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

Authors: Silvano Gnesin*, Justin K. Mikell*, Maurizio Conti, John O. Prior, Thomas Carlier, Thiago V. M. Lima, Yuni K. Dewaraja.

Affiliations:

SG: Institute of Radiation Physics, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland

JKM: Department of Radiation Oncology, University of Michigan and Department of Radiation Oncology, Washington University in St. Louis

MC: Siemens Healthineers, Molecular Imaging

JOP: Department of Nuclear Medicine and Molecular Imaging, Lausanne University Hospital and University of Lausanne, Rue du Bugnon 46, CH-1011, Lausanne, Switzerland

TC: Nuclear Medicine Department, University Hospital of Nantes, France

TVML: Department of Radiology and Nuclear Medicine, Luzerner Kantonsspital, 6004 Luzern, Switzerland

YKD: Division of Nuclear Medicine, Department of Radiology, University of Michigan

*SG and JKM contributed equally to this work

Running title: PET-measured activity of microspheres

Abstract (145/150 words)

Dosimetry-guided treatment planning in selective internal radiation therapy relies on accurate and reproducible measurement of administrated activity. This multi-center (n_{center}=4), multi-device (n_{PET}=5) study compared the manufacturer-declared ^{90}Y activity in vials with quantitative ^{90}Y PET/CT-assessment of the same vials. We compared ^{90}Y PET-measured activity (A_{PET}) for ^{90}Y-labeled glass (n_g=56) and resin (n_r=18) microsphere vials with the calibrated activity specified by the manufacturer (A_M). Additionally, the same analysis was performed for ^{90}Y-chloride vials (n_{cl}=4). The mean A_{PET}/A_M ratio for glass microspheres was 0.79±0.04 [range: 0.71–0.89] and for resin microspheres was 1.15±0.06 [range: 1.05–1.25]. Mean A_{PET}/A_M ratio for ^{90}Y-chloride vials was 1.00±0.04 [range: 0.96–1.06]. Thus, we found an average difference of 46% between glass and resin microsphere activity calibrations while a close agreement was found for chloride solutions. We expect the reported discrepancies will promote further investigations to establish reliable and accurate patient dosimetry and dose-effect assessments.

Keyword: Resin Microspheres; Glass Microspheres; Yttrium-90; PET/CT; Activity.

Introduction

Selective internal radiation therapy (SIRT) with radioactive microspheres is an established liver-directed therapy for both primary liver cancer and liver metastases. Both ^{90}Y glass and resin microspheres are used globally; they are FDA approved in the United States and CE approved in the European Union.

Considerable evidence of dose-effect relationships for both tumor and non-tumoral liver have been demonstrated in ^{90}Y SIRT (1). In particular, for glass microspheres, Garin et al., highlighted a dose-response relationship in a prospective randomized trial, which demonstrated that planned personalized dosimetry improves outcomes compared to standard single compartment dosimetry for locally advanced hepatocellular carcinoma (HCC) (2). Another area of investigation is focused on post-treatment SIRT dosimetry which obviates most of the difficulties linked to the hypothesis that pre-treatment imaging-based dosimetry is a robust surrogate of the actual delivered absorbed dose. In that respect, recent studies suggested the benefit of ^{90}Y PET based dosimetry in HCC or cholangiocarcinoma (3-4).

For reliable dosimetry-guided treatment planning and dose-effect assessment from pre-therapy imaging based absorbed dose estimates, the net administered activity of ^{90}Y microspheres should be accurately determined. Accurate assay of ^{90}Y, an almost pure beta emitter, using activity-meters is challenging compared to other radionuclides commonly employed in nuclear medicine procedures (5). The specific geometry and material composition of the source and its container affects the spectrum of Bremsstrahlung photons; hence affecting the activity-meter measurement.

