U.S. Nuclear Regulatory Commission
Office of the Secretary
Attn: Rulemaking and Adjudications Staff
Washington, DC 20555-0001

Subject: Petition to Amend 10 C.F.R. § 35.3045

Dear Ms. Vietti-Cook:

Pursuant to 10 C.F.R. § 2.802, "Petition for Rulemaking," Lucerno Dynamics, LLC, submits the enclosed petition to amend 10 C.F.R. § 35.2, "Definitions" and 10 C.F.R. § 35.3045, "Report and Notification of a Medical Event." In 1980, the Nuclear Regulatory Commission exempted extravasations from medical event reporting with the understanding that extravasations are virtually impossible to avoid. Since that time, ample evidence has been published demonstrating that nuclear medicine extravasations are, in fact, avoidable and are capable of causing considerable harm to the patients. The enclosed petition asks the Nuclear Regulatory Commission to revisit the policy established in 1980 in light of the existing evidence and require the reporting as medical events of certain extravasations. Reporting of certain extravasations as medical events will not only alert the Commission to instances of serious misuse of byproduct material, but will also incentivize practitioners to improve injection and infusion quality. This petition is intended to ensure that diagnostic and therapeutic nuclear medicine patients are protected from avoidable irradiation and given access to vital information to understand when and how medical events impact their care. Lucerno Dynamics, LLC requests that this petition be made available for public comment.

Thank you for your attention to this matter.

Sincerely,

DocuSigned by:
Ron Lattanze
0C2FCDBE78A7435...

Ronald K. Lattanze
Chief Executive Officer
Lucerno Dynamics, LLC
rlattanze@lucernodynamics.com
(919) 371-6800
140 Towerview Court
Cary, NC 27513

I. STATEMENT OF PETITIONER'S INTEREST

Lucerno Dynamics, LLC, is a North Carolina-based company specializing in the design and development of systems to detect the presence of radiolabeled biomarkers in patients. During the development of the Lara® System, Lucerno discovered the device can help clinicians identify, characterize, and reduce the frequency of nuclear medicine injection extravasations. Through extensive literature research and case studies, the company learned that extravasations can result in patient tissue doses that exceed existing U.S. Nuclear Regulatory Commission (NRC) medical reporting limits and can harm patients in many ways. With an intent to reduce harm, Lucerno has shared these findings with the NRC from December 2018 through the present. The Lara® System is FDA listed, commercially available to help characterize extravasations, and has been used to successfully monitor over 19,000 nuclear medicine injections. The system is one of several methods that licensees can use to identify and characterize an unintended tissue infiltration. Our goal is to help reduce the frequency of extravasations in nuclear medicine.

II. PROBLEM STATEMENT

Consistent with the requirements of 10 C.F.R. § 2.802 to present specified problems that should be addressed through rulemaking, including codified requirements that are incorrect, incomplete, inadequate, or unnecessarily burdensome, Lucerno has identified current NRC regulations governing the reporting of medical events that are both incorrect and inadequate to protect the public. In 1980, during misadministration rulemaking, the NRC determined that extravasations are "virtually impossible to avoid."[1] As a result, the NRC exempted all extravasations from medical event reporting requirements, regardless of the radiation dose to the patient's tissue. More recent evidence, however, demonstrates that extravasations are avoidable, invalidating the NRC's 1980 determination and subsequent exemption of extravasations from medical event reporting requirements. This policy is incorrect because patients may receive localized tissue doses that exceed the dose limits specified in 10 C.F.R. § 35.3045 for other types of radiopharmaceutical misadministrations.

Diagnostic and therapeutic extravasations can result in significant radiation doses to injection site tissue, potentially causing harmful adverse tissue reactions and cancer[2]. An incomplete delivery of a diagnostic radiopharmaceutical into the venous system can also compromise imaging, the patient's ensuing care, and sometimes lead to unnecessary additional radiation dose for repeat imaging studies. An extravasation of a therapeutic radiopharmaceutical prevents the target tumor from receiving the prescribed dose, negatively affecting patient care. Despite these patient risks, the current policy exempts extravasations from medical event reporting requirements, rendering these regulations inadequate to protect the public. Patients would be better protected if the medical community and regulators recognized the potential harmful effects of unintended extravasations during radiopharmaceutical administrations.

Exemption of extravasations from medical event reporting requirements results in a lack of transparency to patients, the public, and the NRC. Under current NRC regulations, reportable medical events must be disclosed to patients. Because extravasations are not reported to the NRC, dosimetry is not performed, and extravasated patients and their physicians are not informed when the patients' tissue has been irradiated with doses that could lead to adverse tissue reactions (deterministic effects) post-extravasation. It is possible that patients and clinicians may not be aware that a radiopharmaceutical misadministration

[1] 45 Fed. Reg. 31701 (1980).
[2] *See infra* note 12.

and localized tissue infiltration may have compromised the diagnostic image or intended therapy. Additionally, the NRC remains unaware when licensees are continually misadministering radiopharmaceuticals resulting in doses that exceed medical event reporting limits.

Extravasations occur with frequency in many nuclear medicine centers. The incorrect administration of a radiopharmaceutical by a licensed facility can result in a high localized radiation dose to patients. The extravasation medical event reporting exemption is premised on incorrect information and, as a result, existing regulations fail to protect the public from unnecessary and unsafe irradiation, and the NRC and patients lack the information needed to understand the associated radiation risks. Reporting serious extravasations to the NRC will increase attention to these issues and help licensees reduce the frequency and seriousness of extravasation events. To ensure that the public is adequately protected and the NRC is aware of misuse of NRC-regulated byproduct material, Lucerno Dynamics respectfully petitions the NRC to revise its regulations to require the reporting of extravasations that exceed a 0.5 Sv (50 rem) dose equivalent to tissue.

III. BACKGROUND

a. Understanding Extravasations

A certified nuclear medicine technologist or nurse begins the administration of a radiopharmaceutical by establishing venous access in a patient. Then they inject or infuse the radiopharmaceutical into the patient's venous system and follow with a saline flush to ensure complete delivery. However, an extravasation is an inadvertent injection or infusion of some or all of the radiopharmaceutical into the tissue surrounding a vein. Extravasations can happen during venous access when a catheter punctures or erodes the venous wall or during the injection or infusion when the injection pressure damages the venous wall.[3] An extravasation results in some or all of the radiopharmaceutical not being administered according to prescribed methods (bolus injection or infusion) into the venous system. During an extravasation, the administered radiopharmaceutical infiltrates and irradiates arm tissue as it decays.

Extravasated radiopharmaceutical ends up within the interstitial space outside of the intended delivery vein. The volume of extravasated radiopharmaceutical and saline will determine the initial volume of tissue that is irradiated. Over time, the radiopharmaceutical will disperse through the interstitial space, thus increasing the volume of infiltrated and irradiated tissue. At the same time, the body's venous and lymphatic systems work to reabsorb the extravasated fluid. Although dispersion and reabsorption may follow, irradiation can often last hours and absorbed dose can be significant.

In an extravasation, some radiopharmaceutical remains in the tissue around the injection site and some leaks back into circulation during the uptake period. Extravasations negatively affect imaging in two ways that combined, reduce the image contrast and sensitivity. Extravasations reduce the number of gamma ray counts available from the target regions of interest and the increased amount of radiopharmaceutical in circulation at imaging time elevates the background concentration as compared to the region of interest. In addition, the unknown biological availability of the radiopharmaceutical over time negatively affects the quantification results.[4] Certain nuclear medicine procedures require very low levels of injected

[3] R.E. Helm et al., *Accepted but Unacceptable*, 38 J. INFUSION NURSING 189–203 (2015).
[4] J.W. Kiser et al., *Impact of an 18F-FDG PET/CT Radiotracer Injection Infiltration on Patient Management—A Case Report*, 5 FRONT. MED. 143 (2018); M.C. Adams et al., *A Systematic Review of the Factors Affecting Accuracy*

radioactivity. A small extravasation of these injections can represent a high percentage of the administered dose and can have a potentially large negative effect on image quality. At this time, there is no way to remedy an extravasation once it has occurred.

b. Regulatory History of 10 C.F.R. § 35.3045

10 C.F.R. § 35.3045 requires the reporting of certain medical events to the NRC. Per the Advisory Committee on the Medical Use of Isotopes (ACMUI) Subcommittee on Patient Intervention, "[t]he purpose of reporting Medical Events [is] for the NRC to evaluate if there was a breakdown in the licensee's program for ensuring that byproduct material or radiation from byproduct material was administered as directed by the Authorized User (AU), or if there was a generic issue that should be reported to other licensees, thereby reducing the likelihood of other medical events."[5] Since 1980, extravasations have been interpreted to not be reportable as medical events (or misadminstrations, as such events were referred to at the time).[6] In reaching the decision that an extravasation should not be reported as a misadministration, the NRC concluded that "extravasations frequently occur in otherwise normal intravenous and intraarterial injections and are virtually impossible to avoid."[7]

In 2008, the NRC asked the ACMUI to reconsider the 1980 reporting exemption. At that time, the NRC expressed concern for patient safety given recent changes in practice. Specifically, the NRC was concerned about the higher probability of patient harm from extravasations due to the significant increase in the use of positron-emitting diagnostic radiopharmaceuticals and the development of alpha- and beta-emitting radiotherapeutics.[8] Despite discussing how extravasations could negatively affect patient safety, the ACMUI recommended the NRC retain the reporting exemption, citing the increased administrative reporting burden associated with the frequent occurrence of extravasations.[9]

On April 2, 2019, Lucerno provided evidence to the NRC that extravasation events can be reduced, challenging the 1980 claim that extravasations are "virtually impossible to avoid."[10] Lucerno requested that the NRC and the ACMUI reevaluate the 1980 interpretation regarding extravasations and begin requiring medical event reporting of radiopharmaceutical extravasations that exceed Subpart M reporting limits. On April 3, 2019, Lucerno presented findings regarding nuclear medicine extravasations to the

---

of SUV Measurements, 195 AM. J. ROENTGENOLOGY 310–320 (2010); R. Boellard, et al. *Effects of Noise, Image Resolution, and ROI Definition on the Accuracy of Standard Uptake Values: A Simulation Study*, 45 J. NUCLEAR MED. 1519–1527 (2004).

[5] U.S. Nuclear Regulatory Commission Advisory Committee on the Medical Use of Isotopes, Subcommittee on Patient Intervention Draft Report. March 5, 2020 (hereinafter ACMUI Patient Intervention Draft Report 2020), *available at*: https://adamswebsearch2.nrc.gov/webSearch2/main.jsp?AccessionNumber=ML20078M712.

[6] 45 Fed. Reg. 31701 (1980).

[7] *Id.*

[8] Nuclear Regulatory Commission, Advisory Committee on the Medical Uses of Isotopes, Meeting Materials October 27-28, *available at*: https://www.nrc.gov/docs/ML0900/ML090060121.pdf; Nuclear Regulatory Commission, Advisory Committee on the Medical Uses of Isotopes, Official Transcript of Proceedings for Thursday, December 18, 2008 (hereinafter ACMUI December 2008 Transcript), *available at*: https://www.nrc.gov/docs/ML0903/ML090340745.pdf.

[9] *See* ACMUI December 2008 Transcript, *supra* note 8; Nuclear Regulatory Commission, Advisory Committee on the Medical Uses of Isotopes, May 7-8, 2009 Meeting Summary, *available at*: https://www.nrc.gov/docs/ML0917/ML091730001.pdf; Nuclear Regulatory Commission, Advisory Committee on the Medical Uses of Isotopes, Official Transcript of Proceedings for Friday, May 8, 2009, *available at*: https://www.nrc.gov/docs/ML0920/ML092090025.pdf.

[10] For evidence documenting that extravasations are avoidable, *see infra* V.a.

ACMUI. At the end of the presentation, the Chair of the ACMUI formed the Subcommittee on Extravasation to evaluate the 1980 decision that exempted extravasations from medical event reporting.

On September 10, 2019, the Subcommittee shared its recommendations with the full Committee membership and NRC Medical Branch staff. A majority of Subcommittee members supported retaining the 1980 exemption. The Subcommittee then determined that extravasations should be considered a type of "patient intervention," which is otherwise exempted from medical event reporting requirements.[11] The patient advocate on the Subcommittee disagreed with the Subcommittee's recommendations and provided a written dissenting opinion indicating that extravasations that exceed the reporting dose limit should be reported to the NRC.

c. Radiation Harm from Extravasations

Extravasations can have immediate, medium-, and long-term negative effects on the health and safety of the public. In the short- and medium-term, extravasation of radionuclides can cause adverse tissue reactions including a burning sensation, erythema, swelling, lesions, wet and dry desquamation, severe tissue damage, and radionecrosis.[12] In the longer-term, some patients can develop aggressive skin cancer following an extravasation.[13] Despite the lack of NRC reporting requirements, some extravasations have been reported to other government agencies. Data available in the FDA Adverse Event Report System (FAERS) and the European Database on Medical Devices (EUDAMED) document at least 55 examples of patient harm associated with extravasations.[14]

The NRC has consistently recognized that patients face potential harm even from relatively minor unintentional irradiation. In 1991, the NRC received a comment regarding a proposed rule change that suggested low doses "would not produce any discernible harmful effects to the individual to warrant

---

[11] U.S. Nuclear Regulatory Commission Advisory Committee on the Medical Use of Isotopes, Subcommittee on Extravasation Final Report. October 23, 2019, *available at*: https://www.nrc.gov/docs/ML1931/ML19316E067.pdf (hereinafter NRC ACMUI Extravasation Final Report 2019). *See also*, 10 C.F.R. § 35.2; 10 C.F.R. § 35.3045.

[12] A. Baus et al., *Complex Upper Arm Reconstruction Using an Antero-Lateral Thigh Free Flap After an Extravasation of Yttrium-90-ibritumomab Tiuxetan: A Case Report and Literature Review*, 63 ANNALES DE CHIRURGIE PLASTIQUE ESTHÉTIQUE 175–181 (2018); J. Kawabe, et al. *Subcutaneous Extravasation of Sr89: Usefulness of Bremsstrahlung Imaging in Confirming Sr89 Extravasation and in the Decision Making for the Choice of Treatment Strategies for Local Radiation Injuries Caused by Sr89 Extravasation*. 1 ASIA OCEANIA J. NUCLEAR MED. BIO. 56-59 (2013); D.V. Bonta, et al. *Extravasation of a Therapeutic Dose of 131I-Metaiodobenzylguanidine: Prevention, Dosimetry, and Mitigation*, 52 J. NUCLEAR MED. 1418–1422 (2011); Sergio Vano-Galvan et al., *Technetium and Blood Extravasation before Gammagraphy: A Case Report*, 2 CASES JOURNAL 141 (2009); B.M. Siebeneck. *Extravasation of Yttrium-90 Ibritumomab Tiuxetan: A Case Study*, 12 CLIN. J. ONCOLOGY NURSING 275–278 (2008); G. Williams et al., *Case Report: Extravazation of Therapeutic Yttrium-90-Ibritumomab Tiuxetan (Zevalin®): A Case Report*, 21 CANCER BIOTHERAPY & RADIOPHARM. 101–105 (2006); E.H. Erken, *Radiocolloids in the Management of Hemophilic Arthropathy in Children and Adolescents*, 264 CLIN. ORTHOPAEDICS & RELATED RESEARCH 129-135 (1991); H.S. Patton & R.G. Millar. *Accidental Skin Ulcerations from Radioisotopes: Recognition, Prevention and Treatment*, 143 J. AM. MED. ASSOC. 554–555 (1950).

