Practical Tools for Patient-specific Characterization and Dosimetry of Radiopharmaceutical Extravasation

Sean Wilson,1 Dustin Osborne,2 Misty Long,3 Josh Knowland,4 and Darrell R. Fisher5

Abstract—Extravasation during radiopharmaceutical injection may occur with a frequency of more than 10%. In these cases, radioactivity remains within tissue and deposits unintended radiation dose. Characterization of extravasations is a necessary step in accurate dosimetry, but a lack of free and publicly available tools hampers routine standardized analysis. Our objective was to improve existing extravasation characterization and dosimetry methods and to create and validate tools to facilitate standardized practical dosimetric analysis in clinical settings. Using Monte Carlo simulations, we calculated dosimetric values for sixteen nuclear medicine isotopes: $^{11}$C, $^{64}$Cu, $^{18}$F, $^{67}$Ga, $^{68}$Ga, $^{123}$I, $^{131}$I, $^{111}$In, $^{17}$Lu, $^{15}$N, $^{82}$Rb, $^{153}$Sm, $^{89}$Sr, $^{90}$Y. We validated our simulation results against five logical alternative dose assessment methods. We then created three new characterization tools: a worksheet, a spreadsheet, and a web application. We assessed each tool by recalculating extravasation dosimetry results found in the literature and used each of the tools for patient cases to show clinical practicality. Average variation between our simulation results and alternative methods was 3.1%. Recalculation of published dosimetry results indicated an average error of 7.9%. Time required to use each characterization tool ranged from 1 to 5 min, and agreement between the three tools was favorable. We improved upon existing methods by creating new tools for characterization and dosimetry of radiopharmaceutical extravasation. These free and publicly available tools will enable standardized routine clinical analysis and benefit patient care, clinical follow-up, documentation, and event reporting.

Health Phys. 123(5):343–347; 2022

Key words: dosimetry; medical radiation; nuclear medicine; radiopharmaceuticals

BACKGROUND

Radio pharmaceuticals are typically administered to patients through intravenous injection or infusion. As previously reported, diagnostic radiopharmaceutical extravasation may occur with a frequency of more than 10% (Hall et al. 2006; Bains et al. 2009; Krumrey et al. 2010; Osman et al. 2011; Silva-Rodriguez et al. 2014; Muzaffar et al. 2017; Wong et al. 2019; Currie and Sanchez 2020). Extravasations degrade diagnostic images (Slavin et al. 1996; Fleming et al. 2004; Naddaf et al. 2004; Burrell and MacDonald 2006; Waxman et al. 2009; Murray et al. 2013; Ozdemir et al. 2014; Minoshima et al. 2016; QIBA SPECT Biomarker Committee 2017; Erthal et al. 2017; Schaefferkoetter et al. 2017; van der Pol et al. 2017; Bennett et al. 2018; Kiser et al. 2018; Murthy et al. 2018; Qubhi 2018) and cause unintentional radiation dose to the patient’s tissue and skin. Prompt identification of potentially serious extravasations is important for mitigation (e.g., massage, elevation). Characterization and dosimetry are then necessary to inform long-term patient care, clinical follow-up, event documentation, and reporting as applicable.

Tissue-absorbed dose resulting from extravasation depends on patient- and procedure-specific factors including the initial amount of paravenous radioactivity, the mass of infiltrated tissue, the radiopharmaceutical used, and residence time. For example, the length of time that extravasated radiopharmaceutical remains near the injection site can depend on the patient’s anatomy, vascular health, and properties of the drug, such as the rate at which it is able to permeate interstitial space. Likewise, the volume of infiltrated tissue can vary with administration technique; for instance, use of a straight stick needle for injection as opposed to an intravenous catheter precludes flushing with saline and thus limits dilution and dispersion of residual radioactivity. Because the amount of extravasated radioactivity and the volume of infiltrated tissue both change over time, conventional static nuclear

1Carilion Clinic, Roanoke VA and Blue Ridge Medical Physics, Daleville, VA; 2University of Tennessee Graduate School of Medicine, Knoxville TN; 3Siemens Medical Solutions, Knoxville TN; 4Lucerno Dynamics, Cary NC; 5University of Washington Department of Radiology and Versant Medical Physics and Radiation Safety, Richland, WA.

The authors declare no conflicts of interest.