^{90}Y PET imaging is also challenging due to the low true coincidence count-rates associated with the low yield of positron emission (0.0032%). Despite this, there have been multiple reports demonstrating the quantification accuracy of ^{90}Y PET in phantom studies when using state-of-the-art time-of-flight (TOF) scanners (6-8). It should be noted that almost all phantom studies to date use ^{90}Y in the form of a chloride solution, and not the microsphere devices themselves. Reasons may include the difficulty to suspend microspheres in a uniform distribution throughout a phantom compartment.

In this work, we use quantitative ^{90}Y PET/CT imaging to measure the ^{90}Y microsphere vial activity ‘in-air’ prior to SIRT with resin and glass microspheres at multiple institutions. Additional data came from PET measurements of vials containing ^{90}Y in chloride solution and as a liquefied resin. We compared the PET measured activity with the activity on the calibration certificate supplied by the vendor for each vial with appropriate decay correction.

Material and methods

In this work we adopted the term “activity meter’’ for the reentrant well type ionization chamber that is calibrated to convert a measured ionization current to an activity; this device is also colloquially referred to as a “dose calibrator” in North America. We reserved the use of “dose’’ for the absorbed dose in units of Gy.

We analyzed ^{90}Y vials from three different manufacturers: n_g=56 ^{90}Y-labeled glass microsphere vials (TheraSphere®, Boston Scientific), n_r=17 ^{90}Y-labeled resin microsphere vials (SIR-Spheres®, Sirtex Medical), and n_{cl}=4 vials containing ^{90}Y chloride solution (n=2 from Curium and n=2 from Eckert & Ziegler) and n_{rs}=1 vial containing a solution of dissolved ^{90}Y-labeled resin microspheres (liquefied resin). All vials were imaged with a single bed position 'in air' centered on the three tomographic directions of the PET scanner to yield peak sensitivity.

Glass microspheres. A first dataset of n=43 ^{90}Y-labeled glass microspheres vials (0.7–6.3 GBq) was imaged using a Biograph Vision 600 (PET-1, Siemens Healthineers, Erlangen, Germany) available at the Lausanne University Hospital (CHUV). A subgroup of n=8 vials (0.7–6.3 GBq) where additionally measured on a Discovery 690 (PET-2, General Electric Healthcare, Milwaukee, MI) at the same institution. Another dataset of n=13 glass microsphere vials (2.3–8.6 GBq) was imaged on a Biograph mCT 40 (PET-3, Siemens Healthineers, Erlangen, Germany) at the University of Michigan Hospital.

Resin microspheres. ^{90}Y-labeled resin microsphere vials (3.3–4.6 GBq) were imaged on PET-1 (n=11) and PET-2 (n=1) at the Lausanne University Hospital CHUV and on PET-4 (Biograph Vision 600, Siemens Healthineers, Erlangen, Germany), at the Luzerner Kantonsspital (n=6), both in Switzerland.

Chloride solution. In addition to microspheres vials, we acquired PET/CT data for vials of liquid ^{90}Y chloride solution. Of these n=2 (0.4 GBq, 2.5 GBq) were acquired on PET-1 at CHUV and n=2 (0.4 GBq, 4.4 GBq) were acquired on PET-3 at the University of Michigan Hospital.

Liquified resin microspheres. The vial with the solution of dissolved ^{90}Y-labelled resin microspheres was from a prior study evaluating the reliability of measuring ^{90}Y activity using PET performed at the University Hospital of Nantes in collaboration with the French National Standard Laboratory (LNHB-CEA, Paris, France). For this purpose, a reference activity of resin microspheres (2.95 GBq) was first dissolved (9), measured using the triple to double coincidence ratio method with Cherenkov counting at LNHB-CEA and then shipped to the University Hospital of Nantes for a PET/CT acquisition (PET-5, Siemens Biograph 40 mCT, Siemens Healthineers, Erlangen, Germany).