[13] C.J. Martin, et al. *Unintended and Accidental Medical Radiation Exposures in Radiology: Guidelines on Investigation and Prevention*. 37 J. RADIOL. PROT. 883-906; K.E. Benjegerdes, S.C. Brown & C.D. Housewright, *Focal Cutaneous Squamous Cell Carcinoma Following Radium-223 Extravasation*, 30 BAYLOR UNIVERSITY MEDICAL CENTER PROCEEDINGS 78–79 (2017); *see also* J.A. Siegel, Guide for Diagnostic Nuclear Medicine (2001) at 4-6, *available at*: https://www.nrc.gov/materials/miau/miau-reg-initiatives/guide_2002.pdf.

[14] *See* FDA Adverse Events Reporting System (FAERS) at: https://fis.fda.gov/sense/app/d10be6bb-494e-4cd2-82e4-0135608ddc13/sheet/7a47a261-d58b-4203-a8aa-6d3021737452/state/analysis; European Database on Medical Devices (EUDAMED) at: https://ec.europa.eu/idabc/en/document/2256/5637.html.

immediate reporting." The NRC responded "[d]oses of the order of 25 rems (5 times the 5-rem [1991] annual dose limit) can produce discernible biological effects in the body in the form of chromosome aberrations and changes in the white blood cell populations. Although the majority of these effects are temporary, they could be discerned." The NRC continued, "[h]owever, irrespective of the potential for discernible effects, doses at these levels represent a major breakdown in the licensee's control over the radioactive material, and the Commission believes that it is important that NRC be promptly notified so that it can take actions, if necessary, to limit further consequences."[15]

Avoidance of unintended or accidental medical exposures is a requirement of the International Atomic Energy Agency's Basic Safety Standards Requirement 41, stating "licensees shall ensure that all practicable measures are taken to minimize the likelihood of unintended or accidental medical exposures. Registrants and licensees shall promptly investigate unintended or accidental medical exposures and, if appropriate, shall implement corrective actions."[16] These statements are consistent with leading guidance from the Joint Government Relations Committee of the American College of Nuclear Physicians and the Society of Nuclear Medicine and Molecular Imaging, which recognizes that ionizing radiation can result in deterministic and stochastic effects, and that the "risk of stochastic effects increases as a function of radiation dose."[17] Because extravasations can exceed 25 rem dose equivalent to tissue, they can produce discernable biological effects in the body, pose potential patient harm, and would be reportable to the NRC if not for the 1980 policy.

In 2017, van der Pol et al. conducted a systematic review of both diagnostic and therapeutic extravasations. Excerpts from their article provide insight on the topic of extravasation that the NRC should consider:

- "Because of the character of the radiation, extravasation of therapeutic radiopharmaceuticals has the highest tendency to result in tissue damage, although some cases of tissue damage following the extravasation of diagnostic radiopharmaceuticals have been reported."
- "Lack of clinical follow-up after diagnostic nuclear medicine scans, but also a conservative attitude towards reporting and publishing of complications may have possibly lead [sic] to under-reporting of skin lesions."
- "Clearance evaluation and dosimetry are often advised to be part of extravasation management. Different methods have been used, yielding a large range of tissue doses, due to uncertainties such as retained activity and the volume of the infiltrated tissue, as well as the use of worse case scenarios. Sequential activity measurements with probes or gamma-camera can give useful insight in biological half-life, as well as effectiveness of applied interventions."[18]

[15] 56 Fed. Reg. 23385 (1991).
[16] International Atomic Energy Agency, RADIATION PROTECTION AND SAFETY OF RADIATION SOURCES: INTERNATIONAL BASIC SAFETY STANDARDS, at: 84. *See also*, International Commission on Radiological Protection (ICRP), *Radiological protection in therapy with radiopharmaceuticals*, 140 ANN. OF THE ICRP 5 (2019).
[17] Siegel, *supra* note 13, at 4-6.
[18] J. van der Pol et al., *Consequences of Radiopharmaceutical Extravasation and Therapeutic Interventions: A Systematic Review*, 44 EURO. J. NUCLEAR MED. & MOLEC. IMAGING 1234–1243 (2017).

d. Clinical Impact of Extravasations on Imaging and Therapy

In addition to the radiation harm posed to patients, extravasations can also negatively impact the course of patient care. Of the approximately 2.5 million PET/CT procedures each year in the US, over 90% are used to help oncologists diagnose, stage, choose therapy, plan treatments, assess tumor response, or longitudinally monitor cancer patients.[19] A few years after PET/CT scan reimbursement was approved by the Centers for Medicaid and Medicare Services (CMS), data from 40,863 PET/CT procedures performed at 1,368 centers were reported in the National Oncologic PET Registry (NOPR). The impact of PET/CT imaging was assessed for 18 cancer types in patients with pathologically confirmed cancer. PET/CT images caused clinicians to change their intended management for 38% of patients. The NOPR demonstrated that PET/CT scans are a very sensitive imaging modality with respect to cancer, and that the scan results play an important role in therapeutic decision-making.[20] Importantly, extravasations have a negative effect on the sensitivity of PET/CT. Possible clinical implications of an extravasation on a PET/CT study for the management of cancer patients include:

Under-staging the disease. Extravasations can lead to unnecessary or ineffective surgery and its associated morbidity and cost, and delay initiation of necessary systemic treatment (e.g., a lung cancer patient's metastatic disease is missed and the patient may receive unnecessary surgery for what is thought to be a single lung lesion).[21] The ways in which under-staging can occur include:

- Failure to detect metastatic disease due to degraded PET/CT image quality and inaccurate quantification results. Due to low count rates, some metastatic disease may not be seen, or if visible, may be considered to be benign.[22]

---

[19] L. Muschlitz. *Report Finds Slowing in PET Annual Growth Rate, at*: https://www.auntminnie.com/index.aspx?sec=ser&sub=def&pag=dis&ItemID=95998. Accessed March 14, 2018; H. Jadvar et al., *Appropriate Use Criteria for18F-FDG PET/CT in Restaging and Treatment Response Assessment of Malignant Disease*, 58 J. NUCLEAR MED. 2026–2037 (2017); D. Groheux & E. Hindie. *Breast Cancer Staging: To Which Women Should 18F-FDG PET/CT Be Offered?* 56 J. NUCLEAR MED. 1293 (2015); O. Humbert, et al. *Role of Positron Emission Tomography for the Monitoring of Response to Therapy in Breast Cancer.* 20 ONCOLOGIST 94-104 (2015); S. Ng et al., *Impact of Pretreatment Combined 18F-Fluorodeoxyglucose (FDG) Positron Emission Tomography/ Computed Tomography Staging on Radiation Therapy Treatment Decisions in Locally Advanced Breast Cancer: A Prospective Evaluation*, 90 INT. J. RADIATION ONC., BIO., AND PHYSICS (2014); X-Y Wang, et al. *Utility of PET/CT in diagnosis, staging, assessment of resectability and metabolic response of pancreatic cancer*. 20 WORLD J. GASTROENTEROLOGY 15580- 15589 (2014); J. Cuaron, M. Dunphy & A. Rimner, *Role of FDG-PET Scans in Staging, Response Assessment, and Follow-Up Care for Non-Small Cell Lung Cancer*, 2 FRONTIERS IN ONCOLOGY (2013); N. Daher. *US Nuclear Medicine and PET Imaging Systems Market, at:* https://cds.frost.com/p/71559/#!/ppt/c?id=NCFC-01-00-00-00&hq=US%20Nuclear%20Medicine%20and%20PET%20Imaging%20Systems%20Market. Accessed May 6, 2014; S. Rankin, *PET/CT for Staging and Monitoring Non Small Cell Lung Cancer*, 8 CANCER IMAGING S27-31 (2008).

[20] B.E. Hillner et al., *Impact of Positron Emission Tomography/Computed Tomography and Positron Emission Tomography (PET) Alone on Expected Management of Patients With Cancer: Initial Results From the National Oncologic PET Registry*, 26 J. CLIN. ONCOLOGY 2155–2161 (2008); Bruce E. Hillner et al., *Relationship Between Cancer Type and Impact of PET and PET/CT on Intended Management: Findings of the National Oncologic PET Registry*, 49 J. NUCLEAR MED. 1928–1935 (2008).

[21] *See* Kiser, et al., *supra* note 4.

[22] van der Pol et al., *supra* note 18; P.A. Bennett, et al. *Specialty Imaging: PET Positron Emission Tomography with Correlative CT and MR.* Vol 1: Elsevier (2018); J.D. Schaefferkoetter, M. Osman & D.W. Townsend, *The Importance of Quality Control for Clinical PET Imaging*, 45 J. NUCLEAR MED. TECH. 265–266 (2017); E. Ozdemir et al., *Hot-Clot Artifacts in the Lung Parenchyma on F-18 Fluorodeoxyglucose Positron Emission Tomography/CT*

- Masked metastatic disease caused by significant extravasation artifacts in image.[23]
- Misinterpreting metastatic disease, identified near an expected injection site location, as an extravasation.[24]

Over-staging the disease. Extravasations can lead to treatment for metastatic disease, which withholds potentially lifesaving regional therapy from the patient (e.g., an incorrect finding of metastatic disease in a lung cancer patient with a single lesion results in systemic treatment for metastatic disease rather than regional surgery or radiation therapy). The ways in which over-staging can occur include:

- False positive lymph nodes with no obvious evidence of extravasations (due to the transport of extravasated radiopharmaceuticals through lymph channels to regional lymph nodes) may result in unnecessary invasive procedures like fine needle aspiration cytology (FNAC) or changes in chemotherapy regimens.[25]
- False positive bone scans.[26]

---

due to Faulty Injection Techniques: Two Case Reports, 15 KOREAN J. RADIOLOGY 530 (2014); P. Bennett, Dose Infiltration, February 2, 2018, at: https://www.instagram.com/p/BespZWGjUxy/?hl=en&taken-by=nuclear_radiology.

[23] T.V. Bogsrud & V.J. Lowe. *Normal variants and pitfalls in whole-body PET imaging with 18F FDG*. 35 APPLIED RADIOLOGY 16-30 (2006).

[24] L.I. Sonoda et al., *FDG Injection Site Extravasation: potential pitfall of misinterpretation and missing metastases*, 37 CLIN. NUCLEAR MED. 1115–1116 (2012).

[25] Bogsrud & Lowe, *supra* note 23; Sonoda et al. *supra* note 24; van der Pol, et al., *supra* note 18; Y. Liu. *Fluorodeoxyglucose uptake in absence of CT abnormality on PET-CT: What is it?* 5 WORLD JOURNAL OF RADIOLOGY 460-467 (2013); N.M. Long & C.S. Smith, *Causes and imaging features of false positives and false negatives on 18F-PET/CT in oncologic imaging*, 2 INSIGHTS INTO IMAGING 679–698 (2011); T. Wagner et al., *A false-positive finding in therapeutic evaluation: hypermetabolic axillary lymph node in a lymphoma patient following FDG extravasation*, 14 NUCLEAR MED. REV. 109–111 (2011); B. Mittal et al., *New axillary lymph nodal F-18 fluoro-deoxy glucose uptake in an interim positron emission tomography scan - not always a sign of disease progression*, 26 INDIAN J. NUCLEAR MED. 192 (2011); S. Vallabhajosula, et al. *Altered biodistribution of radiopharmaceuticals: role of radiochemical/pharmaceutical purity, physiological, and pharmacologic factors*. 40 SEM. NUCLEAR MED. 220-241 (2010); S.B. Chiang et al., *Potential False-Positive FDG PET Imaging Caused by Subcutaneous Radiotracer Infiltration*, 28 CLIN. NUCLEAR MED. 786–788 (2003); J. Stauss, T.S. Treves & L.P. Connolly, *Lymphatic Tc-99m DMSA Localization After Partial-Dose Extravasation*, 28 CLIN. NUCLEAR MED. 618–619 (2003); A.G. Pitman, et al. *Inadvertent 2-deoxy-2-[18F]fluoro-D-glucose lymphoscintigraphy: a potential pitfall characterized by hybrid PET-CT*. 4 MOLEC. IMAGING BIO. 276-278 (2002); W-J Shih, et al. *Visualization in the ipsilateral lymph nodes secondary to extravasation of a bone-imaging agent in the left hand: a case report*. 29 J. NUCLEAR MED. TECH. 154-155 (2001); W-J Shih, et al. *Axillary lymph node uptake of Tc-99m MIBI resulting from extravasation should not be misinterpreted as metastasis*. 13 ANN. NUCLEAR MED. 269-271 (1999); W-J Shih, et al. *Lymph node visualization in the elbow region*. 37 J. NUCLEAR MED. 1913 (1996); J.D. Slavin, W.K. Jung & R.P. Spencer, *False-Positive Renal Study With Tc-99m DTPA Caused by Infiltration of Dose*, 21 CLINICAL NUCLEAR MEDICINE 978–980 (1996); F. Ongseng et al. *Axillary lymph node uptake of technetium-99mMDP*. 36 J. NUCLEAR MED. 1797-1799 (1995); P.J. Peller, V.B. Ho & M.J. Kransdorf, *Extraosseous Tc-99m MDP uptake: a pathophysiologic approach.*, 13 RADIOGRAPHICS 715–734 (1993); J.W. Wallis, S. Fisher & R.L. Wahl, *99Tcm-MDP uptake by lymph nodes following tracer infiltration*, 8 NUCLEAR MED. COMM. 357–363 (1987); F. Vieras. *Serendipitous lymph node visualization during bone imaging*, 11 CLIN. NUCLEAR MED. 434 (1986); H.F. Penney & C.B. Styles, *Fortuitous Lymph Node Visualization After Interstitial Injection of Tc-99m-MDP*, 7 CLIN. NUCLEAR MED. 84–85 (1982).

[26] M.P. Andrich & C.C. Chen, *Bone Scan Injection Artifacts*, 21 CLIN. NUCLEAR MED. 260–262 (1996); A.S. Dogan & K. Rezai. *Incidental lymph node visualization on bone scan due to subcutaneous infiltration of Tc-99m MDP. A potential for false positive interpretation*, 18 CLIN. NUCLEAR MED. 208- 209 (1993).

