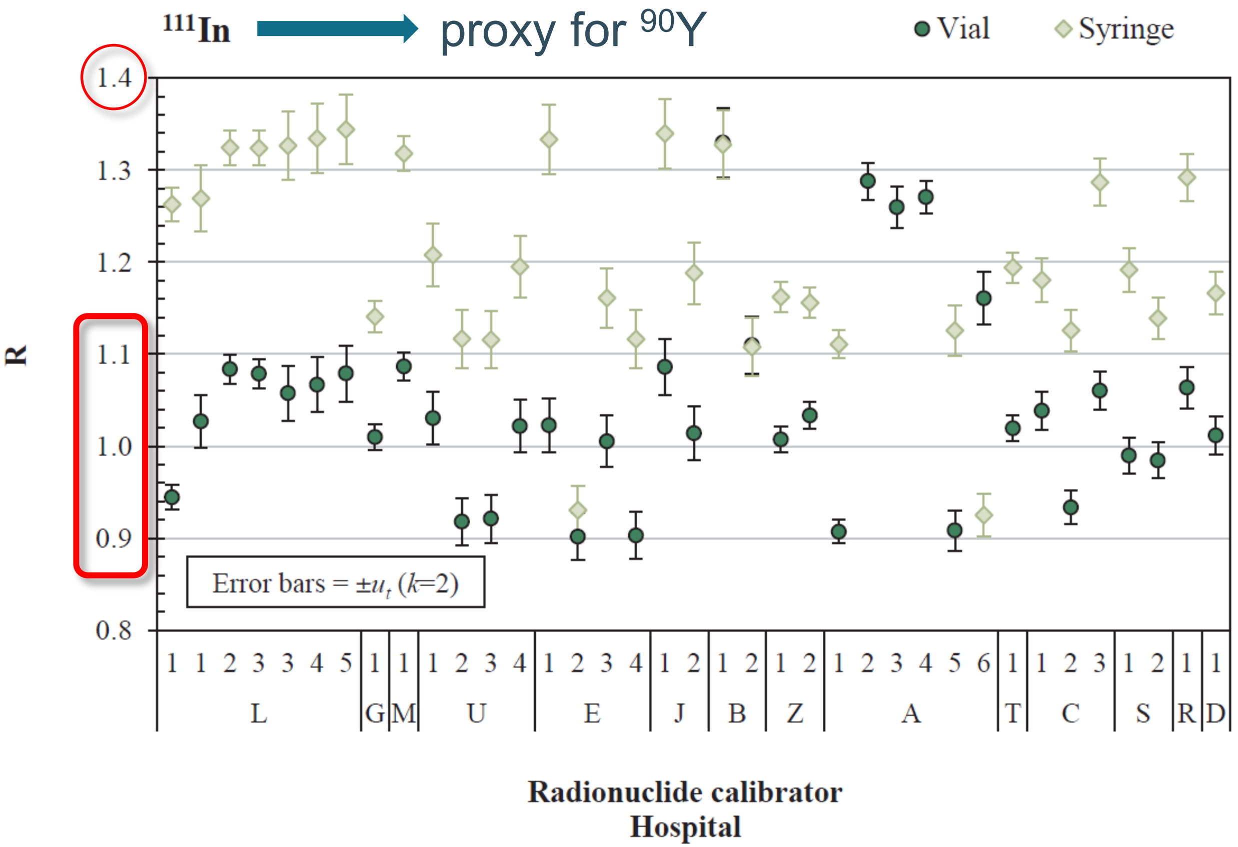
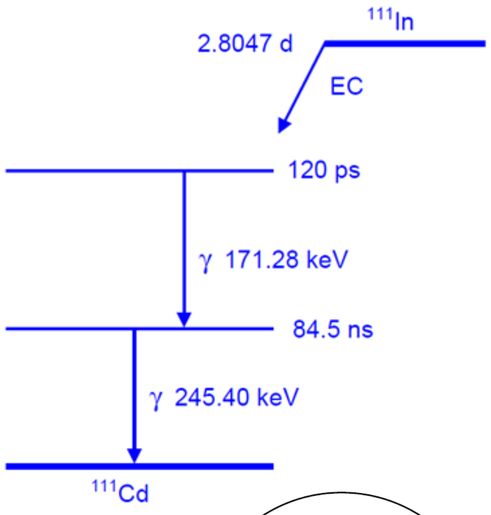
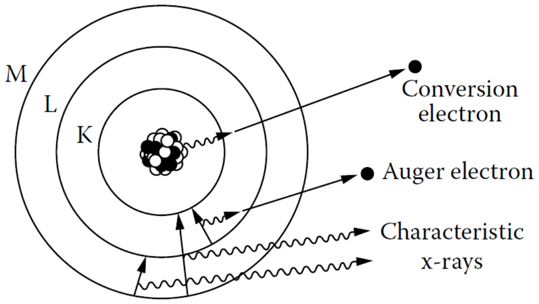