PET/CT reconstruction and quantification. Supplemental Table S1 summarizes acquisition and reconstruction parameters for the measurements performed on the different PET/CT devices included in this study. Manufacturer recommendations for ^{90}Y were used for the reconstruction parameters. Considering the measurements on Siemens Healthineers PET/CT Biograph Vision 600 devices, we tested both absolute and relative scatter corrections available with the manufacturer software. The relatively high noise associated with low-count ^{90}Y PET can affect the scatter correction with relative scaling and some bias can appear in the final quantification as reported previously (6). Since the preliminary quantitative assessment showed, as expected, no significant difference between the two scatter methods in the low-scatter setting ('in-air') of the current experiment (Supplemental Table S2 and S3), we focus on results obtained with the absolute scatter correction.

In all PET scanners used in the current study, the software enables ^{90}Y quantitation automatically from the local ^{18}F system cross-calibration, accounting for the ^{90}Y specific physical decay and positron branching ratio. The quantitative PET data were decay corrected to the start of the PET acquisition. We defined cylindrical (50 mm diameter, 5 cm high) volume of interests (VOIs) on the PET images to encompass the vials (diameters of 25, 35 and 25 mm for resin, glass and ^{90}Y chloride respectively), to minimize any signal loss due to partial volume effects.

Manufacturer specified activity assessment.

The manufacturer-specified calibrated activity was reported in a specific document shipped with the vial to the different hospitals. In this document, the manufacturer indicates the vial activity and the time of the calibration. Following the manufacturer specified procedure for establishing a local calibration factor, we routinely verified the activity by measuring the received vial in the local activity meter. Specifically, nominal manufacturer activity was used for resin microspheres, while the manufacturer measured total activity (not nominal) was used for glass microspheres. The local vs. certified manufacture activity was found to be within 5% in all centers.

Comparison of PET-derived activity with manufacturer specified value.

For each measurement, the total PET activity measured in the vial VOI (A_{PET}) was compared with the vial activity reported in the manufacturer calibration sheet (A_M) decay corrected to the start time of the PET acquisition, using the ratio A_{PET}/A_M. We assessed statistical difference of A_{PET}/A_M ratios for the same microsphere type obtained in different PET scanners applying ANOVA and multiple comparison tests using the MATLAB R2021a statistical toolbox. A significant difference was considered for $p<0.05$.

Results

Figure 1 shows a dot-plot representation of the A_{PET}/A_M distribution across all 4 vial types and different centers. Table 1 present the summary statistics for all the measurements (full data available in Supplemental Presentation 1). The mean A_{PET}/A_M ratio for ^{90}Y glass spheres was 0.79±0.04 [range: 0.71–0.89]. No statistical differences were found between the mean A_{PET}/A_M for ^{90}Y glass spheres acquired between PET-1 and PET-3 ($p=0.43$). Statistical differences were found between PET-1 and PET-2 ($p=0.009$) and between PET-2 and PET-3 ($p=0.002$). The mean A_{PET}/A_M ratio for the resin spheres was 1.15±0.06 [range: 1.05-1.25]. In this case, no statistical difference was found between PET-1 and PET-4 ($p=0.072$).

The mean A_{PET}/A_M measured in ^{90}Y-chloride vials was 1.00±0.04 [range: 0.96–1.06] (Table 1 and Supplemental Table S4). The A_{PET}/A_M measured for the liquefied resin-spheres in PET-5 was 1.22±0.12 while a good agreement was found between the LNHB-CEA reference activity and the PET activity measurements with a ratio of 1.01

Discussion

In this study, we used PET as an independent measure of activity for ^{90}Y microsphere vials in air and compared with the activity reported in the respective manufacturer's calibration sheet for ^{90}Y-labeled resin and glass microspheres and ^{90}Y in chloride solution and liquefied resin. While we report substantial discrepancies for resin and glass microspheres, close agreement is reported for the chloride solution. Furthermore, activity measurement of the liquefied resin with PET is in excellent agreement with the national metrology laboratory reference measurement, suggesting an accurate PET quantification.