- Spurious lung lesions caused by radioactive clots from extravasations; such spurious lesions may require investigation by diagnostic CT and sometimes rescanning to ensure there is not a lung lesion.[27]

The negative effects of extravasations are not limited just to PET/CT imaging procedures. Negative clinical outcomes can also result from extravasations of gamma camera procedures. Approximately 15 million gamma camera procedures are performed each year in the US. Extravasations during these procedures have similar implications to those found during PET/CT procedures: misinterpretation of results may lead to patient harm and unnecessary invasive procedures. Extravasations have negatively impacted imaging quality and patient care in renal scan/glomerular filtration rate studies,[28] Tc-99m Sestambi cardiac studies,[29] multigated acquisition chemotherapy monitoring studies,[30] dopamine transporter imaging studies,[31] ventilation perfusion pulmonary embolism studies,[32] and planar bone scans.[33] When extravasations are recognized to have compromised the image, some licensees choose to repeat the diagnostic procedure. These repeated procedures result in patients receiving additional radiation that would have been unnecessary if the patient had not been extravasated.

[27] Bogsrud & Lowe, *supra* note 23; Liu, *supra* note 25; Ozdemir et al., *supra* note 22; D.L. Simpson, et al. *FDG PET/CT: Artifacts and Pitfalls*, 40 CONTEMP. DIAGNOSTIC RADIOLOGY 108 (2017); J. Giron et al., *Accuracy of positron emission tomography may be improved when combined with postcontrast high-resolution computed tomography scan In Regard to Pepek et al.* 5 PRACTICAL RADIATION ONCOLOGY e549-e550 (2014); M. Farsad, et al. *Focal lung uptake of 18F-fluorodeoxyglucose (18FFDG) without computed tomography findings*, 26 NUCLEAR MED. COMM. 827-830 (2005).

[28] A.W. Murray, et al. *Assessment of Glomerular Filtration Rate Measurement with Plasma Sampling: A Technical Review*. 41 J. NUCLEAR MED. TECH. 67-75 (2013); J.S. Fleming, et. a. *Guidelines for the measurement of glomerular filtration rate using plasma sampling*. 25 NUCLEAR MED. COMMUN. 759-769 (2004); J.D. Slavin, et al. *False-positive renal study with Tc-99m DTPA caused by infiltration of dose*. 21 CLIN. NUCLEAR MED. 978-980 (1996).

[29] S. Burrell & A. MacDonald. *Artifacts and pitfalls in myocardial perfusion imaging*. 34 J. NUCLEAR MED. TECH. 193-211; quiz 212-194 (2006).

[30] J.A. Ponto. *Preparation and Dispensing Problems Associated with Technetium Tc-99m Radiopharmaceuticals. Correspondence Continuing Education Courses for Nuclear Pharmacists and Nuclear Medicine Professionals* [2004; Volume 11, lesson 1, at: https://pharmacyce.unm.edu/nuclear_program/freelessonfiles/Vol11Lesson1.pdf.

[31] Alliance QIB. QIBA Profile: Quantifying Dopamine Transporters with 123Iodine Labeled Ioflupane in Neurodegenerative Diseases. In: QIBA, ed. QIBA Profile; 2017. Agency EM. DaTSCAN, INN- Ioflupane (123I) Injection issues. 2004.

[32] S. Hur, et al. *Optimizing the Ventilation–Perfusion Lung Scan for Image Quality and Radiation Exposure*. 42 J. NUCLEAR MED. TECH. 51-54 (2014); S. Mallick & D. Petkova. *Investigating suspected pulmonary embolism during pregnancy*. 100 RESPIR. MED. 1682-1687 (2006). 85. S. Goel, et al. *Recognition of dose infiltration on pulmonary ventilationperfusion scintigraphy*. 6 RADIOLOGY CASE REPORTS 562 (2011).

[33] S. Y. Naddaf, et al. *Technical Errors in Planar Bone Scanning*. 32 J. NUCLEAR MED. TECH. 148-153 (2004).

IV. PROPOSED CHANGES TO 10 C.F.R. § 35.3045

a. Regulatory Authority

The NRC is obligated to provide for the radiation safety of workers and the general public in and outside of the medical context. The purpose of NRC regulation is to assure radioactive materials are used properly, including when used in medical diagnosis, treatment, or research.[34] The NRC Medical Use Policy Statement describes the NRC's approach to regulating the medical use of byproduct material. The NRC's approach is governed by four guiding principles: 1) The NRC will continue to regulate the medical use of radioisotopes as necessary to provide for the radiation safety of workers and the general public. 2) The NRC will not intrude into the medical judgements affecting patients, except as necessary to provide for the radiation safety of workers and the general public. 3) The NRC will, when justified by the risk to patients, regulate the radiation safety of patients primarily to assure the use of radionuclides is in accordance with the physician's direction. 4) The NRC, in developing a specific regulatory approach, will consider industry and professional standards that define acceptable approaches of achieving radiation safety.[35] Per this Policy Statement, the NRC has the obligation to regulate nuclear medicine procedures to ensure the safety of the general public by limiting unnecessary radiation exposure. Additionally, the NRC has the obligation and ability to intrude into medical judgments affecting patients as necessary to provide for the radiation safety of workers and the general public. As such, the NRC has both the ability and obligation to regulate extravasations as necessary to provide for the radiation safety of workers and the general public.

b. Interpretation of Existing Authority

Existing regulatory authority generally requires licensees to report the unintentional administration of byproduct material or radiation from byproduct material that exceed certain radiation dose limits.[36] While medical events are generally reportable to the NRC, medical events that qualify as patient interventions need not be reported. Patient interventions are defined in 10 C.F.R. § 35.3045 as "actions by the patient or human research subject, whether intentional or unintentional, such as dislodging or removing treatment devices or prematurely terminating the administration."[37] The 2019 ACMUI Subcommittee on Extravasation Final Report and Subcommittee on Patient Intervention Draft Report each recommended that extravasations be considered a patient intervention, thereby exempting extravasations from the reporting requirements of 10 C.F.R. § 35.3045.[38] In doing so, the Subcommittees classified extravasations as a "passive" patient intervention, a concept neither defined nor referenced in existing regulations but described by the Patient Intervention Subcommittee as an unintentional treatment outcome due to anatomic or physiological anomaly of the patient.[39]

---

[34] U.S. Nuclear Regulatory Commission, NRC Library. Backgrounder on Risks Associated with Medical Events, *available at*: https://www.nrc.gov/reading-rm/doc-collections/fact-sheets/risks-assoc-medical-events.html.
[35] 65 Fed. Reg. 47654 (2000).
[36] *See* 10 C.F.R. § 35.3045.
[37] 10 C.F.R. § 35.2.
[38] ACMUI Patient Intervention Draft Report 2020, *supra* note 5; NRC ACMUI Extravasation Final Report 2019, *supra* note 11.
[39] NRC ACMUI Extravasation Final Report 2019, *supra* note 11; ACMUI Patient Intervention Draft Report 2020, *supra* note 5. 10 C.F.R. § 35.2 defines "patient intervention" as "actions by the patient or human research subject,

The plain language of the existing regulation, however, contradicts the notion that an extravasation could be considered a patient intervention. The definition of patient intervention requires that an action be taken – intentionally or unintentionally – by the patient for an otherwise reportable medical event to be exempt from reporting requirements. An intentional action, for example, would include a situation in which the patient actively chose to remove an intravenous needle or refused to continue a course of treatment. An involuntary action, per the Code of Federal Regulation, still requires that patient action or status results in the medical event. Intentional and unintentional patient interventions inherently involve circumstances created by the patient. Extravasations, on the other hand, are avoidable and under the control of the practitioner – not the patient. With adequate training, skill, tools, and injection quality monitoring, practitioners are capable of improving injection quality independent of any action of the patient. Rather than classifying an extravasation as a patient intervention, it would be more appropriate and within the NRC's authority to classify an extravasation as a reportable medical event when the unintended absorbed dose and the resulting dose equivalent to injection site tissue is determined to be more than 0.5 Sv (50 rem) dose equivalent. The proposed modifications to 10 C.F.R. § 35.3045 and 10 C.F.R. § 35.2 below clarify that extravasations that exceed reporting thresholds are best treated as medical events that must be reported to the NRC.

c. Requested Modifications to 10 C.F.R. § 35.2 and 10 C.F.R. § 35.3045

To ensure the safety of the public as it relates to nuclear medicine extravasations, the NRC should make the following modifications to 10 C.F.R. § 35.2 and 10 C.F.R. § 35.3045:

10 C.F.R. § 35.2 should be amended to include a definition of "extravasation" as follows:

> "Extravasation means the inadvertent injection or infusion of some or all of a radiopharmaceutical dosage into the tissue surrounding a vein or artery."

10 C.F.R. § 35.3045(a)(1) should be amended by adding the following item iv.:

> "(iv) An extravasation that leads to an irradiation resulting in a localized dose equivalent exceeding 0.5 Sv (50 rem)."

The effect of these modifications would be to require reporting of extravasations resulting in a localized dose equivalent exceeding 0.5 Sv (50 rem).

To allow practitioners to improve their injection technique and to avoid a temporarily burdensome number of medical event reports, the Commission could issue an enforcement guidance memorandum that exempts licensees from the requirement to report extravasation events to the NRC for 12 months. While the memorandum would allow practitioners the opportunity to improve their injection technique before needing to report extravasations to the NRC, it would not exempt licensees from their obligation to report extravasation events that exceed reporting limits to patients and their physicians during this 12-month period.

whether intentional or unintentional, such as dislodging or removing treatment devices or prematurely terminating the administration." 10 C.F.R. § 35.2 does not define or include passive patient interventions.

V. RATIONALE FOR PROPOSED CHANGES

a. Extravasations are Unlike Other Exempted Events because Extravasations are Avoidable

Unlike patient interventions which are ostensibly outside of the control of a physician or other practitioner, extravasations are avoidable. Ample evidence stemming from quality improvement efforts demonstrates that extravasations are avoidable and, therefore, not a result of the voluntary or involuntary actions of the patient. In injection processes for patient populations similar to nuclear medicine patient populations, monitoring and reporting requirements have led to continual quality improvement efforts, and extravasation rates have declined to low levels as a result. Despite this improvement, clinicians continue to make large scale efforts to drive these rates even lower.[40] Chemotherapy extravasation rates in the 1980s and 1990s ranged from 3-6%.[41] A recent attempt to create a national benchmark of the chemotherapy extravasation rate assessed 739,832 patients and documented an overall extravasation rate was 0.10%, with peripheral IV and central venous access methods contributing estimated extravasation rates of 0.18% and 0.01%, respectively.[42] Similar efforts to reduce non-ionic iodinated contrast medium extravasation rates have also proven successful. CT extravasation rates from 1991-2007 were 0.45%. In 2015, A National Data Registry and Practice Quality Improvement Initiative involving 454,497 CT scans showed that rates had improved to 0.24%.[43]

Low extravasation rates can also be accomplished in nuclear medicine injections. For example, a 2019 study by Wong, et al. utilized a design, measure, analyze, improve, control quality improvement methodology to address PET/CT injection quality. Of the seven centers that participated, four designed quality improvement plans based on extravasation contributing factors specific to their centers and improved and sustained their baseline extravasation rates.[44] Their aggregated rate had a statistically significant decrease, from 8.9% to 4.6% ($p<0.0001$). These results were accomplished in approximately six to eight months from the time the centers began measuring their baseline extravasation rates. These findings suggest that, not only are extravasations avoidable, but that investments in quality improvement can significantly lower the rate of extravasation.

The anatomical or physiological conditions of the patient need not contribute to the rate of extravasation. In its Draft Report dated March 5, 2020, the ACMUI Subcommittee on Patient Intervention recommended that "patient intervention" in 10 C.F.R. § 35.2 be interpreted to include "medical outcomes resulting from the anatomical or physiological conditions of the patient, such as extravasation, migration of implanted radioactive seeds, arterial spasm, and the onset of other underlying medical diseases and disorders which

---

[40] C.E. Coyle, J. Griffie & L.M. Czaplewski, *Eliminating Extravasation Events*, 38 J. INFUSION NURSING Suppl 6:S43-50 (2015).
[41] N.W. Lemmers et al., *Complications of venous access ports in 132 patients with disseminated testicular cancer treated with polychemotherapy*, 14 J. CLIN. ONCOLOGY 2916–2922 (1996); D.M. Boyle & C. Engelking. *Vesicant extravasation: myths and realities*, 22 ONCOLOGY NURSING FORUM 57-67 (1995).
[42] J. Jackson-Rose J, et al. *Chemotherapy Extravasation: Establishing a National Benchmark for Incidence Among Cancer Centers*, 21 CLIN. J. ONCOLOGY NURSING 438-445 (2017).
[43] T.M. Dykes TM, M. Bhargavan-Chatfield M & R.B. Dyer. *Intravenous contrast extravasation during CT: a national data registry and practice quality improvement initiative*. 12 J. AM. COLL. RADIOLOGY 183- 191 (2015); C.L.Wang, et al. *Frequency, Management, and Outcome of Extravasation of Nonionic Iodinated Contrast Medium in 69,657 Intravenous Injections*, 243 RADIOLOGY 80-87 (2007).
[44] T. Z. Wong, et al., *Quality Improvement Initiatives to Assess and Improve PET/CT Injection Infiltration Rates at Multiple Centers*, 47 J. NUCLEAR MED. TECH. 326–331 (2019).

interfere with the prescribed treatment." Setting aside that 10 C.F.R. § 35.2 only includes actions taken by the patient, rather than inaction, passive actions, or the anatomical or physiological conditions of the patient, the framing of extravasations as a result of "anatomical or physiological conditions of the patient" belies the existing evidence that extravasations are, in fact, preventable and are not due exclusively to the anatomical or physiological conditions of the patient. Indeed, extravasation quality initiatives resulting in reduced extravasation rates demonstrate conclusively that extravasations are due to practitioner skills, tools, and training rather than the anatomical or physiological conditions of the patient.[45]

b. Reporting Extravasations as Medical Events Will Increase the Likelihood that Radionuclides are Used in Accordance with Physicians' Direction

The NRC Medical Use Policy Statement states that the NRC will, when justified by the risk to patients, regulate the radiation safety of patients primarily to assure the use of radionuclides is in accordance with the physician's direction.[46] By definition, when an extravasation occurs, the radionuclides are not used in accordance with the physician's direction. Medical event reporting can address this lapse in patient safety and care quality by documenting the incidence of extravasations, incentivizing practitioners to monitor their extravasation rates, and alerting the NRC to practices that fail to assure the use of radionuclides in accordance with physicians' directives.

Studies suggest that an average of 15% (range between 2-23%) of nuclear medicine intravenous injections may result in an extravasation.[47] Stated differently, approximately 15% of nuclear medicine intravenous injections result in radionuclides being delivered contrary to a physician's direction. While extravasations in excess of 0.5 Sv (50 rem) dose equivalent may pose substantial risks to patients and constitute a misuse of NRC-regulated byproduct material, the vast majority of extravasations result in irradiation far below this limit. The modifications proposed by this petition are structured such that extravasations below the existing reporting limit would not need to be reported to the NRC. As with other medical event reports, by limiting the reports to only those events that exceed 0.5 Sv (50 rem) dose equivalent to tissue, the NRC will only receive reports of higher risk misadministrations. Therefore, licensees that rarely extravasate or exceed reportable limits will be unaffected by the proposed modifications to 10 C.F.R § 35.3045.