Fig. 4. Ratio of the massic activity obtained from radionuclide calibrator measurements and the reference value for samples of ^{111}In in a vial and a syringe container. RCs 1 and 3 from hospital L were measured twice (first and second measurement campaigns).





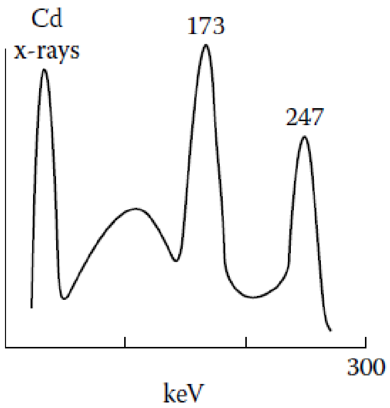


TABLE 3. Nuclear Data for ^{111}In

Principal radiation	E_i (keV)*	n_i	Equilibrium dose constant, Δ_i (rad g μCi^{-1} h^{-1})	Equilibrium dose constant, Δ_i (Gy kg Bq^{-1} s^{-1})
Auger electron	2.7	0.98	5.68E−03	4.27E−16
	19.3	0.156	6.41E−03	4.82E−16
Conversion electron	144.6	0.078	2.40E−02	1.80E−15
	167.3	0.0106	3.78E−03	2.84E−16
	170.5	0.00203	7.37E−04	5.54E−17
	171.2	0.000424	1.55E−04	1.16E−17
	218.7	0.0493	2.30E−02	1.73E−15
	241.4	0.00785	4.04E−03	3.03E−16
	244.6	0.00151	7.87E−04	5.91E−17
	245.3	0.000301	1.57E−04	1.18E−17
x-ray	3.1	0.069	4.60E−04	3.46E−17
	23	0.235	1.15E−02	8.64E−16
	23.2	0.443	2.19E−02	1.64E−15
	26.1	0.145	8.06E−03	6.06E−16
γ	171.3	0.902	3.29E−01	2.47E−14
	245.4	0.94	4.91E−01	3.69E−14

*Average electron energies.

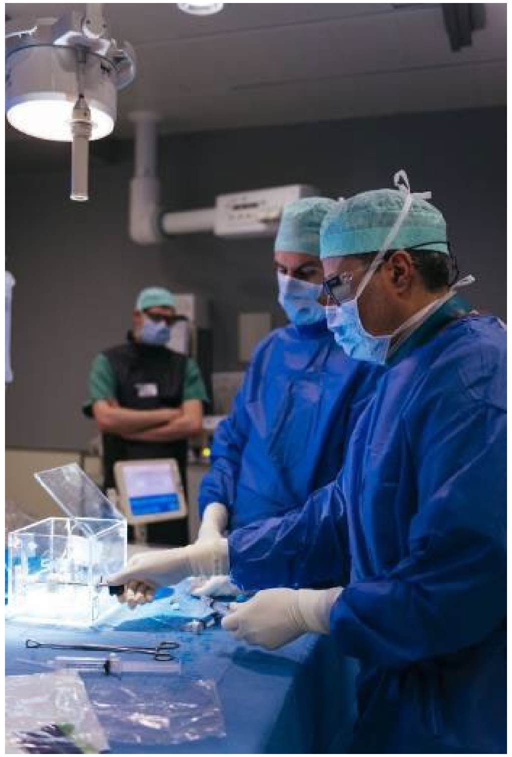
E_i = mean energy per particle or photon; n_i = mean number of particles or photons per nuclear transition; Δ_i = mean energy emitted per nuclear transition.