For correspondence contact: Josh Knowland, 140 Towerview Ct., Cary, NC 27513, or email at jknowland@lucernodynamics.com.

(Manuscript accepted 29 April 2022)

Copyright © 2022 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the Health Physics Society. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

DOI: 10.1097/HP.0000000000001600

www.health-physics.com

McIntosh C, Abele J. Frequency of interstitial radiotracer injection for patients undergoing bone scan. The 79th Annual Scientific Meeting of the Canadian Association of Radiologists. Montreal, Canada. 2016.
medicine imaging by itself can be an inadequate tool for dosimetry characterization. Serial imaging of the injection site or monitoring with nuclear uptake probes have been proposed as improved ways to inform characterization (Breen and Dreidger 1991; Williams et al. 2006; Bonta et al. 2011; Terwinghe et al. 2012; Kawabe et al. 2013; Esser 2017; Tylski et al. 2018).

Even with measurements from serial imaging or uptake probes, extravasation dosimetry requires effort to determine appropriate dose rates and clearance times. A recent publication (Osborne et al. 2021) proposed pre-calculated dose rates for a standardized tissue volume of 5 cm³—a tissue volume also used by others (Castronovo et al. 1988; Narkevich et al. 2019)—in analysis of radiopharmaceutical extravasations. The method uses injection-site radioactivity measurements to estimate the rate of biological clearance and is applicable to clinical extravasation characterization and dosimetry.

In this work, we built upon the efforts of Osborne et al. (2021) by pre-calculating dosimetric data for several additional isotopes. We then created and validated three free and publicly available tools for characterization and dosimetry of extravasations to facilitate routine use, standardization, and conformity.

**MATERIALS AND METHODS**

We calculated dose rates for sixteen common nuclear medicine isotopes: $^{11}C$, $^{64}Cu$, $^{18}F$, $^{67}Ga$, $^{68}Ga$, $^{123}I$, $^{131}I$, $^{11}In$, $^{177}Lu$, $^{15}N$, $^{15}O$, $^{82}Rb$, $^{153}Sm$, $^{89}Sr$, $^{99m}Tc$, and $^{90}Y$. These data were generated using Monte Carlo simulations of 5 cm³ water-filled spherical volumes each containing a uniformly distributed activity of 100 kBq. Simulations were run using version 9.1 of the GATE Monte Carlo framework (Jan et al. 2004). Within GATE, source isotopes were defined by their characteristic ionic forms. Ionic sources represent an accurate source type within GATE because they incorporate all emissions and nuclear processes, including ingrowth and decay of progeny products, as applicable. Simulated events within each of the 5 cm³ volumes were generated, recorded, and analyzed to determine the energy deposited per nuclear transition.

To validate the Monte Carlo simulations, we compared our results against five alternative dose-assessment methods that represent logical approaches one may take. The first alternative method was the IDAC-Dose 2.1 software version 1.04 (Andersson et al. 2017), which is freely available and endorsed for radiopharmaceutical dosimetry by the International Commission on Radiological Protection (ICRP). We used the “spheres” module within IDAC-Dose to calculate absorbed dose to spherical volumes. The second method we employed was the sphere dose calculation function of OLINDA® version 2.2.3 (Hermes Medical Solutions, Stockholm, Sweden). For consistency of comparison against the Monte Carlo simulations, both IDAC-Dose and OLINDA were configured to calculate dose resulting from 100 kBq within water-filled spheres of mass 5 g. The third alternative method consisted of a Monte Carlo simulation using discrete emissions. The fourth method was a simplification of the third and used only one emission of each type with energy equal to the weighted average of their respective constituents. For example, electron and positron emission energies were summed according to their individual yield intensities and were then represented by one electron of equivalent energy. Likewise, all photons were represented using a weighted average of their underlying emissions. Finally, the fifth alternative method assumed complete absorption of non-penetrating emissions and no absorption of penetrating emissions.

We created three new extravasation characterization and dosimetry tools: a manual worksheet, a computer spreadsheet, and an online web application. We validated each of the tools through recalculation of and comparison against three previously reported examples of extravasation dosimetry (Castronovo et al. 1988).