For the resin spheres, we reported an average $A_{PET}/A_M = 1.15\pm0.06$ (i.e., $A_{M,resin}$ underestimates A_{PET} by 13%), this value is compatible with HPGe NIST-referred results recently published by Graves et al where a ratio of 1.233±0.030 was reported (10). In addition, we provided original data for the glass spheres showing an opposite trend compared to resin, $A_{PET}/A_M = 0.79\pm0.04$ (i.e., $A_{M,glass}$ systematically overestimating A_{PET} by 27%). Therefore, a relative difference of about 46% exists between the two manufacturer's ^{90}Y activity calibrations, i.e., 1 Bq of ^{90}Y measured in the activity reference frame of the glass microsphere manufacturer corresponds to 1.46 Bq measured within the resin microsphere manufacturer's activity reference.

Quantitative PET-imaging of ^{90}Y is challenging, but it is enhanced by state-of-the-art TOF systems used in this study. However an error in the PET reconstructed activity could arise from a potential inaccurate attenuation correction due to inadequate modeling of higher density materials such as glass. The ^{90}Y Chloride and resin microsphere containers have minimal glass thicknesses. Such thicknesses will have minor effects on PET reconstructed activity. The following observations support this claim, 1) our A_{PET}/A_M for resin microspheres is consistent with prior studies (10,11) reporting A_M is being underestimated using a different measurement approach than PET, 2) our A_{PET}/A_M is near unity for ^{90}Y Chloride for which activity meter measurements are well known with a traceable standard, and, 3) the near unity value of the LNHB-CEA reference activity to the PET activity. However, for glass microspheres, the combination of a thick glass v-vial bottom and microspheres settling in that vicinity may lead to large glass thicknesses- this could potentially introduce a bias in the attenuation correction. To estimate the potential bias, we used cone beam CT of a glass microsphere vial to create a high resolution (0.1 mm) model of the geometry/material used in our study. Nominal linear attenuation coefficients were then assigned, and attenuation correction factors (ACF) calculated along a few lines of response. We compared ACFs from the high resolution model with ACFs calculated from the CT-derived attenuation map used in the PET reconstruction. Assuming nominal values for diameter and total number of microspheres with a packing ratio of 0.6, we estimated the potential ACF bias along evaluated lines of response to vary from -11% to +13%. The average ACF bias was no greater than 6%. Which would move our results only slightly toward unity, leaving the A_{PET}/A_M ratio at or below 0.85. The sensitivity of attenuation correction was also tested by increasing the CT numbers above 600 HU by 20% and then performing PET reconstruction. The resulting activity concentration image had a maximum difference of 3.6%, demonstrating minimal sensitivity to changes in HU.

Although primary measurements from national laboratories have been reported for both devices (12,13) any changes from the specific source and container tied to these measurements will impact the ^{90}Y Bremsstrahlung energy spectrum and thereby the activity meter assay. One study

reported a systematic bias of 4% due to likely changes in the acrylic shield used by glass microspheres (14). Monte Carlo simulations that model the composition and geometry of the vials as well as the devices could provide more insight on their impact on both the PET measurement and activity meter calibration but is beyond the scope of this work.

To the best of our knowledge, we believe this is the first report of such observed differences for ^{90}Y glass microspheres between PET and vendor stated activity. The purpose of this study is not to fully explain the discrepancies we have observed, but to share our observations which suggest a significant bias exists when comparing PET quantification with vendor stated activity for both glass and resin ^{90}Y microsphere devices. Such differences would likely not affect clinical practice given the large number of patients safely and effectively treated to date with activities as stated by the vendors. However, it is important from a metrological standpoint to know the activities administered to patients; reporting “true” activities should enable more accurate radiobiological modeling and dosimetry comparisons across devices and modalities. For example, our results should be considered within the context of studies reporting lower biologic effect per Gy for glass vs. resin microspheres when treating the same hepatic disease (15).