Additionally, it is reasonable to expect that nuclear medicine licensees that extravasate injections at a high rate will undertake greater injection quality controls. These centers would use the 12-month reporting exemption period to focus on identifying and characterizing extravasations and estimating the dose to tissue. They would undergo the training necessary to bring their extravasation rates down. During this period of increased focus on extravasations, nuclear medicine practitioners should not expect that

---

[45] *See infra* V.a.

[46] 65 Fed. Reg. 47654 (2000).

[47] Wong, *supra* note 44; R. Muzaffar, et al. *Novel Method to Detect and Characterize (18)F-FDG Infiltration at the Injection Site: A Single-Institution Experience*. 45 J. NUCLEAR MED. TECH. 267-271 (2017); J. Silva-Rodriguez, et al. *Correction for FDG PET dose extravasations: Monte Carlo validation and quantitative evaluation of patient studies*. 41 MED. PHYSICS 052502 (2014); M.M. Osman, et al. *FDG Dose Extravasations in PET/CT: Frequency and Impact on SUV Measurements*. 1 FRONTIERS IN ONCOLOGY 41 (2011); A. Bains, et al. *Contamination in 18F-FDG PET/CT: An initial experience*. 50 J. NUCLEAR MED. 2222 (2009); S. Krumrey, et al. *FDG manual injection verses infusion system: A comparison of dose precision and extravasation*. 50 J. NUCLEAR MED. 2031 (2009); N. Hall, et al. *Impact of FDG extravasation on SUV measurements in clinical PET/CT. Should we routinely scan the injection site?* 47 J. NUCLEAR MED. 115P (2006); T.Z. Wong, et al. *Multi-Center Quality Improvement Project to Assess and Improve PET/CT 18F-FDG Injection Infiltration Rates* (submitted to JACR, December 11, 2018).

investigating the extravasation severity would result in a substantial increase in the burden of care for these patients. Existing practice standards already require the imaging of an injection site if an extravasation is suspected.[48] Furthermore, a novel dosimetry method presented at the 2020 SNMMI and ACNM Mid-Winter meeting and currently under peer-review for publication provides a more accurate way to assess dose to tissue. Centers that identify and characterize extravasations would modify their procedures to ensure patient safety and to ensure that radionuclides are delivered in accordance with physician directions. These efforts will lead to fewer extravasations overall and even fewer extravasations that would require reporting to the NRC.

c. Ethical Obligation to Inform Patients when Extravasations Occur

Physicians have a well-documented and long-understood ethical obligation to disclose adverse events to patients. Indeed, even when the information is irrelevant to the patient's treatment or therapeutic options, "[p]atients have a right to know their past and present medical status, including conditions that may have resulted from medical error."[49] Existing NRC regulations codify this ethical obligation in 10 C.F.R. § 35.3045(e) by requiring licensees to notify the referring physician and patient following a reportable medical event, unless the referring physician personally informs the licensee either that he or she will inform the individual or that, based on medical judgment, telling the individual would be harmful. In setting this requirement, the NRC stated that it "continue[s] to believe that patient notification enables patients, in consultation with their personal physicians, to make timely decisions regarding any remedial and prospective medical care. This approach also codifies existing medical ethical standards requiring physicians to provide complete and accurate information to their patients."[50] Like other reportable medical events, extravasations have the potential to harm patients and may require remedial actions by the patient's care team. A patient has the right to, and practitioners have the ethical obligation to empower each patient to have, an understanding of the medical events that may impact the patient's health or treatment. Modifying 10 C.F.R. § 35 to require the medical event reporting of extravasations exceeding 0.5 Sv (50 rem) dose equivalent to tissue will ensure that patients receive information about their health and treatment, consistent with existing, long-standing ethical obligations of the medical community. This ethical obligation also counsels in favor of immediate implementation of the requirement to notify patients when an extravasation occurs, while nevertheless permitting a 12-month exemption from reporting to the NRC. Implemented in this way, the NRC will ensure that practitioners meet their ethical obligations to patients without overburdening either practitioners or the NRC with medical event reports.

d. The NRC is Obligated to Protect the Public

Nuclear Safety Culture is a guiding tenet of the NRC's policy mission. Per the NRC's Nuclear Safety Culture Policy Statement, Nuclear Safety Culture is "the core values and behaviors resulting from a collective commitment by leaders and individuals to emphasize safety over competing goals to ensure protection of people and the environment."[51] Medical event reporting, as required by 10 C.F.R. Part 35 *et seq.* is a pillar of the NRC's commitment to safety and is intended to provide for the radiation safety of

[48] R. Boellaard, et al. *FDG PET/CT: EANM Procedure Guidelines for Tumour Imaging: Version 2.0*. 42 EUR. J. NUCLEAR MED. MOL. IMAGING 328-354 (2015).
[49] American Medical Association Code of Medical Ethics Opinion 8.6, *available at*: https://www.ama-assn.org/delivering-care/ethics/promoting-patient-safety.
[50] 67 Fed. Reg. 20249, 20297 (2002).
[51] 76 Fed. Reg. 34777 (2011).

workers, the general public, patients, and human research subjects.[52] Indeed, the NRC cites problem identification and resolution, personal accountability, and continuous learning as positive traits of safety culture.[53] Consistent with this purpose, the NRC regulates the use of radionuclides in medical practice and requires the reporting of medical events, balancing the safety of the public with deference to physician judgment in the practice of medicine. Extravasations have the potential to irradiate patient tissue and result in high absorbed doses. Extravasations can also compromise diagnostic images and patient healthcare and can negatively affect the delivery of radiotherapeutics. They can also result in repeat imaging that provides patients with unnecessary irradiation and exposure, which is contrary to the principle of "as low as reasonably achievable" (ALARA). The risk of unintentional tissue dose justifies NRC intervention to protect the public. Unintended tissue doses resemble the type of error that warrants NRC attention—such as the administration of the wrong radiopharmaceutical to the patient or the administration of a radiopharmaceutical to the wrong patient.

Harms associated with staging, diagnosis, and treatment selection also pose major risks to patients. In its analysis, the ACMUI repeatedly referred to such harms as outside of the purview of the NRC because such medical events constitute "the practice of medicine."[54] Even if accepting, for the sake of argument, that these medical events do indeed constitute the practice of medicine, or "medical judgments affecting patients" as it is referred to in the NRC Medical Use Policy Statement, the NRC is not wholly excluded from regulating physicians and physician practice.[55] Rather, NRC policy states that it will not intrude into the medical judgments affecting patients, *except as necessary to provide for the radiation safety of workers and the general public*. The NRC is required, therefore, to go beyond the analysis of whether a medical event or incident occurs within the practice of medicine, but also to assess whether NRC action is necessary to provide for the radiation safety of medical patients as members of the general public. The risks posed by extravasations justify NRC intervention to protect the public. Lucerno proposes that the most reasonable way to do so is by removing the exemption of extravasations from medical event reporting requirements.

In the same way that a radiopharmaceutical contamination *on* skin may result in a reportable radiation dose,[56] an extravasation *into* the patient's tissue resulting in a dose equivalent that exceeds 0.5 Sv should also be reported to the NRC. Required reporting for both events would fulfill the Commission's "expectation that all individuals and organizations, performing or overseeing regulated activities involving nuclear materials, should take the necessary steps to promote a positive safety culture . . . ."[57] The reporting of extravasations as medical events is necessary to provide for the radiation safety of the

---

[52] 10 C.F.R. § 35.1 (2020). *See also* NCRP Report No. 180, MANAGEMENT OF EXPOSURE TO IONIZING RADIATION: RADIATION PROTECTION GUIDANCE FOR THE UNITED STATES (2018) at 36 ("Radiation protection culture includes the core values and behaviors resulting from a collective commitment by leaders and individuals within an organization18 to emphasize radiation protection over competing goals (nonsafety related) to ensure protection of people and the environment. The overriding principle is to "put safety first." Positive radiation protection culture fosters traits to effectively establish and implement a radiation protection program that applies to an organization's environment.")

[53] 76 Fed. Reg. 34777-327778 (2011).

[54] ACMUI Patient Intervention Draft Report 2020, *supra* note 5.

[55] *See* 65 Fed. Reg. 47654 (2000).

[56] *See, e.g.*, U.S. Nuclear Regulatory Commission Operations Center, Event Notification Report for June 11, 2018, Event Number 53434, at: https://www.nrc.gov/reading-rm/doc-collections/event-status/event/2018/20180611en.html.

[57] 76 Fed. Reg. 34778 (2011).

general public and, therefore, the NRC should modify 10 C.F.R. Part 35 to protect patients from unnecessary and unsafe irradiation.

VI. CONCLUSION

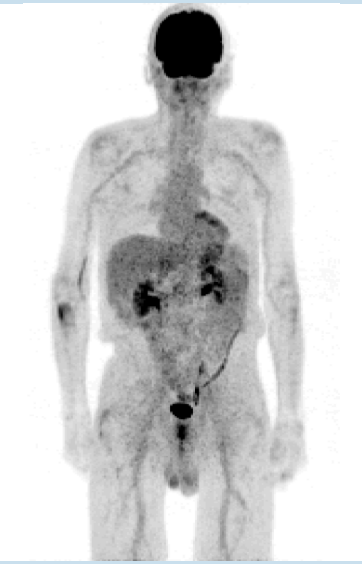
Extravasations occur frequently at many nuclear medicine centers. The incorrect administration of a radiopharmaceutical can result in a high localized radiation dose to patients. To understand whether an extravasation represents a serious patient health event that constitutes misuse of NRC-regulated byproduct material, licensees should correctly characterize the extravasation. Technology exists today that can help clinicians identify when extravasations occur. This technology may assist licensees with the characterization of an extravasation and facilitate tissue dose calculation. Over 20 examples of significant extravasations that exceed 0.5 Sv (50 rem) dose equivalent to tissue have been previously submitted to the NRC as evidence (Appendix 1). A requirement to report serious extravasations to the NRC will increase attention to these issues and will motivate licensees to implement practices that will reduce the frequency and seriousness of extravasation events.

The current lack of reporting requirements for extravasations exceeding the dose equivalent reporting thresholds in 10 C.F.R. § 35.3045 are inconsistent with the NRC's obligation to ensure the radiation safety of the public. Since its determination in 1980 that extravasations are "virtually impossible to avoid," ample evidence has emerged demonstrating that extravasations can cause radiation harm to the patient, can negatively affect the patient's health care, and can be avoided. The NRC has the obligation to intervene as necessary to provide for the radiation safety of workers and the public. For these reasons, Lucerno Dynamics respectfully requests that the NRC, pursuant to 10 C.F.R. § 2.802, amend 10 C.F.R. § 35.2, "Definitions" and 10 C.F.R. § 35.3045, "Report and Notification of a Medical Event" to require the reporting of extravasations exceeding existing medical event reporting thresholds. By requiring the reporting of extravasations, the NRC will have the opportunity to monitor for systemic breakdowns in injection quality, protect patients from unnecessary irradiation, and provide transparency to patients receiving nuclear medicine injections.

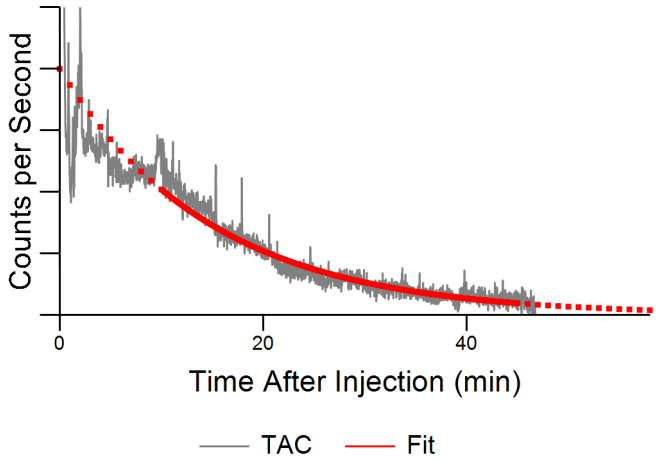
Appendix 1

Scan #1010

Absorbed Dose: 0.2 to 1.2 Gy



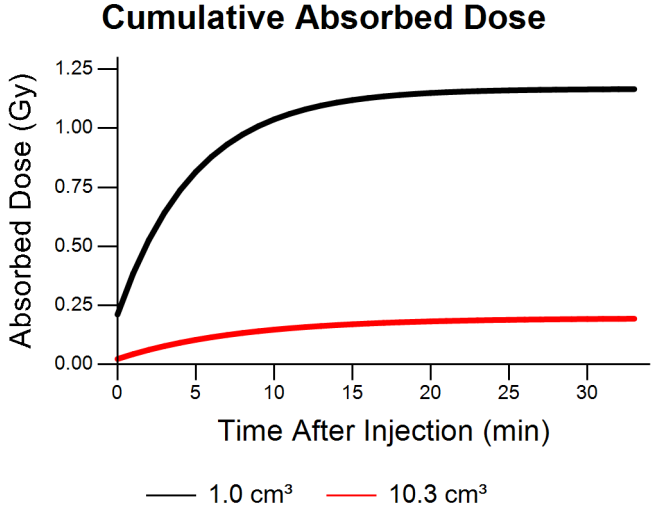
Isotope	F-18
Injection Method	Manual
Injection Location	R Antecubital
Injected Activity	14.29 mCi
Radiotracer Volume	1.50 mL
Saline Flush Volume	10.0 mL
Imaging Time	56.9 min
% Extravasation	18 %
Initial Activity	2.63 mCi
Imaging Time Activity	0.04 mCi
Reabsorption Rate	10.3 min
Dose Calculation Volume	1.00 to 10.28 cm^3
Dose Rate	80.5 to 8.9 mGy/mCi-min
Total Absorbed Dose	1.2 to 0.2 Gy



As part of an 18F-FDG study, this patient was injected in the right antecubital with 14.29 mCi comprising 1.5 mL. Additionally, the injection was flushed with 10 mL of saline.

Based on PET image measurements and dynamic time-activity data, the initial infiltration was estimated to be 2.63 mCi or 18%.

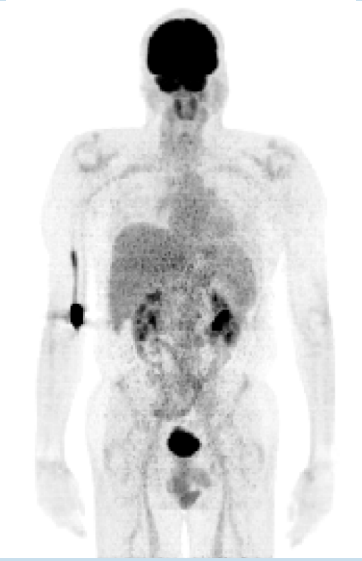
Using an initial infiltrated tissue volume of 1 cm^3, absorbed dose was calculated to be 1.2 Sv. Assuming complete infiltration of the saline flush would result in 0.2 Sv of absorbed dose to 10.28 cm^3 of tissue.