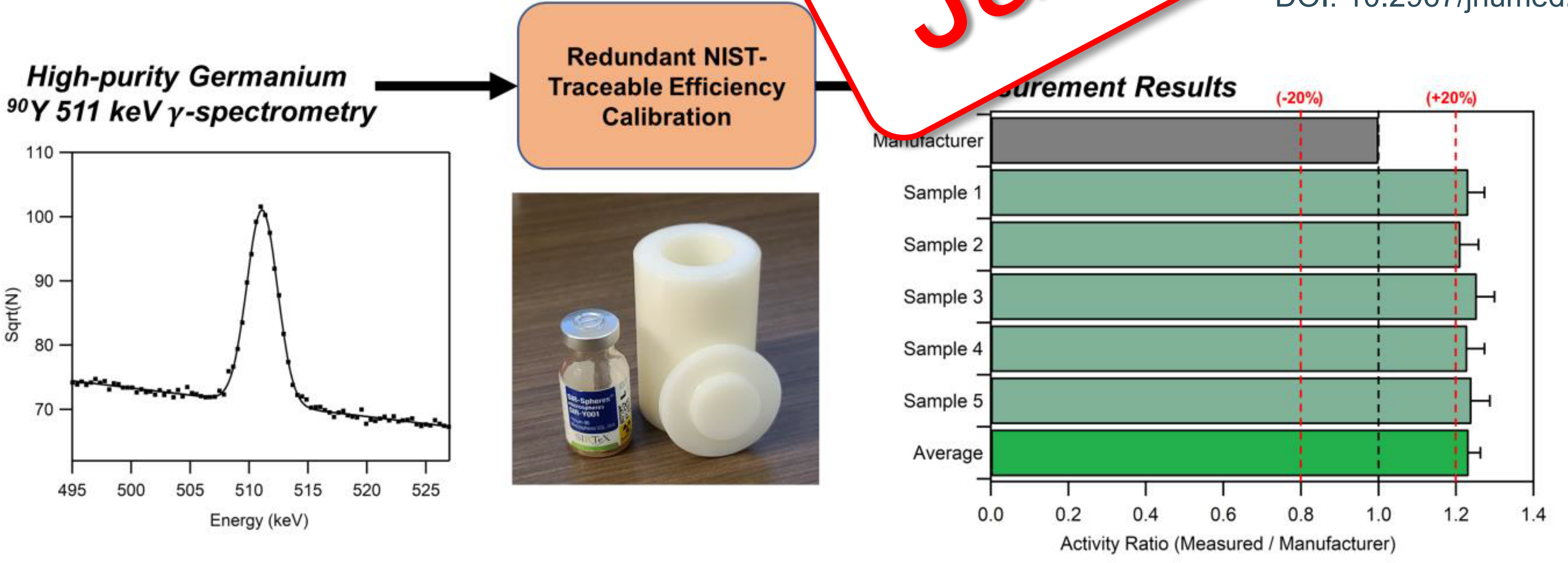
^{111}In has the following properties: physical half-life, 67.3 h; decay constant, 0.0103 h^{-1}; and decay mode, electron capture.

Saldarriaga Vargas C, et al. *Phys Med*. 2018;45:134-142.