To determine clinical practicality of the tools, we applied them to seven cases of diagnostic nuclear medicine extravasation and recorded the time required for each characterization. At our institutions, we routinely monitor nuclear medicine injections and record injection site count-rate data throughout the pre-imaging uptake time using Lara® external uptake probes (Lucerno Dynamics, Cary, NC). When probe feedback indicated possible extravasation, technologist staff would include the injection site in the imaging field-of-view. We performed quantitative image-based activity measurements using syngo® via version 6.5 (Siemens Healthineers AG, Erlangen, Germany) with volumes of interest (VOIs) centered about the maximal local voxel and defined by a 10% threshold value.

**RESULTS**

Tables 1 and 2 show dose factors and mean absolute percent error values, respectively, for the six calculation methods. Table 3 compares doses obtained using each of the characterization tools against published values (Castronovo et al. 1988). Table 4 shows the results of characterization for clinical cases of extravasation.

**DISCUSSION**

In this work, we developed three tools for characterization and dosimetry of radiopharmaceutical extravasations. We validated all three tools against published data and demonstrated their practicality within a clinical workflow. All three tools are available at no charge online⁷ or from the authors.

---

⁷ Radiopharmaceutical Infiltration Dosimetry Estimator (RIDE), http://gsm.utmck.edu/research/MITRP/RIDE.cfm. Accessed 26 April 2022.
Dose rates from our simulations compared favorably with alternative methods of calculation. Differences between our simulation of ion sources and alternative calculation methods one through four (IDAC-Dose 2.1, OLINDA 2.2.3, simulation of discrete emissions, and simulation of weighted average emissions) were all less than 4%. With respect to the OLINDA dosimetry software, it is important to point out that recent code updates have improved the spheres module performance. For this work, agreement between OLINDA and the other calculation methods was poor until the software was updated to version 2.2.3. The difference between our ion simulations and an assumption of complete absorption of non-penetrating emissions only (alternative calculation method five) was almost 10%. This assumption may be considered naïve but has been previously proposed as a solution (Shapiro et al. 1987) with the reasoning that for relatively small volumes, the absorbed fraction for photons will tend to be insignificant compared to that of electrons. This simplification can lead to significant bias. In our simulation of $^{18}$F, only 2.6% of the emitted annihilation photon energy was deposited within the 5 cm$^3$ sphere, but this photon energy accounted for 10% of the total energy deposited. An assumption of no photon absorption resulted in an underestimate of overall absorbed energy.

Application of the characterization tools to a clinical workflow showed that the tools have practical value and can be used within a normal clinical setting. Characterization and dosimetry required, on average, between 8 and 15 min—of which only 1 to 5 min were in addition to actions already recommended by medical guidelines for cases of extravasation (Boellaard et al. 2015). At our institutions, we routinely monitor radiopharmaceutical injections using high temporal-resolution uptake probes. This practice simplifies characterization, but other data collection methods may also be appropriate. For example, periodic measurement with a mobile ion chamber (Berry and Kendrick 2022) or serial imaging of the injection site, depending on the availability of technology and personnel, would be obvious options.

We used syngo.via for quantitative image analysis because of availability and our own experience, but we would expect software from other vendors to produce comparable results. Dosimetry results from each of the three characterization tools indicated favorable agreement. We analyzed the results statistically for significant differences and relationships. Data were indicated to be within normality standards and of equal variance. Pearson correlation coefficients between groups were greater than 96% with $P < 0.001$. No statistical difference was detected between groups by one-way ANOVA.