Report generated May 18, 2020

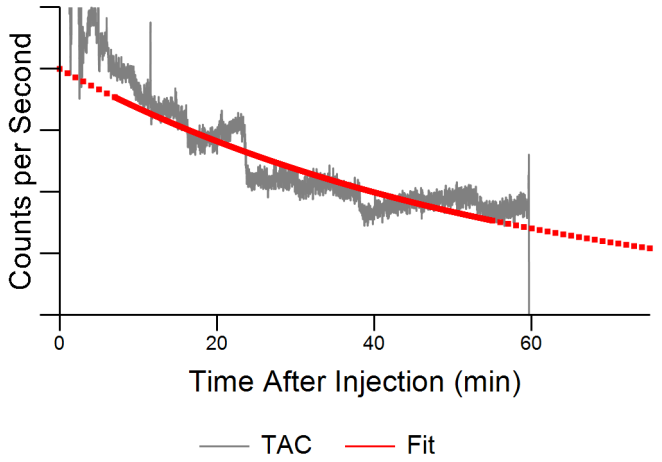
Scan #1070

Absorbed Dose: 0.2 to 0.5 Gy



Isotope	F-18
Injection Method	Manual
Injection Location	R Antecubital
Injected Activity	16.87 mCi
Radiotracer Volume	1.50 mL
Saline Flush Volume	10.0 mL
Imaging Time	67.0 min
% Extravasation	3 %
Initial Activity	0.49 mCi
Imaging Time Activity	0.10 mCi
Reabsorption Rate	39.8 min
Dose Calculation Volume	1.00 to 11.00 cm^3
Dose Rate	84.4 to 8.7 mGy/mCi-min
Total Absorbed Dose	0.5 to 0.2 Gy

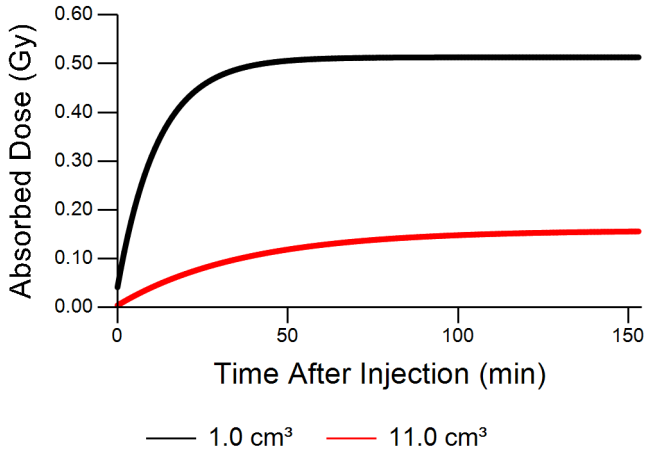
TAC with Exponential Fit



This patient underwent PET/CT imaging using 18F-FDG. The injection was performed in the right antecubital through an IV with no saline flush. We estimate that 0.49 mCi, or 3%, of the injected activity was extravasated into the arm tissue. At imaging time, only 0.1 mCi remained at the injection site.

The estimated absorbed dose to the arm tissue is between 0.2 and 0.5 Sv.

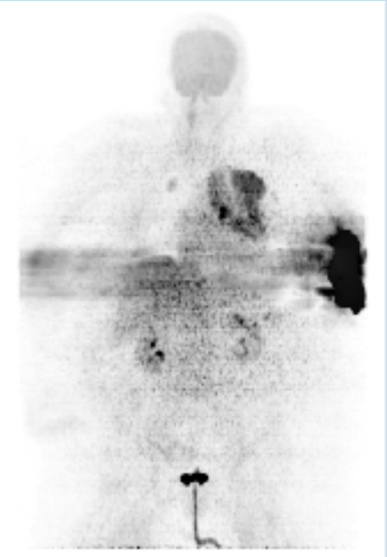
Cumulative Absorbed Dose



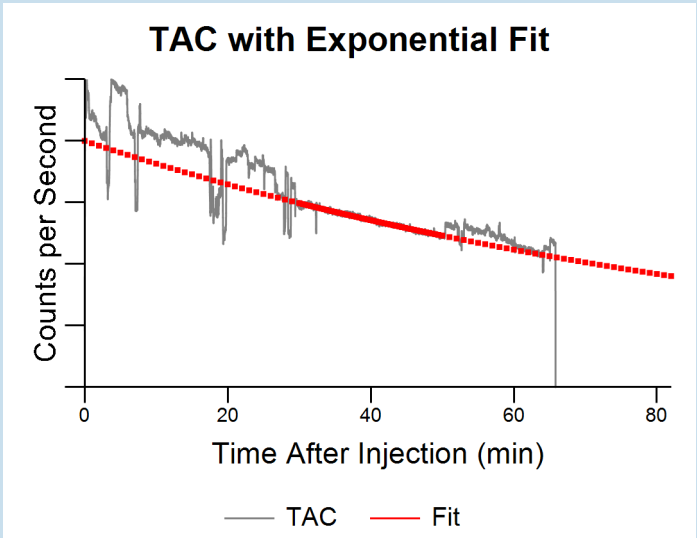
Report generated May 18, 2020

Scan #2078

Absorbed Dose: 1.5 to 4.9 Gy



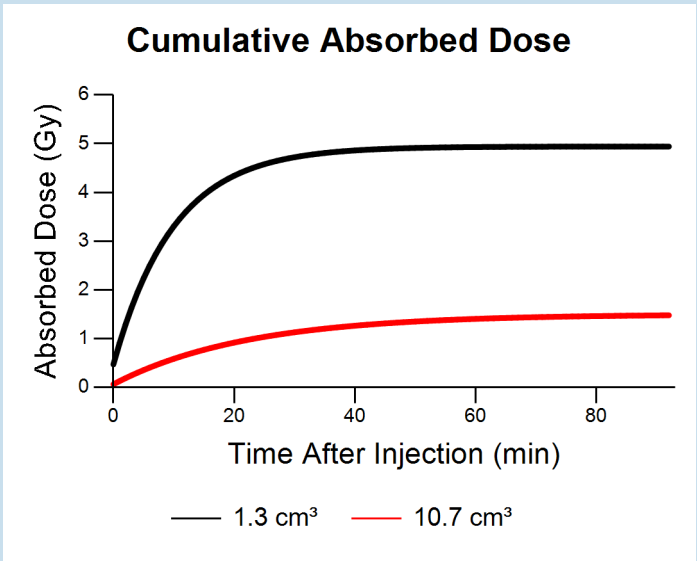
Isotope	F-18
Injection Method	Manual
Injection Location	L Antecubital
Injected Activity	17.33 mCi
Radiotracer Volume	1.50 mL
Saline Flush Volume	10.0 mL
Imaging Time	76.6 min
% Extravasation	45 %
Initial Activity	7.75 mCi
Imaging Time Activity	2.27 mCi
Reabsorption Rate	71.4 min
Dose Calculation Volume	1.34 to 10.67 cm^3
Dose Rate	61.0 to 8.6 mGy/mCi-min
Total Absorbed Dose	4.9 to 1.5 Gy



The patient was injected in the left antecubital with 17.33 mCi of 18F-FDG in 1.5 mL. Subsequent flush consisted of 10 mL of saline.

At imaging time, PET measurements indicate 2.27 mCi of activity remained at the injection site, and significant image artifacts were noted.

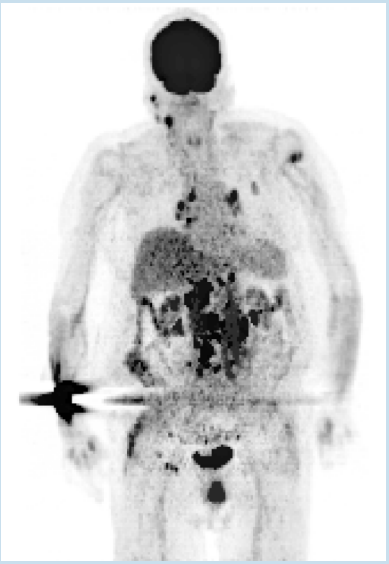
Based on PET image measurements and time-activity curve data, the initial infiltration amount was estimated to be 7.75 mCi or 45%. Absorbed dose was calculated for infiltrated tissue volumes of 1.3 cm^3 and 10.7 cm^3, and resulted in between 1.5 Sv and 4.9 Sv.



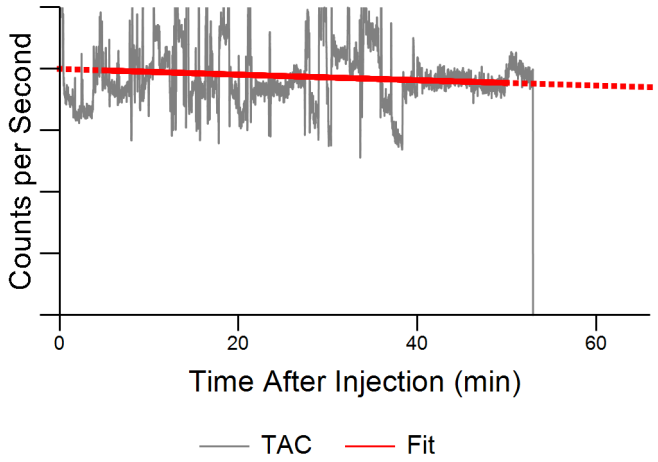
Report generated May 18, 2020

Scan #2169

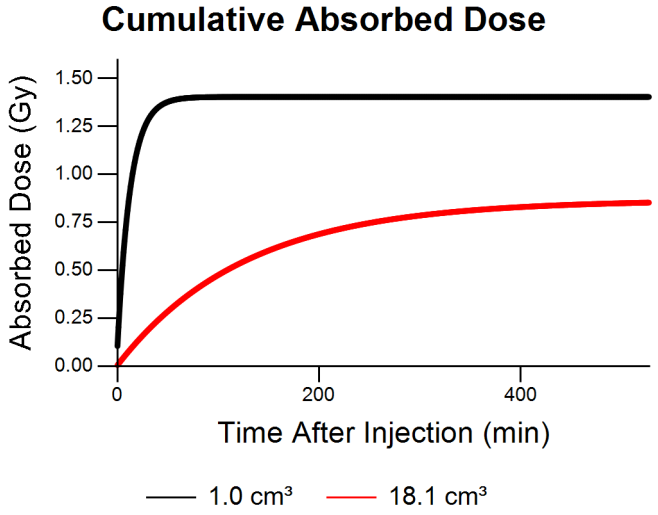
Absorbed Dose: 0.9 to 1.4 Gy



Isotope	F-18
Injection Method	Manual
Injection Location	R Forearm
Injected Activity	16.11 mCi
Radiotracer Volume	1.50 mL
Saline Flush Volume	18.0 mL
Imaging Time	64.9 min
% Extravasation	8 %
Initial Activity	1.32 mCi
Imaging Time Activity	0.81 mCi
Reabsorption Rate	594.3 min
Dose Calculation Volume	1.00 to 18.12 cm^3
Dose Rate	80.5 to 5.2 mGy/mCi-min
Total Absorbed Dose	1.4 to 0.9 Gy



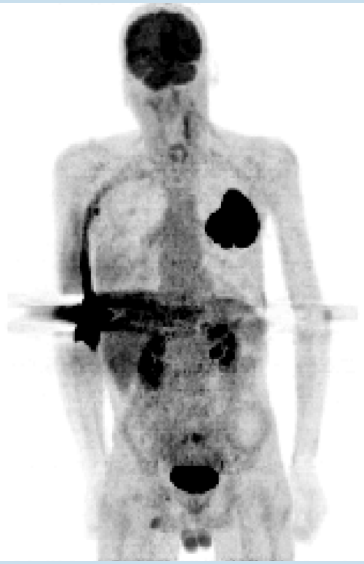
Administration of 18F-FDG consisted of 16.11 mCi injected through an IV in the right forearm followed by 18 mL of saline. Using PET images and TAC data, the extravasation was estimated to be approximately 8% of injected activity. Total absorbed dose to be 1.4 Sv for a tissue volume of 1 cm^3 and 0.87 Sv for a tissue volume of 18.1 cm^3.



Report generated May 18, 2020

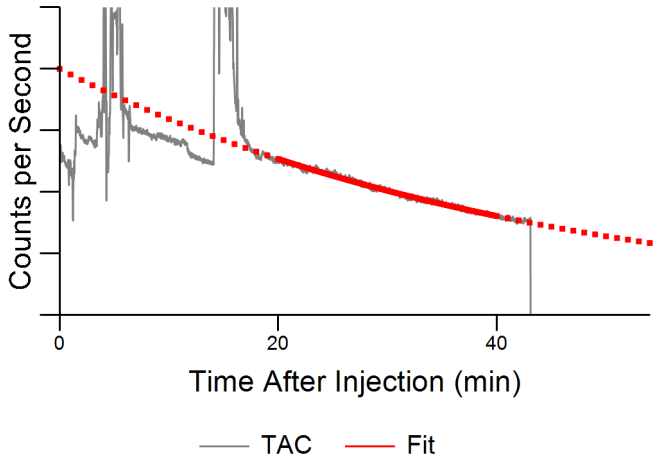
Scan #2189

Absorbed Dose: 2.4 to 5.2 Gy



Isotope	F-18
Injection Method	Manual
Injection Location	R Antecubital
Injected Activity	17.20 mCi
Radiotracer Volume	1.50 mL
Saline Flush Volume	14.0 mL
Imaging Time	61.8 min
% Extravasation	91 %
Initial Activity	15.59 mCi
Imaging Time Activity	2.59 mCi
Reabsorption Rate	30.5 min
Dose Calculation Volume	2.72 to 15.36 cm^3
Dose Rate	31.2 to 6.1 mGy/mCi-min
Total Absorbed Dose	5.2 to 2.4 Gy

TAC with Exponential Fit



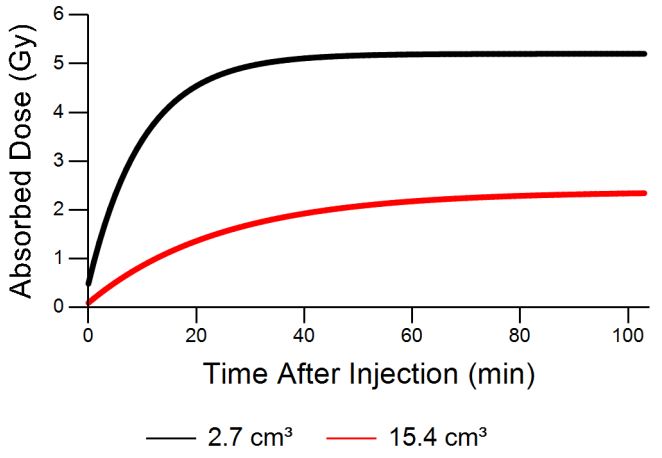
For a lung cancer imaging study, the patient was injected in the right antecubital with 17.2 mCi of FDG comprising 1.5 mL. The injection was followed by a saline flush of 14 mL. After an uptake time period of 62 minutes, PET imaging indicated 2.59 mCi remained at the injection site.