Accuracy of activity for ^{90}Y-SIRT

- SIRT = selective internal radiation therapy of liver cancer
- gamma spectrometry reveals that the ^{90}Y primary SIR-Spheres® activity calibration appears to be a significant underestimate of true activity: 1.233 ± 0.030





January 2022

Stephen A Graves, *et al.*
JNM, Jan 2022,
DOI: 10.2967/jnumed.121.262650

Accuracy of activity for ^{90}Y-SIRT

Silvano Gnesin, *et al.*
JNM, Nov 2022,
DOI: 10.2967/jnumed.122.2644

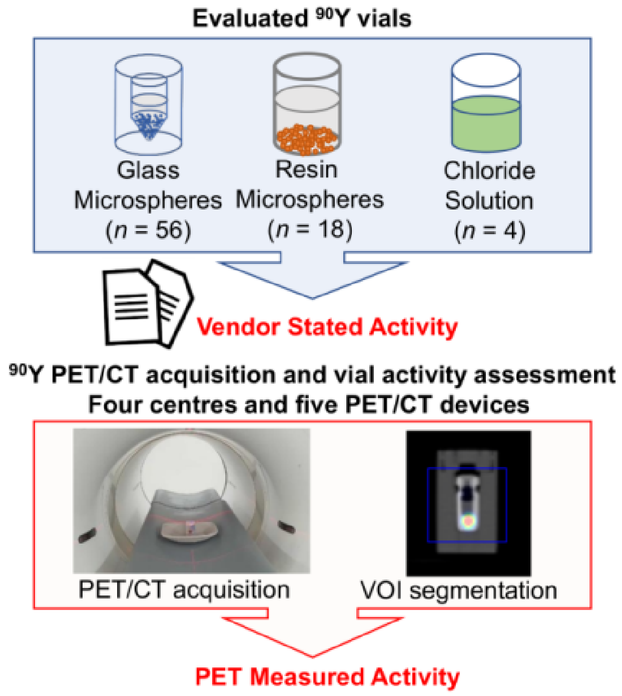
- confirmation of previous study and observations

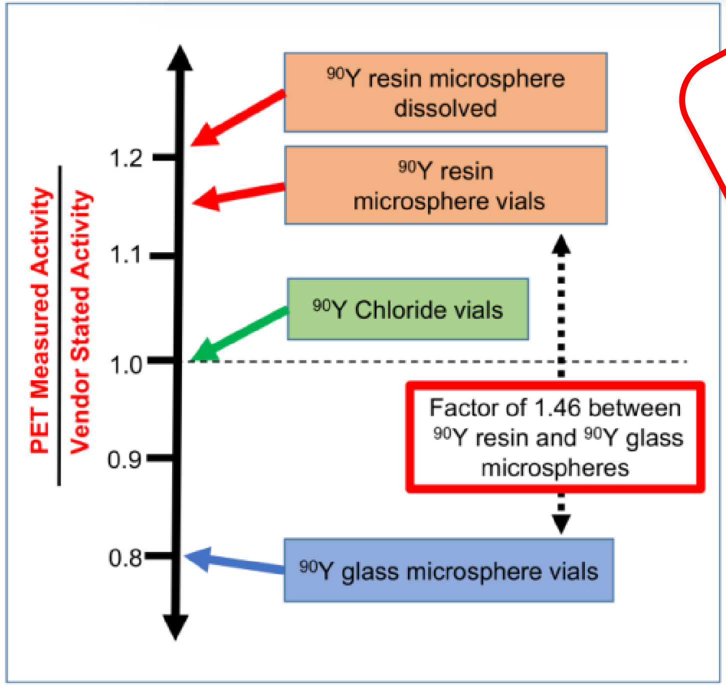
Title: A multicenter study on observed discrepancies between vendor-stated an
^{90}Y activities for both glass and resin microsphere devices

Authors: Silvano Gnesin*, Justin K. Mikell*, Maurizio Conti
Thiago V. M. Lima, Yuni K. Dewaraja.

November 2022

Graphical Abstract





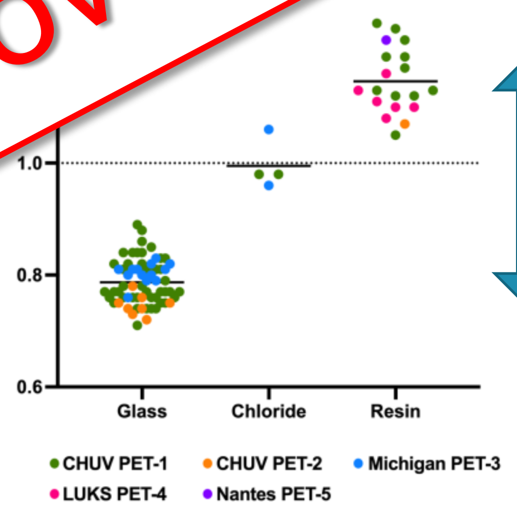
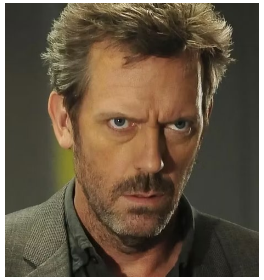