### Table 1. Self-dose factors (mGy/MBq) for six different calculation methods.

| Isotope | Ion Source Simulation | IDAC-Dose 2.1 | OLINDA 2.2.3 | Discrete Emission Simulation | Weighted Average Emission Simulation | Non-Penetrating Emissions Only |
|---------|-----------------------|---------------|--------------|-----------------------------|-------------------------------------|-------------------------------|
| C-11    | 21.8                  | 21.8          | 22.1         | 23.6                        | 22.1                                | 20.3                          |
| Cu-64   | 267.8                 | 266.8         | 268.0        | 278.7                       | 270.3                               | 255.9                         |
| F-18    | 78.7                  | 78.3          | 79.0         | 87.6                        | 78.4                                | 70.8                          |
| Ga-67   | 584.3                 | 576.3         | 536.0        | 579.9                       | 518.1                               | 478.3                         |
| Ga-68   | 120.2                 | 120.9         | 126.0        | 129.9                       | 126.9                               | 116.0                         |
| I-123   | 78.1                  | 78.3          | 77.2         | 78.2                        | 70.9                                | 61.8                          |
| I-131   | 6,276.0               | 6,268.5       | 6,330.0      | 6,414.7                     | 6,384.5                             | 5,986.1                       |
| In-111  | 545.1                 | 543.4         | 538.0        | 543.6                       | 507.9                               | 385.0                         |
| Lu-177  | 3,871.2               | 3,880.5       | 3,940.0      | 3,905.0                     | 3,958.6                             | 3,843.1                       |
| N-13    | 13.1                  | 13.1          | 13.4         | 14.1                        | 13.3                                | 12.3                          |
| O-15    | 3.7                   | 3.7           | 3.9          | 4.0                         | 3.8                                 | 3.5                           |
| Rb-82   | 3.6                   | 3.6           | 3.8          | 3.9                         | 3.9                                 | 3.5                           |
| Sm-153  | 2,045.3               | 2,042.1       | 2,030.0      | 2,076.6                     | 2,045.4                             | 2,023.0                       |
| Sr-89   | 105,833.4             | 103,405.0     | 108,000.0    | 109,467.2                   | 108,543.8                           | 105,799.6                     |
| Tc-99m  | 19.6                  | 19.4          | 19.6         | 19.4                        | 18.8                                | 16.2                          |
| Y-90    | 8,075.2               | 7,971.8       | 8,530.0      | 8,569.8                     | 8,528.5                             | 8,072.2                       |

### Table 2. Mean absolute percent error for alternative dose rate methods as compared to ion source simulation.

| Calculation method                  | Error  |
|-------------------------------------|--------|
| IDAC-Dose 2.1                       | 0.29%  |
| OLINDA 2.2.3                        | 1.06%  |
| Discrete Emission Simulation        | 3.96%  |
| Weighted Average Emission Simulation| 0.11%  |
| Non-Penetrating Emissions Only      | 9.83%  |

### Table 3. Results for recalculation of work published by Castronovo et al. (1988) (absorbed dose, Gy).

| Isotope            | Castronovo et al. Worksheet | Spreadsheet | Web Application |
|--------------------|-----------------------------|-------------|----------------|
| $^{99m}$Tc Microspheres | 1.78                        | 1.70        | 1.69           | 1.78 |
| $^{99m}$Tc MDP      | 2.74                        | 2.28        | 2.96           | 2.42 |
| $^{67}$Ga Citrate   | 1.65                        | 1.50        | 1.83           | 1.74 |
(F = 0.035, P = 0.966). A Tukey post-hoc analysis confirmed no statistically significant difference in means with P > 0.97 for all comparisons.

For image-based activity measurements, we used VOIs defined using a threshold of 10% of local maximum and relied on multiplication of average enclosed activity (Bq mL\(^{-1}\)) by volume (cm\(^3\)). This approach may underestimate the residual activity because in cases of extravasation, even 10% of the maximal voxel’s value can be significantly higher than background. However, the potential loss of accuracy is offset by a reduction in effort and complexity. We expect that a larger number of VOI segments would result in increased accuracy but decreased utility.

Osborne et al. (2021) previously reported that for cases of radiopharmaceutical extravasation, deep tissue dose can be significantly higher than dose to overlying skin. Additionally, appropriate tools already exist for the complex task of skin dosimetry (e.g., VARSKIN) (Hamby and Mangini 2018). For these reasons, we chose instead to concentrate only on calculation of tissue absorbed dose.

We acknowledge that the set of radionuclides included in this work is not exhaustive and does not include, for example, therapeutic alpha emitters. Although extravasation of alpha emitting radiopharmaceuticals can be serious (Benjegerdes et al. 2017; Frantellizzi et al. 2020), dosimetry for these cases would involve assumptions different from those made in this work (e.g., the degree of equilibrium, biodistribution of radioactive progeny over time). The radionuclides presented in this work encompass most nuclear medicine procedures, but we do anticipate the creation of tools to enable straightforward characterization and dosimetry of additional use cases.

### CONCLUSION

Accurate extravasation dosimetry requires characterization of the event. In this work, we developed three extravasation characterization and dosimetry tools, validated each against published data, and demonstrated their utility in a realistic clinical workflow. Free and publicly available tools for practical and rapid characterization of extrasations will be beneficial to patient care, clinical follow-up, documentation, and event reporting.