Conclusions

We presented original data comparing quantitative PET and manufacturer-declared total activity in ^{90}Y-labeled microspheres and ^{90}Y-chloride vials. Manufacturer-declared vial activities were substantially different when measured by quantitative PET for glass (mean ratio 0.79) and resin (mean ratio 1.15), which showed opposite trends with a large relative difference of 46% between them. In ^{90}Y-chloride vials, PET and manufacturer-declared activities were in close agreement. We expect the reported discrepancies will promote further investigations to establish reliable and accurate patient injected activity measurement and thus consistent dosimetry and dose-effect relation assessments.

Disclosure

Maurizio Conti is full-time employee of Siemens Medical Solutions USA, Inc. No other potential conflicts of interest relevant to this article exist.

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Key Points

QUESTION: How accurate are vendor specified calibrated activities used for therapy and absorbed dose assessment in ^{90}Y SIRT?

PERTINENT FINDINGS: We compared quantitative Y-90 PET measurements against vendor specified calibrated activities in both glass and resin microsphere vials across multi-center and devices. We found a large difference between PET measurements and reported vial activities (average –21% for glass and +15% for resins).

IMPLICATIONS FOR PATIENT CARE: Accounting for the observed differences can lead to a shift of reported administered activity and absorbed dose thresholds in dose-effect studies.

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Table

Product	Manufacturer	# of vials	Center	PET scanner	A_{PET}/A_M mean	A_{PET}/A_M SD	A_{PET}/A_M Range
Glass	Boston Scientific	43	CHUV (PET-1)	Siemens Biograph Vision 600	0.79	0.04	(0.71; 0.89)
Glass	Boston Scientific	8	CHUV (PET-2)	GE Discovery 690	0.74	0.02	(0.72; 0.78)
Glass	Boston Scientific	13	University of Michigan (PET-3)	Siemens Biograph mCT 40	0.80	0.02	(0.76; 0.83)
Glass	Boston Scientific	64	All	All	0.79	0.04	(0.71; 0.89)
Resin	Sirtex Medical	11	CHUV (PET-1)	Siemens Biograph Vision 600	1.16	0.06	(1.05; 1.25)
Resin	Sirtex Medical	1	CHUV (PET-2)	GE Discovery 690	1.07		
Resin	Sirtex Medical	6	Luzerner Kantonsspital (PET-4)	Siemens Biograph Vision 600	1.11	0.03	(1.08; 1.16)
Resin	Sirtex Medical	18	All	All	1.15	0.06	(1.05; 1.25)
Resin* Liquified	Sirtex Medical; liquefied by LNHB-CEA, Paris	1	University Hospital of Nantes (PET-5)	Siemens Biograph mCT 40	1.22		
Chloride	Curium	2	CHUV (PET-1)	Siemens Biograph Vision 600	0.98	0.01	(0.98; 0.98)
Chloride*	Eckert & Ziegler	2	University of Michigan (PET-3)	Siemens Biograph mCT 40	1.01	0.07	(0.96; 1.06)
Chloride	All	4	All	All	1.00	0.04	(0.96; 1.06)

Table 1. Summary of A_{PET}/A_M results, for the different types of product tested, with indication of the test center and the PET device used for the measures. Absolute scatter correction was applied except for data labelled by (*) that indicates the use of the relative scatter.