The time-activity curve indicates a reabsorption half-time of 30.5 minutes, resulting in an estimated initial infiltration of 15.6 mCi or 91%. Using the injected volumes, we calculated dose for tissue volumes of 2.70 cm^3 and 15.4 cm^3.

Dose rates for this case ranged from 31.2 mSv/mCi-min to 6.1 mSv/mCi-min and resulted in estimated doses to tissue of 5.2 Sv to 2.4 Sv.

The clinical aspects of this case have been published. doi:10.3389/fmed.2018.00143

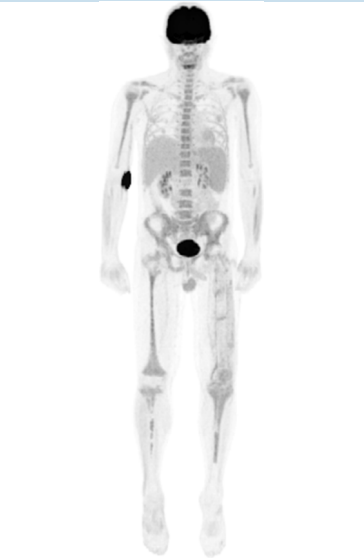
Cumulative Absorbed Dose



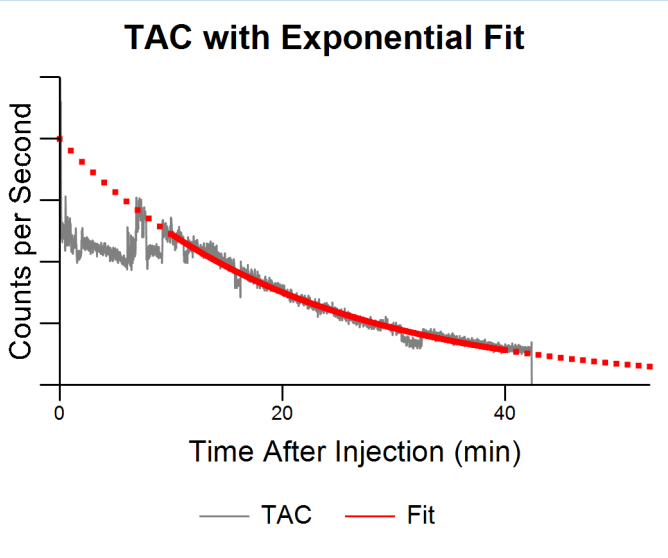
Report generated May 18, 2020

Scan #4679

Absorbed Dose: 0.4 to 2.1 Gy



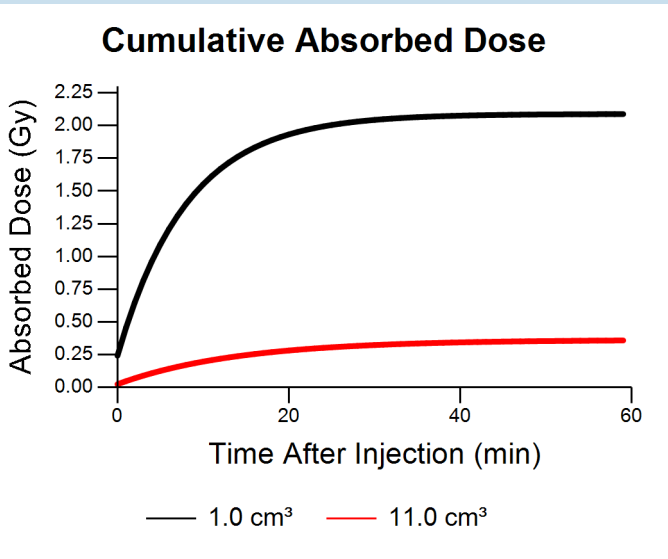
Isotope	F-18
Injection Method	Manual
Injection Location	R Antecubital
Injected Activity	10.44 mCi
Radiotracer Volume	1.50 mL
Saline Flush Volume	10.0 mL
Imaging Time	54.0 min
% Extravasation	28 %
Initial Activity	2.87 mCi
Imaging Time Activity	0.15 mCi
Reabsorption Rate	14.2 min
Dose Calculation Volume	1.00 to 11.00 cm^3
Dose Rate	84.4 to 8.7 mGy/mCi-min
Total Absorbed Dose	2.1 to 0.4 Gy



For an FDG-PET scan, the patient was injected in the right antecubital fossa with 10.44 mCi of 18F-FDG in 1.5 mL. The injection was followed by a 10 mL flush of saline.

Based on the time-activity curve data and activity quanitification at imaging time, we estimated that 2.87 mCi (27.5%) of the injected radiopharmaceutical was extravasated which resolved over 54 minutes to 0.15 mCi.

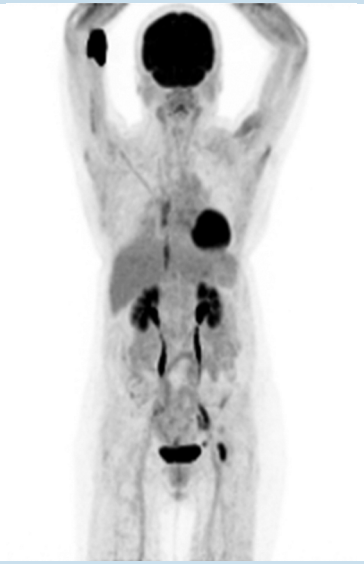
For tissue volumes of 1 and 11 cm^3, absorbed dose was calculated to be 2.1 and 0.4 Gy.



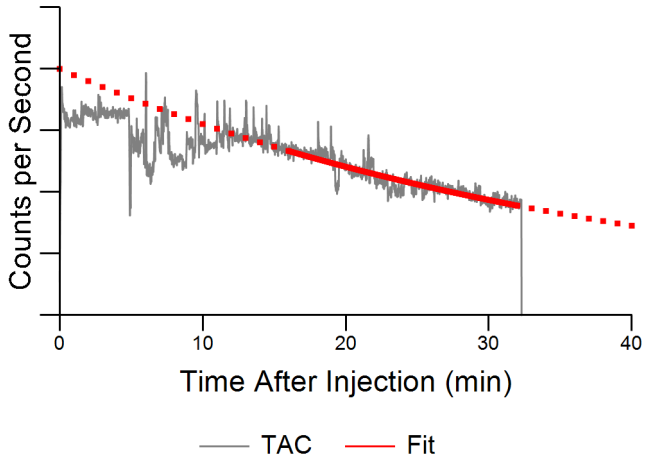
Report generated May 18, 2020

Scan #8634

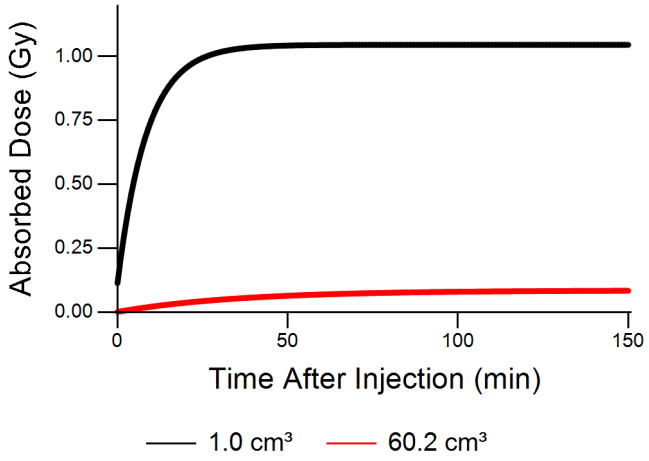
Absorbed Dose: 0.1 to 1.0 Gy



Isotope	F-18
Injection Method	Autoinjector
Injection Location	R Antecubital
Injected Activity	9.98 mCi
Radiotracer Volume	1.50 mL
Saline Flush Volume	60.0 mL
Imaging Time	56.5 min
% Extravasation	14 %
Initial Activity	1.42 mCi
Imaging Time Activity	0.24 mCi
Reabsorption Rate	27.4 min
Dose Calculation Volume	1.00 to 60.21 cm^3
Dose Rate	80.5 to 1.7 mGy/mCi-min
Total Absorbed Dose	1.0 to 0.1 Gy

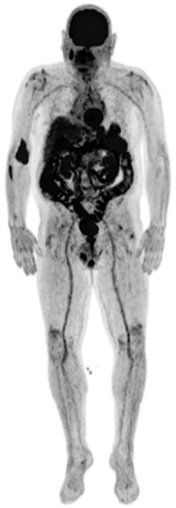


Administration of 18F-FDG consisted of 9.98 mCi injected with an auto-injector through an IV in the right antecubital followed by 60 mL of saline. Using PET images and TAC data, the extravasation was estimated to be approximately 14% of injected activity. Total absorbed dose to be 1.05 Sv for a tissue volume of 1 cm^3 and 0.09 Sv for a tissue volume of 60.2 cm^3.



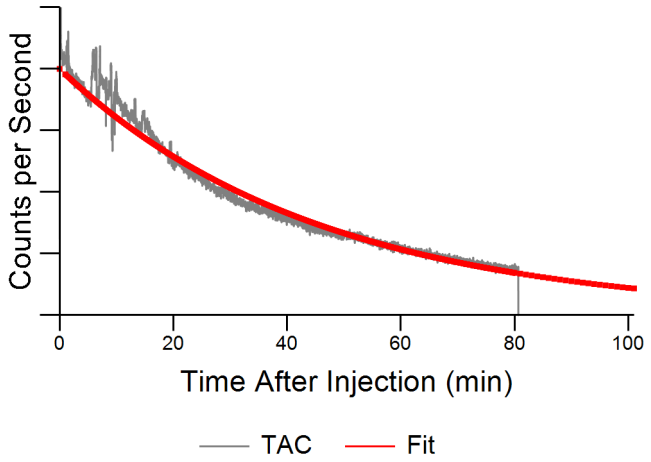
Scan #9535

Absorbed Dose: 0.1 to 1.2 Gy



Isotope	F-18
Injection Method	Manual
Injection Location	R Antecubital
Injected Activity	11.96 mCi
Radiotracer Volume	1.50 mL
Saline Flush Volume	20.0 mL
Imaging Time	107.2 min
% Extravasation	7 %
Initial Activity	0.89 mCi
Imaging Time Activity	0.04 mCi
Reabsorption Rate	31.5 min
Dose Calculation Volume	1.00 to 21.00 cm^3
Dose Rate	84.4 to 4.7 mGy/mCi-min
Total Absorbed Dose	1.2 to 0.1 Gy

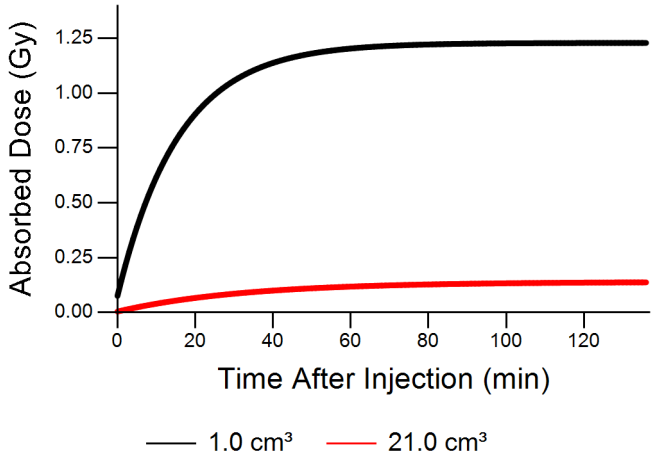
TAC with Exponential Fit



For a PET scan, the patient was injected with 11.96 mCi of 18F-FDG in 1.5 mL which was followed by 20 mL of saline. We estimate that 7.5% of the injection was extravasated into the right antecubital tissue.

For tissue volumes between 1 and 21 cm^3, absorbed dose calculations resulted in 1.23 to 0.14 Gy.

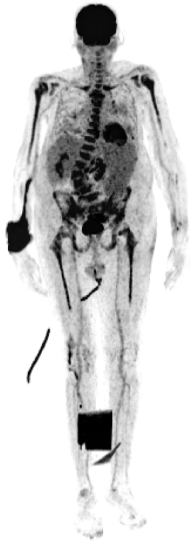
Cumulative Absorbed Dose



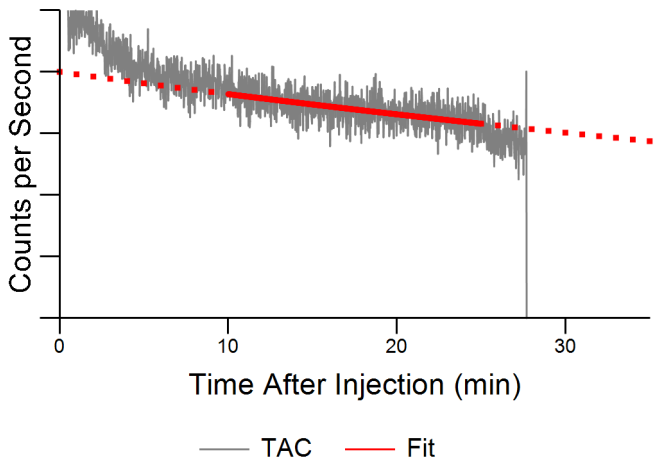
Report generated May 18, 2020

Scan #9571

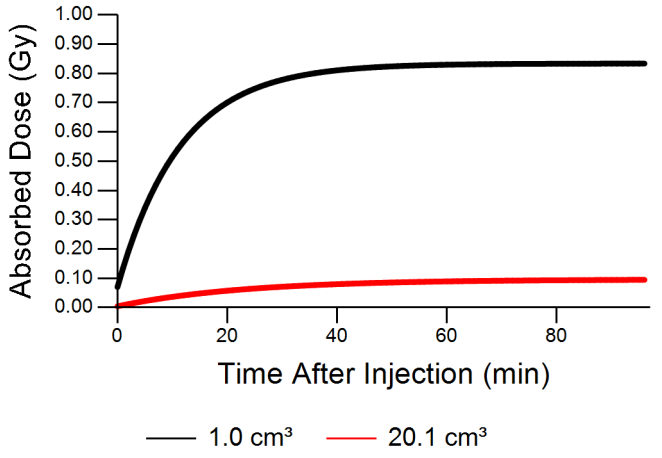
Absorbed Dose: 0.1 to 0.8 Gy



Isotope	F-18
Injection Method	Manual
Injection Location	R Forearm
Injected Activity	9.90 mCi
Radiotracer Volume	1.50 mL
Saline Flush Volume	20.0 mL
Imaging Time	74.0 min
% Extravasation	9 %
Initial Activity	0.87 mCi
Imaging Time Activity	0.27 mCi
Reabsorption Rate	73.4 min
Dose Calculation Volume	1.00 to 20.13 cm^3
Dose Rate	80.5 to 4.7 mGy/mCi-min
Total Absorbed Dose	0.8 to 0.1 Gy



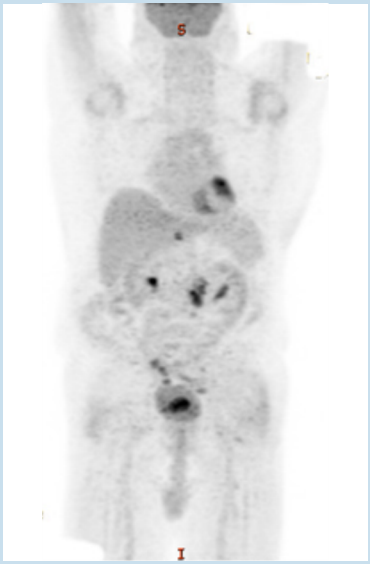
Administration of 18F-FDG consisted of 9.9 mCi injected through an IV in the right forearm followed by 20 mL of saline. Using PET images and TAC data, the extravasation was estimated to be approximately 9% of the injected activity. Total absorbed dose to be 0.83 Sv for a tissue volume of 1 cm^3 and 0.1 Sv for a tissue volume of 20.1 cm^3.