### Acknowledgments

The authors would like to acknowledge the assistance of Carl Von Gall.

The authors declare no conflicts of interest. Dustin Osborne is conducting research with Lucerno Dynamics unrelated to this manuscript and received no compensation for this work. Misty Long is an employee of Siemens Healthineers. Josh Knowland is an employee of Lucerno Dynamics; Versant Medical Physics and Radiation Safety has provided consultant services to Lucerno Dynamics but did not contribute to or receive payment for this work.

### REFERENCES

Andersson M, Johansson L, Eckerman K, Mattsson S. ldac-dose 2.1, an internal dosimetry program for diagnostic nuclear medicine based on the ICRP adult reference voxel phantoms. EJNMNI Res 7:88; 2017.

Bains A, Botkin C, Oliver D, Nguyen N, Osman M. Contamination in 18F-FDG PET/CT: an initial experience. J Nucl Med 50: 2222; 2009.

Benjegerdes KE, Brown SC, Housewright CD. Focal cutaneous squamous cell carcinoma following radium-223 extravasation. Proc Bayl Univ Med Cent 30:78–79; 2017.

Bennett PA, Mintz A, Perry B, Trout A, Vergara-Wentland P. Specialty imaging: PET. Philadelphia: Elsevier; 2018.

Berry K, Kendrick J. Lutathera (lu-177) extravasation. Health Phys. 123(2):160–164; 2022.

Boellaard R, Delgado-Bolton R, Oyen WJG, Gimanmarie F, Tatsch K, Eschner W, Verzijlbergen PJ, Barrington SF, Pike LC, Weber WA, Stroobants S, Delheke D, Donohoe KJ, Holbrook S, Graham MM, Testanera G, Hoekstra OS, Zijlstra J, Visser E, Hoekstra CJ, Pruim J, Willemsen A, Arends B, Kotzerke J, Bockisch A, Beyer T, Chiti A, Krause BJ. FDG PET/CT: EANM procedure guidelines for tumour imaging: Version 2.0. Eur J Nucl Med Mol Imaging 42:328–354; 2015.

Bonta DV, Halkar RK, Alazraki N. Extravasation of a therapeutic dose of 131I-metaiodobenzylguanidine: prevention, dosimetry, and mitigation. J Nucl Med 52:1418–1422; 2011.

Breen SL, Dredger AA. Radiation injury from interstitial injection of iodine-131-iodocholesterol. J Nucl Med 32:892; 1991.

Burrell S, MacDonald A. Artifacts and pitfalls in myocardial perfusion imaging. J Nucl Med Technol 34:193; 1988.

Currie G, Sanchez S. Topical sensor for the assessment of injection quality for 18F-FDG, 68GA-psma, 68GA-dotatate positron emission tomography. J Med Imag Radiat Sci 2020.

### Table 4. Results of characterization for clinical cases of extravasation.

| Case | 18F | 18F | 68Ga | 18F | 18F | 18F | 18F |
|------|-----|-----|------|-----|-----|-----|-----|
| Isotope | Administered activity (MBq) | 473.6 | 525.4 | 180.6 | 606.4 | 481.4 | 355.2 | 395.9 |
| | Image-based activity measurement (MBq) | 20.8 | 85.2 | 19.1 | 19.0 | 137.1 | 13.1 | 4.8 |
| | Time between injection and imaging (min) | 68.9 | 79.0 | 78.3 | 78.5 | 60.6 | 65.0 | 53.0 |
| | Effective half-life (min) | 27.2 | 40.8 | 34.7 | 53.9 | 55.3 | 25.8 | 40.3 |
| | Tissue absorbed dose, Worksheet (Gy) | 2.0 | 16.2 | 5.1 | 3.0 | 17.6 | 1.2 | 0.38 |
| | Tissue absorbed dose, Spreadsheet (Gy) | 4.3 | 16.7 | 7.9 | 3.2 | 17.3 | 1.3 | 0.39 |
| | Tissue absorbed dose, Web Application (Gy) | 2.7 | 17.4 | 7.0 | 2.6 | 13.4 | 1.6 | 0.39 |
Erthal L, Erthal F, Beanlands RSB, Ruddy TD, deKemp RA, Dwivedi G. False-positive stress PET-CT imaging in a patient with intestinal injection. J Nucl Cardiol 24:1447–1450; 2017.