Figure

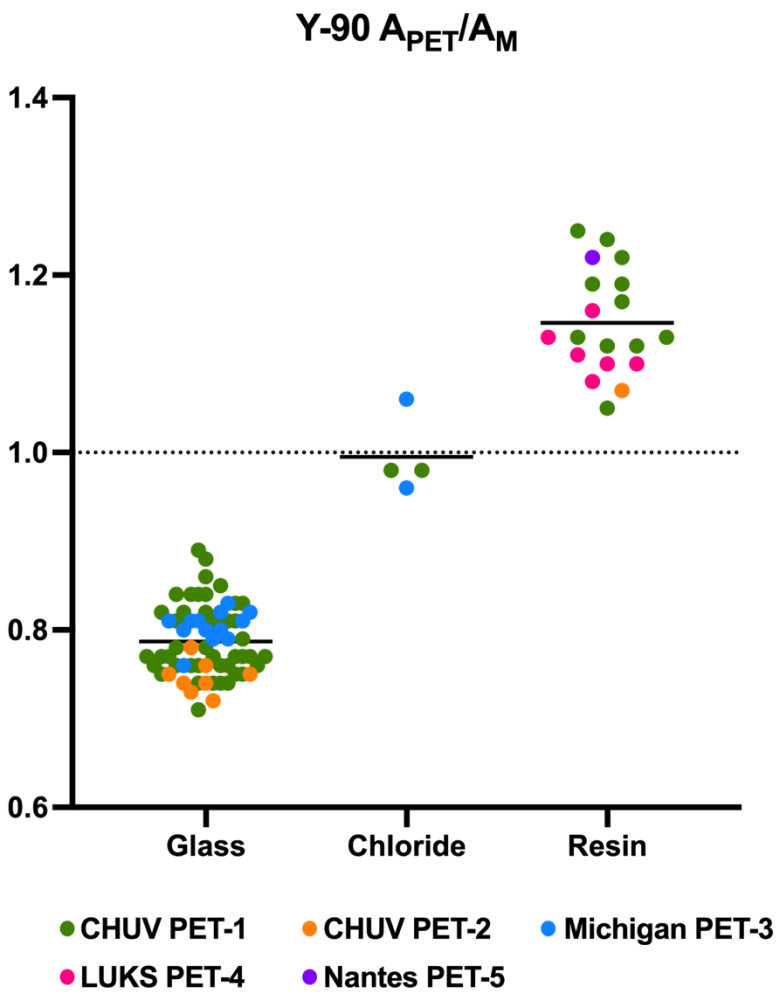
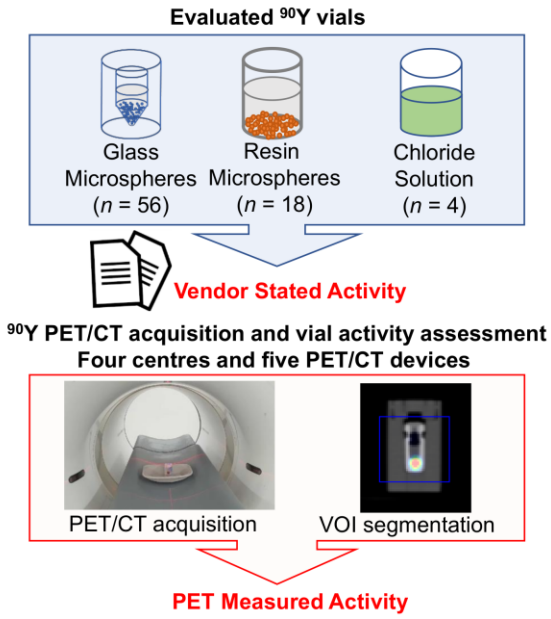
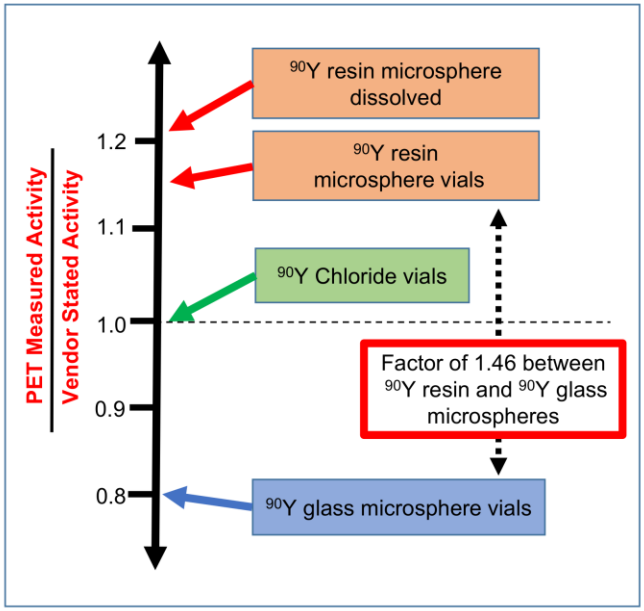


Figure 1. Distribution of A_{PET}/A_M ratios for the four vial products tested in this study (i.e ^{90}Y-labeled glass microspheres, ^{90}Y-Chloride solution, ^{90}Y-labeled resin microspheres and ^{90}Y-labeled liquefied resin).