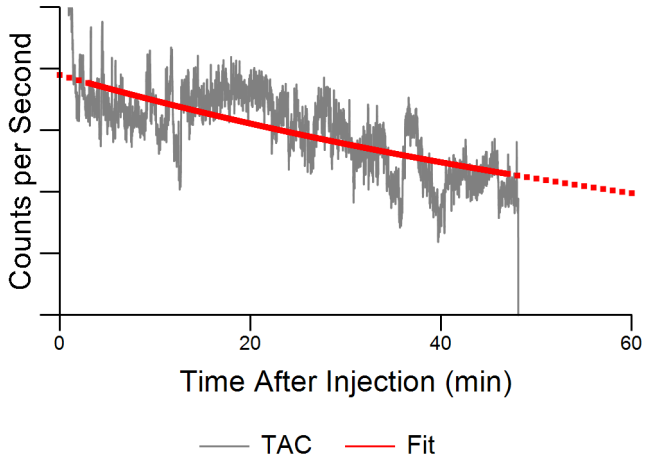
Report generated May 18, 2020

Scan #11490

Absorbed Dose: 5.8 to 21.4 Gy



Isotope	F-18
Injection Method	Manual
Injection Location	L Hand
Injected Activity	13.72 mCi
Radiotracer Volume	1.50 mL
Saline Flush Volume	10.0 mL
Imaging Time	57.0 min
% Extravasation	92 %
Initial Activity	12.62 mCi
Imaging Time Activity	4.63 mCi
Reabsorption Rate	61.4 min
Dose Calculation Volume	2.76 to 11.38 cm^3
Dose Rate	30.8 to 8.0 mGy/mCi-min
Total Absorbed Dose	21.4 to 5.8 Gy

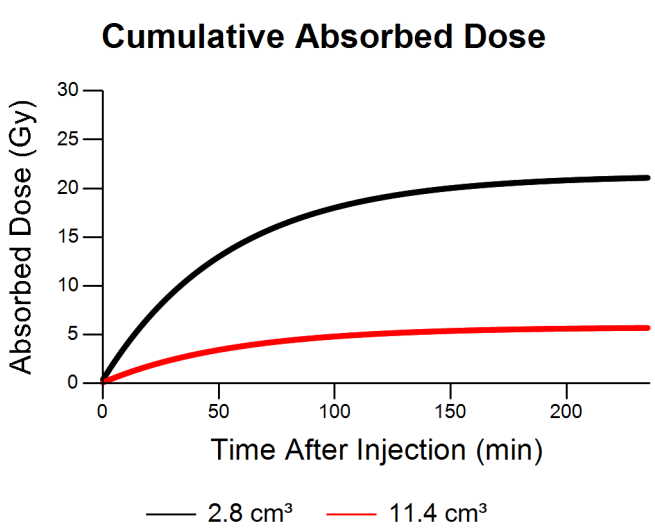


The patient was injected in the left hand with 13.7 mCi of FDG. The injection site was out of the PET imaging field of view. Had Lucerno's Lara® System not identified the presence of excess radiotracer near the injection site, no one would have known that the patient had been infiltrated.

This patient had a repeat scan five days later, and four lesions were studied. The new data showed that the infiltration caused the original SUVs to be understated by 33-54%, and MTV calculations were understated by 32-70%. Using the infiltrated image would likely have impacted patient care.

Using the change in quantifiable measures as an indicator of infiltration severity, we estimated that approximately 92% of the injected activity was infiltrated. We calculated absorbed dose based on initial tissue volumes ranging from 2.8 to 11.4 cm^3.

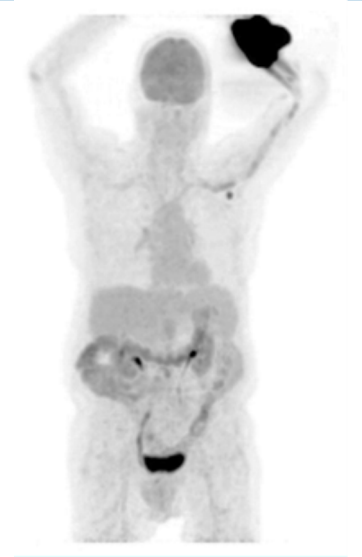
In addition to the negative effect that this infiltration had on the patient's diagnostic study, the patient also received between 5.8 and 21.4 Sv of unintended exposure to their



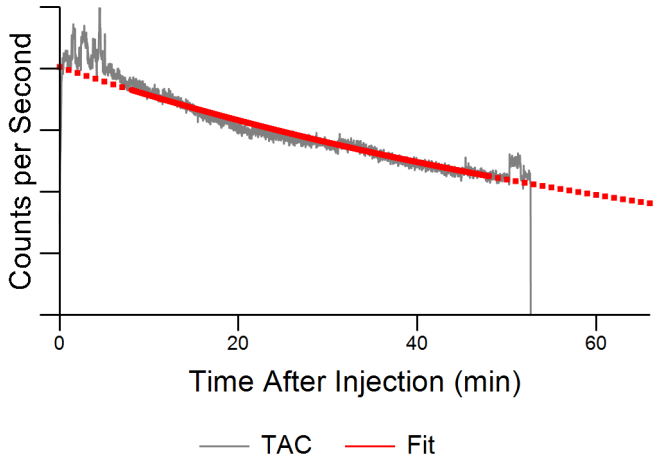
Report generated May 18, 2020

Scan #14547

Absorbed Dose: 1.7 to 6.0 Gy



Isotope	F-18
Injection Method	Manual
Injection Location	L Forearm
Injected Activity	10.22 mCi
Radiotracer Volume	1.50 mL
Saline Flush Volume	30.0 mL
Imaging Time	62.0 min
% Extravasation	100 %
Initial Activity	10.22 mCi
Imaging Time Activity	5.19 mCi
Reabsorption Rate	57.4 min
Dose Calculation Volume	3.00 to 31.50 cm^3
Dose Rate	28.4 to 3.1 mGy/mCi-min
Total Absorbed Dose	6.0 to 1.7 Gy

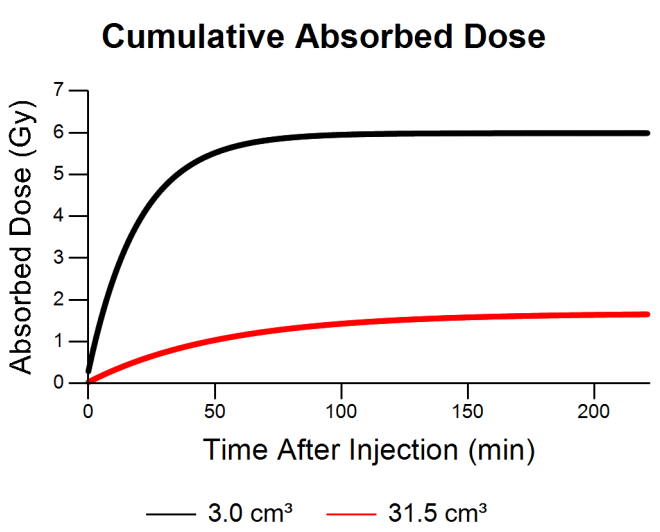


The patient was injected in the left forearm with 10.2 mCi of FDG. Lucerno's Lara® System identified the presence of excess radiotracer near the injection site.

The patient had a repeat scan the next day. Axial images of a pancreatic tumor revealed the infiltration caused the original SUVs to be understated by 65%.

Using PET-measured infiltration activity at imaging time and the time-activity curve data, we estimate that 100% of the injected activity was infiltrated. We calculated absorbed dose based on initial tissue volumes ranging from 3.0 to 31.5 cm^3.

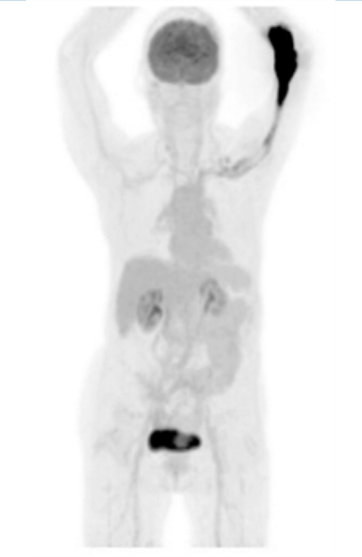
In addition to the negative effect that this infiltration had on the patient's diagnostic study, the patient also received between 1.7 and 6.0 Sv of absorbed dose to their forearm tissue.



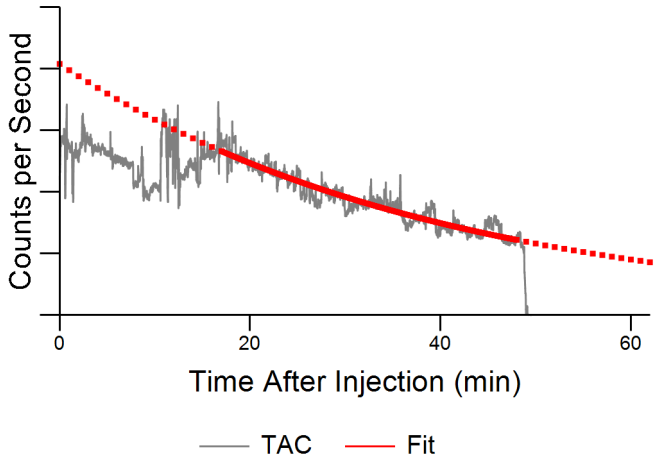
Report generated May 18, 2020

Scan #15170

Absorbed Dose: 0.7 to 2.6 Gy



Isotope	F-18
Injection Method	Autoinjector
Injection Location	L Antecubital
Injected Activity	9.99 mCi
Radiotracer Volume	4.00 mL
Saline Flush Volume	41.0 mL
Imaging Time	62.0 min
% Extravasation	77 %
Initial Activity	7.69 mCi
Imaging Time Activity	1.62 mCi
Reabsorption Rate	27.6 min
Dose Calculation Volume	6.16 to 44.08 cm^3
Dose Rate	14.4 to 2.2 mGy/mCi-min
Total Absorbed Dose	2.6 to 0.7 Gy

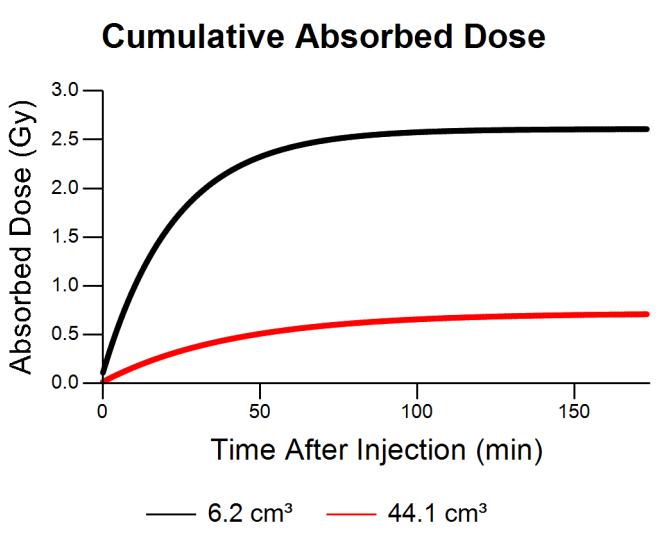


As part of a breast tumor assessment study, the patient was injected in the left antecubital with 10.0 mCi of FDG using an auto-injector. Lucerno's Lara® System identified the presence of excess radiotracer near the injection site even though the auto-injector reported an error-free injection.

This patient had a repeat scan three days later. The repeat PET scan revealed the infiltration caused the SUVs of a breast tumor to be understated by 73%. An assessment based on the infiltrated scan would have erroneously concluded that the disease was responding favorably to the treatment regimen. A revised assessment based on the repeat study showed the disease was recalcitrant.

Using PET-measured infiltration activity at imaging time and the time-activity curve data, we estimated that 77% of the injected activity was infiltrated. We calculated absorbed dose based on tissue volumes ranging from 6.2 to 44.1 cm^3.

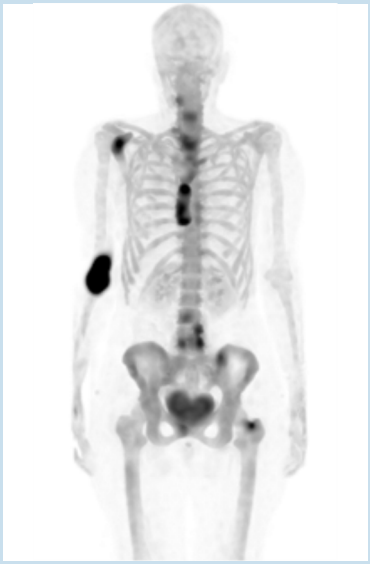
In addition to the negative effect that this infiltration had on the patient's assessment



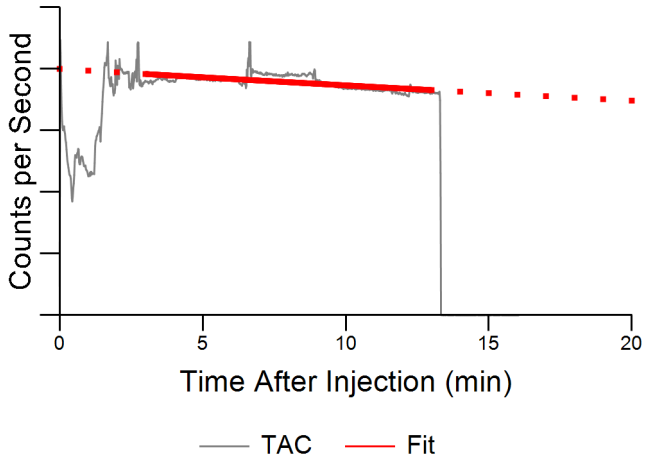
Report generated May 18, 2020

Scan #15771

Absorbed Dose: 0.2 to 1.6 Gy



Isotope	Tc-99m
Injection Method	Manual
Injection Location	R Antecubital
Injected Activity	25.38 mCi
Radiotracer Volume	1.00 mL
Saline Flush Volume	10.0 mL
Imaging Time	214.0 min
% Extravasation	10 %
Initial Activity	2.54 mCi
Imaging Time Activity	0.38 mCi
Reabsorption Rate	100.5 min
Dose Calculation Volume	1.00 to 10.10 cm^3
Dose Rate	6.0 to 0.7 mGy/mCi-min
Total Absorbed Dose	1.6 to 0.2 Gy



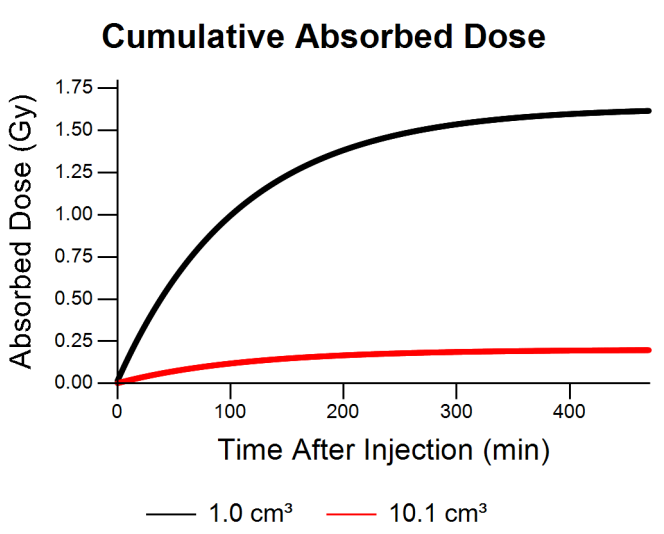
For a therapy assessment scan, the patient was injected in the right antecubital with 25.4 mCi of Tc-99m. Lucerno's Lara® System identified the presence of excess radiotracer near the injection site.