Esser JP, ed. Procedure Guidelines Nuclear Medicine. Neer, Netherlands: Kloosterhof Neer BV; 2017.

Fleming JS, Zivanovic MA, Blake GM, Burniston M, Cosgriff PS. Guidelines for the measurement of glomerular filtration rate using plasma sampling. Nucl Med Comm 25:759–769; 2004.

Franzellizzi V, Pontico M, Pani A, Pani R, De Vincentis G. Analysis of unusual adverse effects after radium-223 dichloride administration. Current Radiopharmaceut 13:159–163; 2020.

Hall N, Zhang J, Reid R, Hurley D, Knopp M. Impact of FDG extravasation on SUV measurements in clinical PET/CT. Should we routinely scan the injection site? J Nucl Med 47:115P; 2006.

Hamby DM, Mangini CD. Varskin 6: a computer code for skin contamination dosimetry. Washington, DC: USNRC; (NUREG/CR-6918, rev. 3); 2018.

Jan S, Santin G, Strul D, Staelsens A, Assie K, Autret D, Avner S, Barbier R, Bardies M, Bloomfield PM, Brasse D, Breton V, Brouyndonckx P, Buvat I, Chatzioannou AF, Choi Y, Chung YH, Comtat C, Donnaire X, Ferrer L, Glick SJ, Groselle CJ, Guez D, Honore PF, Kerboua-Cavita S, Kirov AS, Kostrub G, Koole M, Krieguer M, van der Laan DJ, Lamarre F, Lamarre G, Lartizien C, Lazaro D, Maas MC, Maigne L, Mayet F, Melot F, Merheb C, Pennacchio E, Perez J, Pietrzyk U, Rannou FR, Rey M, Schait DR, Schmidtcrin CR, Simon L, Song TY, Vieira Jr, Visvikis D, Van de Walle R, Wierse E, Morel C. GATE: a simulation toolkit for PET and SPECT. Phys Med Biol 49:4543–4561; 2004.

Kawabe J, Higashiyama S, Kotani K, Yoshida A, Tsushima H, Yamanaga T, Tsuruta D, Shiomii S. Subcutaneous extravasation of Sr-89: usefulness of bremsstrahlung imaging in confirming Sr-89 extravasation and in the decision making for the choice of treatment strategies for local radiation injuries caused by Sr-89 extravasation. Asia Ocean J Nucl Med Biol 1:56–59; 2013.

Kiser JW, Crowley JR, Wyatt DA, Lattanze RK. Impact of an 18F-FDG PET/CT radiotracer injection infiltration on patient management—a case report. Frontiers Med 5:143; 2018.

Krumrey S, Frye R, Tran I, Yost P, Nguyen N, Osman M. FDG manual injection versus infusion system: a comparison of dose precision and extravasation. J Nucl Med 50:2031; 2009.

Minoshima S, Drzezga AE, Barthel H, Bohnen N, Djekidel M, Lewis DH, Mathis CA, McConathy J, Nordberg A, Sabri O, Seibyl JP, Stokes MK, Van Laere K. SNMMI procedure standard/EANM practice guideline for amyloid PET imaging of the brain 1.0. J Nucl Med 57:1316–1322; 2016.

Murray AW, Barnfield MC, Waller ML, Telford T, Peters AM. Assessment of glomerular filtration rate measurement with plasma sampling: a technical review. J Nucl Med Technol 41:67–75; 2013.

Murthy LV, Bateman TM, Beanlands RS, Berman DS, Borges Neto S, Chareonthaitawee P, Cerqueira MD, deKemp RA, DePuey EG, Dilsizian V, Durbala S, Piccaro E, Garcia EV, Gewirtz H, Heller GV, Lewin HC, Malhotra S, Ruddy TD, Schindler TH, Schwartz RG, Slomka PJ, Soman P, Di Carli MF. Clinical quantification of myocardial blood flow using PET: joint position paper of the SNMMI Cardiovascular Council and the ASNC. J Nuc Med 59:269–297; 2018.

Murazzar R, Frye SA, McMunn A, Ryan K, Lattanze R, Osman MM. Novel method to detect and characterize 18F-FDG infiltration at the injection site: a single-institution experience. J Nucl Med Technol 45:267–271; 2017.