Figure 1. Distribution of A_{PET}/A_M ratios for the four vial products tested in this study (i.e ^{90}Y-labeled glass microspheres, ^{90}Y-Chloride solution, ^{90}Y-labeled resin microspheres and ^{90}Y-labeled liquefied resin).

Δ ~ 50%

significant uncertainty for therapy



The value of (legal) metrology

- European Union: 2013/59/EURATOM
  - art. 56 – Optimisation: "…verification of administered activities …"
- Belgium: Medical Exposure Decree (2020)
  - art. 9 – Optimisation: "… verification of administered activities …"
  - art. 60 – Reporting: "… deviation of >10% of the intended activity"
- recipients often do not meet the calibration requirements
- unknown calibration uncertainties on certificate of analysis
- lack of knowledge about the unbroken chain of traceability or calibration path for radioactivity prescription by a physician
- how to compare that to the concept of maximum permitted tolerance on "content" in the EU (76/211/EEC) 😳 ???

Traceability pyramid

CSIR-National Physical Laboratory, New Delhi, India

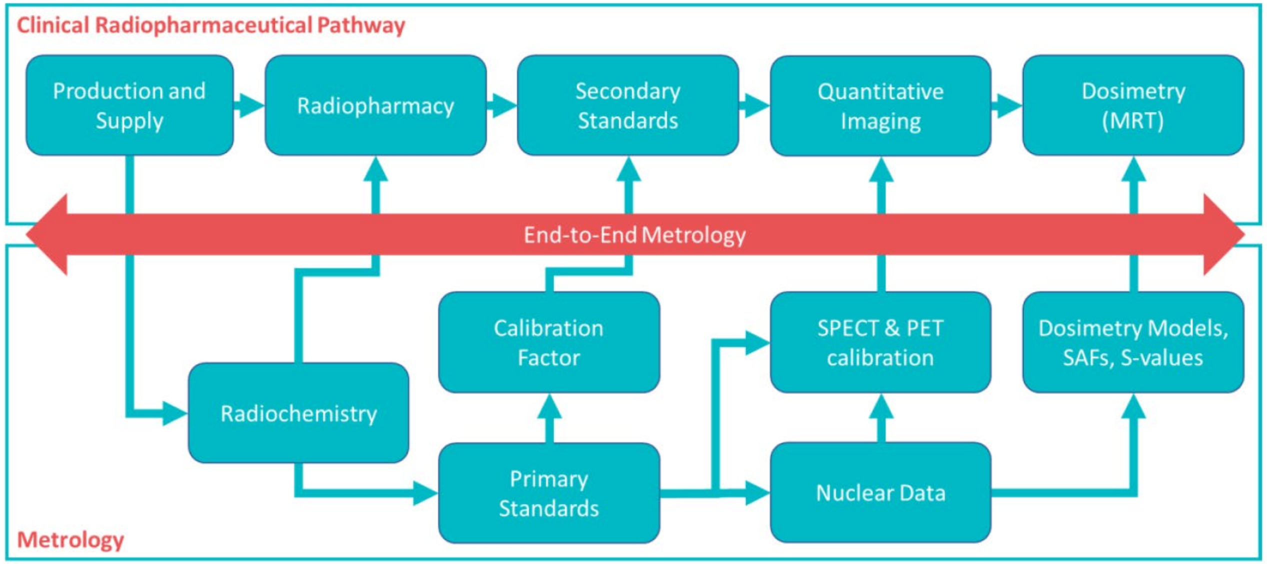
℮

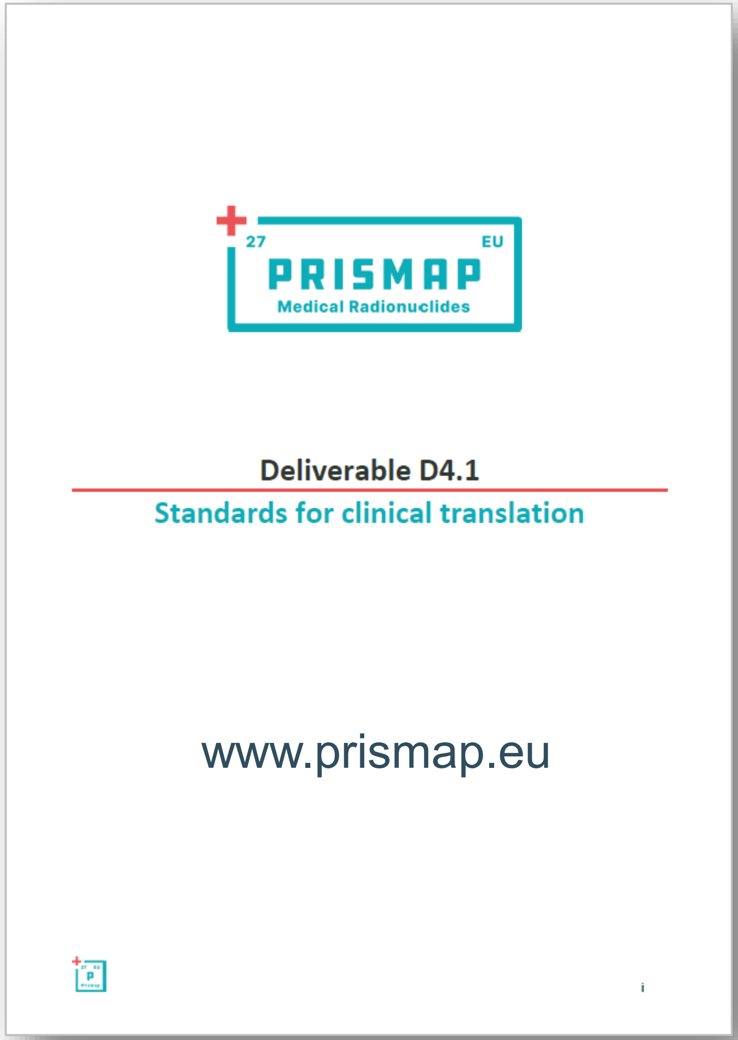
Aswal, D.K. MAPAN 35, 139–150 (2020).
doi.org/10.1007/s12647-020-00376-3

Standards for clinical translation

- PRISMAP recommends the implementation of
  - an end-to-end metrology methodology, and
  - the involvement of medical physics experts (MPE)