Graphical Abstract





Supplemental Table S1. Acquisition and reconstruction parameters used for vial acquisition in the different PET devices present across centres.

PET ID	Device	Centre	Acquisition parameters	Vendor based recon. parameters*	Scatter correction
PET-1	Siemens Healthineers Biograph Vison 600	CHUV Lausanne	List-mode 15 minutes; step and shoot	OSEM3D TOF+PSF 2 iterations × 5 subsets Gaussian FWHM=4mm	Absolute & relative
PET-2	GE Discovery 690	CHUV Lausanne	List-mode 20 minutes; step and shoot	OSEM3D TOF 2 iterations × 24 subsets Gaussian FWHM=6.4mm	Model based
PET-3	Siemens Healthineers mCT 40	University of Michigan Hospital	List-mode 20 minutes; step and shoot	OSEM3D TOF+PSF 2 iterations × 21 subsets Gaussian FWHM=5mm	Absolute (Y-90 spheres) & relative (Y-90 chloride)
PET-4	Siemens Healthineers Biograph Vison 600	Luzerner Kantonsspital	List-mode 15 minutes; step and shoot	OSEM3D TOF+PSF 2 iterations × 5 subsets Gaussian FWHM=4mm	Absolute & relative
PET-5	Siemens Healthineers mCT 40	University Hospital of Nantes	List-mode 30 minutes; step and shoot	OSEM3D TOF+PSF 2 iterations × 21 subsets Gaussian FWHM=5mm	Relative

*Common applied corrections were normalization, dead time, activity decay, random coincidence ad CT-based attenuation correction.

Supplemental Table S2. Y-90 glass microsphere vial data from the CHUV (PET-1, n=43 and PET-2, n=8) and University of Michigan (PET-3, n=13). A_M = vial activity as declared by the manufacturer (vendor calibration sheet), A_{PET} = PET measurements of the vial activity obtained for the tested scatter correction method (absolute and relative). All activities are decay corrected to the PET acquisition time.

Centre/device	Vial ID	A_M (MBq)	A_{PET} (MBq)		A_{PET}/A_M	
			absolute	relative	absolute	relative
CHUV PET-1	1	2259	1789	1778	0.79	0.79
	2	2637	2019	2009	0.77	0.76
	3	1341	1095	1087	0.82	0.81
	4	1260	1054	1049	0.84	0.83
	5	1587	1331	1318	0.84	0.83
	6	1254	1032	997	0.82	0.79
	7	5422	4181	4144	0.77	0.76
	8	814	685	678	0.84	0.83
	9	2292	1782	1791	0.78	0.78
	10	3334	2552	2562	0.77	0.77
	11	728	601	602	0.83	0.83
	12	1221	1003	996	0.82	0.82
	13	1394	1054	1047	0.76	0.75
	14	2811	2156	2129	0.77	0.76
	15	2588	1964	1936	0.76	0.75
	16	1231	1099	1088	0.89	0.88
	17	788	678	653	0.86	0.83
	18	5284	4272	4197	0.81	0.79
	19	1598	1297	1273	0.81	0.80
	20	734	623	599	0.85	0.82
	21	994	880	868	0.88	0.87
	22	965	744	738	0.77	0.76
	23	2015	1536	1521	0.76	0.75
	24	1026	771	758	0.75	0.74
	25	2252	1667	1661	0.74	0.74
	26	2386	1765	1756	0.74	0.74
	27	711	538	533	0.76	0.75
	28	797	595	583	0.75	0.73
	29	2221	1670	1659	0.75	0.75
	30	2841	2114	2111	0.74	0.74
	31	2548	1809	1806	0.71	0.71
	32	2697	1995	1981	0.74	0.73
	33	5174	3963	3949	0.77	0.76