Naddaf SY, Collier BD, Elgazzar AH, Khalil MM. Technical errors in planar bone scanning. J Nucl Med Technol 32:148–153; 2004.

Narkevich BY, Lysak YV, Ryzhov SA. Dosimetric modeling of extravasal administration of therapeutic radiopharmaceutical drugs. Oncol 2:35–41; 2019.

Osborne D, Kiser JW, Knowland J, Townsend D, Fisher DR. Patient-specific extravasation dosimetry using uptake probe measurements. Health Phys 120:339–343; 2021.

Osmann MM, Muzaffar R, Alitynan ME, Teymouri C. FDG dose extrapolations in PET/CT: frequency and impact on SUV measurements. Frontiers Oncol 1:41; 2011.

Ozdemir E, Poyraz NY, Keskin M, Kandemir Z, Turkolmez S. Hot-cot artifacts in the lung parenchyma on F-18 fluorodeoxyglucose emission tomography/CT due to faulty injection techniques: two case reports. Korean J Radiol 15:530–533; 2014.

QIBA SPECT Biomarker Committee. Quantifying dopamine transporters with 123-iodine labeled ioflupane in neurodegenerative diseases. Quantitative Imaging Biomarkers Alliance. Profile Stage: Conformance Testing After Responses to Public Comment. 2017. Available from: http://qibawiki.rsna.org/index.php/Profiles. Accessed 30 June 2022.

Qubti M. Masking effect of radiopharmaceutical dose extravasation during injection on myocardial perfusion defects during SPECT myocardial perfusion imaging: a potential source of false negative result. Mol Imaging Radionucl Ther 27: 141–143; 2018.

Schaefferkoetter JD, Osman M, Townsend DW. The importance of quality control for clinical PET imaging. J Nucl Med Technol 45:265–266; 2017.

Shapiro B, Pillay M, Cox PH. Dosimetric consequences of interstitial extravasation following i.v. administration of a radio-pharmaceutical. Eur J Nucl Med 12:522–523; 1987.

Silva-Rodriguez J, Aguiar P, Sanchez M, Mosquera J, Luna-Vega V, Cortes J, Garrido M, Pombar M, Ruaib A. Correction for FDG PET Dose extrapolations: Monte Carlo validation and quantitative evaluation of patient studies. Med Phys 41:052502; 2014.

Slavin JD Jr, Jung WK, Spencer RP. False-positive renal study with Tc-99m dtpa caused by infiltration of dose. Clin Nucl Med 21: 978–980; 1996.

Terwingehe C, Binnebeek SV, Bergans N, Haustermans K, Van Custem E, Verbruggen A, Deroose CM, Vanbiloen B, Baeoste K, Koole M, Verslype C, Clement PM, Mortelmans L. Extravasation of Y-DOTATOC: case report and discussion of potential effects, remedies and precautions in PRRT. Eur J Nucl Med Molecular Imag 39:155–303; 2012.

Tylski P, Vuillod A, Goutain-Majorel C, Jalade P. Abstract 58, dose estimation for an extravasation in a patient treated with 177Lu-dotatate. Physica Medica 56:32–33; 2018.

van der Pol J, Voo S, Buceriuss J, Mottaghy FM. Consequences of radiopharmaceutical extravasation and therapeutic interventions: a systematic review. Eur J Nucl Med Mol Imag 44:1234–1243; 2017.

Waxman AD, Herholz K, Lewis DH, Herscovitch P, Minoshima S, Ichise M, Drzezga AE, Devous MD, Mountz JM. Procedure guideline for FDG PET brain imaging. Reston, VA: Society of Nuclear Medicine; 2009.

Williams G, Palmer MR, Parker JA, Joyce R. Extravazation of therapeutic yttrium-90-ibritumomab tiuxetan (zevalin): a case report. Cancer Biother Radiopharm 21:101–105; 2006.

Wong TZ, Benefiel T, Masters S, Kiser JW, Crowley JR, Osborne D, Mawlawi O, Barnwell J, Gupta P, Mintz A, Ryan K, Perrin SR, Lattanze RK, Townsend DW. Quality improvement initiatives to assess and improve PET/CT injection infiltration rates in multiple centers. J Nucl Med Technol 47:326–331; 2019.