for the standardization and harmonization of novel radiopharmaceuticals for imaging and therapy




PRISMAP Medical Radionuclides

Deliverable D4.1

Standards for clinical translation

www.prismap.eu

This project has received funding from the European Union's Horizon 2020 research and innovation program under grant agreement No 101008571 (PRISMAP).

Clemens Decristoforo, et al. (2022). https://doi.org/10.5281/zenodo.6599181

Quality assurance & control (2.x)

- novel detector and gantry technology
  - CZT, SiPM, novel system configurations, radionuclide settings
- advanced image correction & reconstruction techniques
  - raw data correction techniques, count rate & dead-time, …
  - offline (in-house) processing (quid EU-MDR 2017/745)
  - quantification in SPECT & PET (dirty isotopes)
- advanced image processing & data extraction techniques
  - (multi-modal) image registration
  - image segmentation – artificial intelligence
  - quantification, dosimetry and therapy planning system
- radionuclide calibrators
  - influence of geometry, recipient, volume, filters, dispensing systems, traceability & metrology
- (technical) regulatory aspects are not in sync with the evolution of NM technology

27 EU

PRISMAP

Medical Radionuclides

Thank You!

This project has received funding from the European Union's Horizon 2020 research and innovation program under grant agreement No 101008571 (PRISMAP).