	34	1788	1370	1357	0.77	0.76
	35	831	635	617	0.76	0.74
	36	1290	977	957	0.76	0.74
	37	695	577	571	0.83	0.82
	38	985	767	772	0.78	0.78
	39	983	826	819	0.84	0.83
	40	763	615	606	0.81	0.79
	41	6277	4847	4844	0.77	0.77
	42	1001	809	790	0.81	0.79
	43	770	587	587	0.76	0.76
	mean				0.79	0.78
	SD				0.04	0.04
CHUV GE PET-2	36	1290	925		0.72	
	37	695	539		0.78	
	38	985	747		0.76	
	39	983	740		0.75	
	40	763	569		0.75	
	41	6277	4630		0.74	
	42	1001	731		0.73	
	43	770	568		0.74	
	mean				0.74	
	SD				0.02	
University of Michigan PET-3	1	6270	4979		0.79	
	2	6666	5305		0.80	
	3	3851	3177		0.82	
	4	7513	6093		0.81	
	5	2759	2226		0.81	
	6	4186	3374		0.81	
	7	3181	2655		0.83	
	8	4083	3247		0.80	
	9	5523	4538		0.82	
	10	7078	5593		0.79	
	11	8604	6540		0.76	
	12	2361	1878		0.80	
	13	7628	6210		0.81	
	mean				0.80	
	SD				0.02	

Supplemental Table S3. Y-90 resin microsphere and liquified resin data from CHUV (PET-1, n=11 and PET-2, n=1), Luzerner Kantonsspital (PET-4, n=6) and University of Nantes (PET-5, n=1). A_M = vial activity as declared by the manufacturer (vendor calibration sheet), A_{PET} = PET measurements of the vial activity obtained for the tested scatter correction method (absolute and relative). All activities are decay corrected to the PET acquisition time.

Centre/device	Vial ID	A_M (MBq)	A_{PET} (MBq)		A_{PET}/A_M	
			absolute	relative	absolute	relative
CHUV PET-1	1	3580	4244	4168	1.19	1.16
	2	3386	3978	3926	1.17	1.16
	3	4388	5214	5161	1.19	1.18
	4	3444	3863	3820	1.12	1.11
	5	4181	5184	5147	1.24	1.23
	6	3477	3942	3841	1.13	1.10
	7	4238	5153	5109	1.22	1.21
	8	3348	4183	4136	1.25	1.24
	9	3586	4060	3985	1.13	1.11
	10	4586	4794	4728	1.05	1.03
	11	3577	4007	3935	1.12	1.10
	mean				1.16	1.15
	SD				0.06	0.06
CHUV PET-2	10	4856	4898		1.07	
Luzerner Kantonsspital PET-4	1	3600	4084		1.13	
	2	3569	4125	4090	1.16	1.15
	3	3608	3907		1.08	
	4	3618	3982	3980	1.10	1.10
	5	3606	4003	3932	1.11	1.09
	6	3664	4036		1.10	
	mean				1.11	1.11
	SD				0.03	0.03
University Hospital of Nantes PET-5	1	2950		3583		1.22

Supplemental Table S4. Y-90 Chloride solution data from CHUV (PET-1, n=2) and University of Michigan (PET-3, n=2). A_M = vial activity as declared by the manufacturer (vendor calibration sheet), A_{PET} = PET measurements of the vials. All activities are decay corrected to the PET acquisition time.

Centre/device	Vial ID	A_M (MBq)	A_{PET} (MBq) absolute	A_{PET}/A_M absolute
			absolute	absolute
CHUV PET-1	1	2534	2494	0.98
	2	351	345	0.98
University of Michigan PET-3	1	425	408	0.96
	2	4373	4634	1.06
	mean			1.00
	SD			0.04