No repeat of the imaging study was ordered in response to this infiltrated injection.

No activity quantification could be made from the SPECT images, but infiltrated tissue volume was measured. Time-activity curve data was used to estimate the rate of reabsorption.

Absorbed dose was calculated for initial infiltrations ranging from 10% to 50% with corresponding initial tissue volumes of 1.0 to 10.1 cm^3 for 10% and 1.0 to 10.5 cm^3 for 50%.

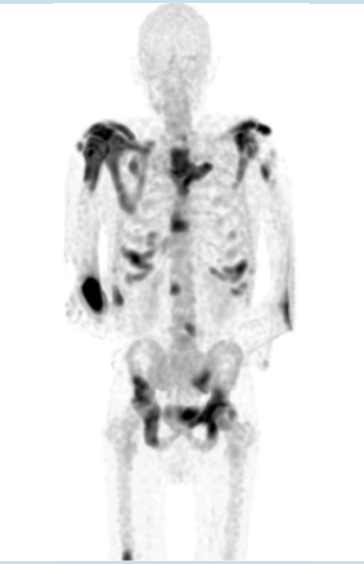
The patient's arm tissue was exposed to unintended absorbed dose between 0.2 and 4.5 Sv.



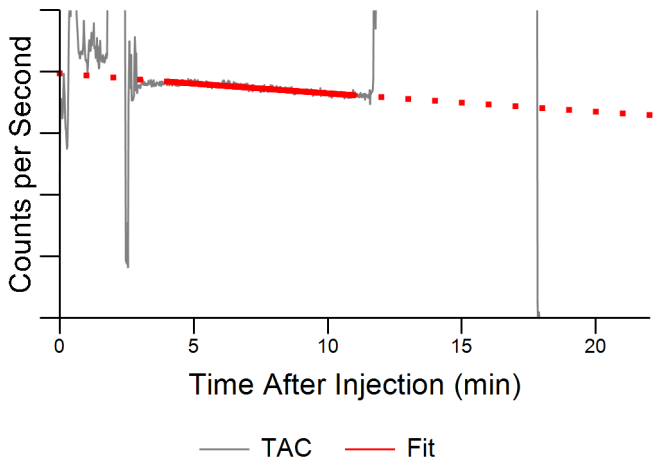
Report generated May 18, 2020

Scan #15819

Absorbed Dose: 1.5 Gy



Isotope	Tc-99m
Injection Method	Manual
Injection Location	R Antecubital
Injected Activity	27.40 mCi
Radiotracer Volume	1.50 mL
Saline Flush Volume	0.0 mL
Imaging Time	247.0 min
% Extravasation	10 %
Initial Activity	2.74 mCi
Imaging Time Activity	0.21 mCi
Reabsorption Rate	81.7 min
Dose Calculation Volume	1.00 cm^3
Dose Rate	6.0 mGy/mCi-min
Total Absorbed Dose	1.5 Gy



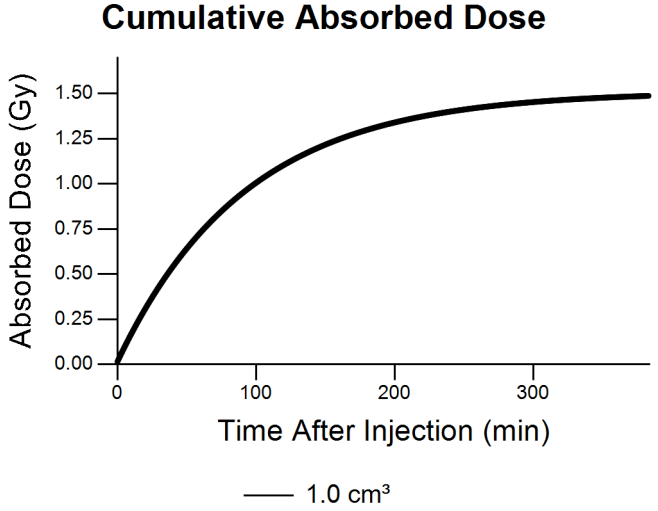
For a bone scan, the patient was injected in the right antecubital with 27.4 mCi of Tc-99m. Lucerno's Lara® System identified the presence of excess radiotracer near the injection site.

No repeat of the imaging study was ordered in response to this infiltrated injection.

No activity quantification could be made from the SPECT images, but infiltrated tissue volume was measured. Time-activity curve data was used to estimate the rate of reabsorption.

This injection was a "straight stick" procedure with no saline flush after the radiotracer injection. When no flush is performed, initial infiltration volumes are very small. We have used 1 cm^3 as the initial infiltrated tissue volume to avoid excessively high estimates of dose for a very small volume.

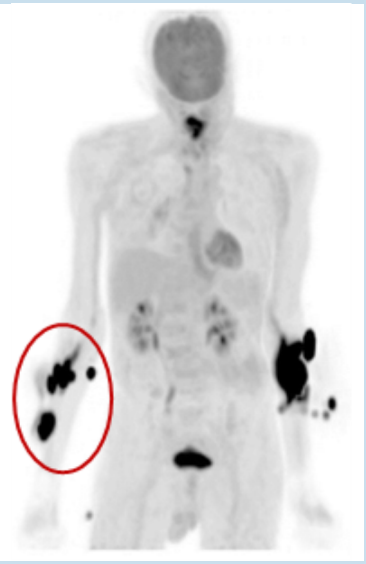
Absorbed dose was calculated for initial infiltrations ranging from 10% to 50%. The



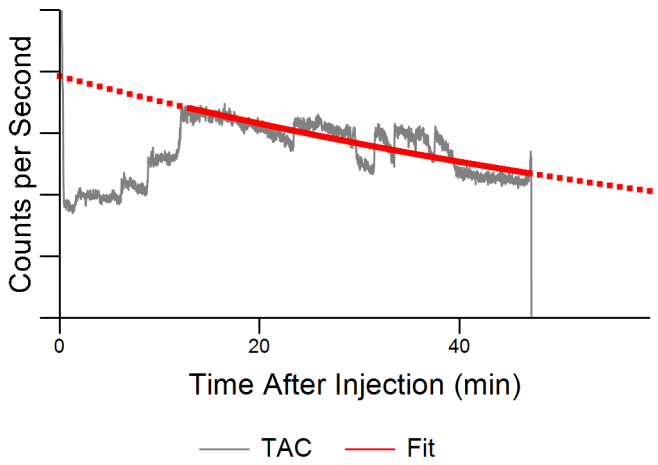
Report generated May 18, 2020

Scan #16031R

Absorbed Dose: 1.0 Gy



Isotope	F-18
Injection Method	Manual
Injection Location	R Antecubital
Injected Activity	4.82 mCi
Radiotracer Volume	0.90 mL
Saline Flush Volume	0.0 mL
Imaging Time	56.0 min
% Extravasation	7 %
Initial Activity	0.36 mCi
Imaging Time Activity	0.20 mCi
Reabsorption Rate	63.5 min
Dose Calculation Volume	1.00 cm^3
Dose Rate	80.5 mGy/mCi-min
Total Absorbed Dose	1.0 Gy

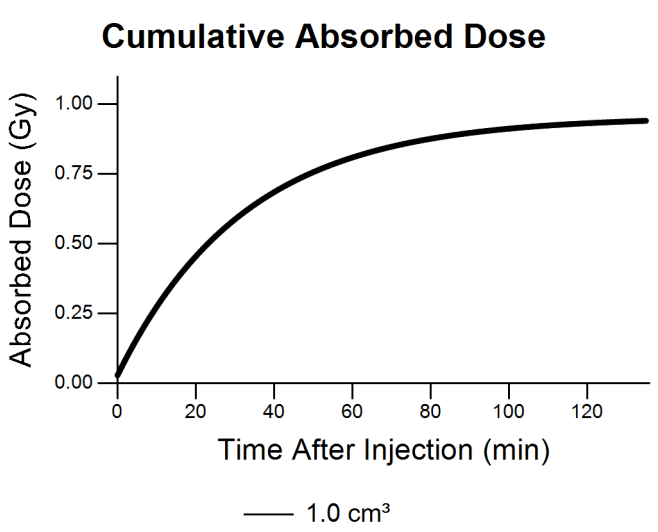


In the course of their PET scan, this patient was injected twice and both injections were infiltrated. The technologist performing the injection reported that they tried to inject in the right antecubital and realized an infiltration was occurring. He withdrew the catheter and started another IV in the left antecubital to finish the procedure.

For our analysis, we assume half of the radiotracer was injected into each arm.

In the first attempt, 4.8 mCi of FDG was injected into the patient's right antecubital and was not flushed. Using PET-measured infiltration activity at imaging time and the time-activity curve data, we estimated that 7% of the 4.8 mCi was infiltrated. We used 1 cm^3 for the initial infiltrated tissue volume.

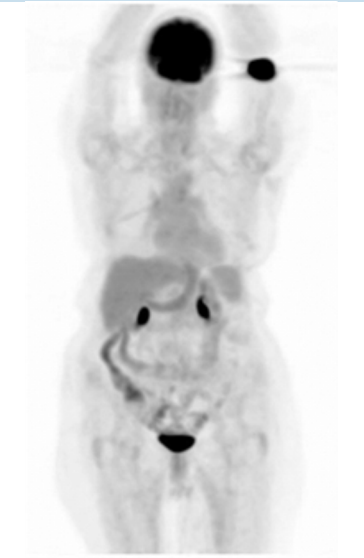
From this first injection, 1 cm^3 of the patient's arm tissue received unintended absorbed dose of 1.0 Sv.



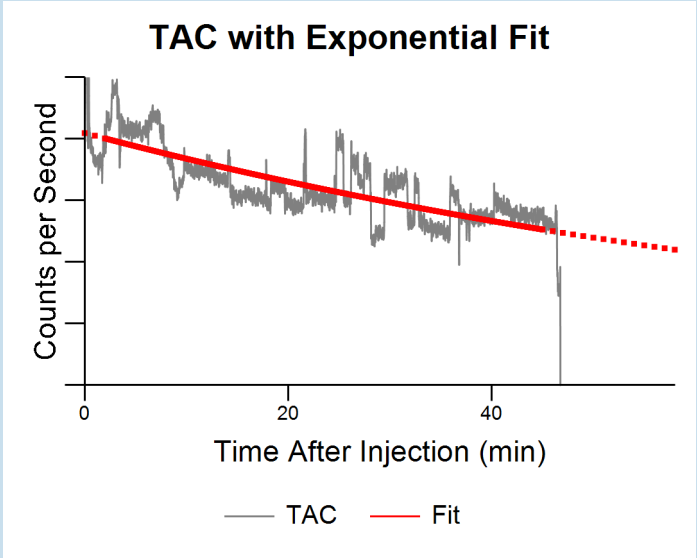
Report generated May 18, 2020

Scan #16074

Absorbed Dose: 1.3 Gy



Isotope	F-18
Injection Method	Manual
Injection Location	L Antecubital
Injected Activity	17.65 mCi
Radiotracer Volume	2.62 mL
Saline Flush Volume	0.0 mL
Imaging Time	67.0 min
% Extravasation	4 %
Initial Activity	0.69 mCi
Imaging Time Activity	0.34 mCi
Reabsorption Rate	64.7 min
Dose Calculation Volume	1.00 cm^3
Dose Rate	80.5 mGy/mCi-min
Total Absorbed Dose	1.3 Gy



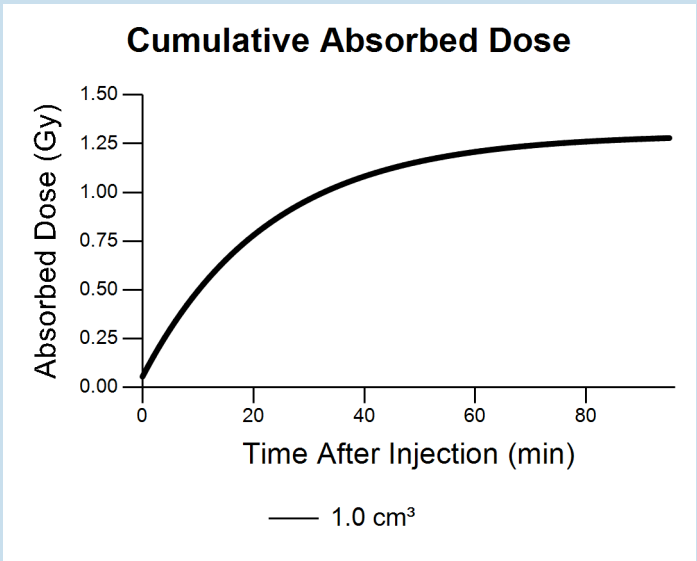
The patient was injected in the left antecubital with 17.7 mCi of FDG. The technologist performing the injection reported that the patient complained of pain near the IV after the radiotracer injection. As such, the technologist did not flush with saline.

No repeat of the imaging study was ordered in response to this infiltrated injection.

Using PET-measured infiltration activity at imaging time and the time-activity curve data, we estimate that 4% of the injected activity was infiltrated.

Because there was no saline flush, the infiltrated volume would be quite small, resulting in high calculated dose. Thus, we used 1 cm^3 as a minimum initial infiltrated volume.

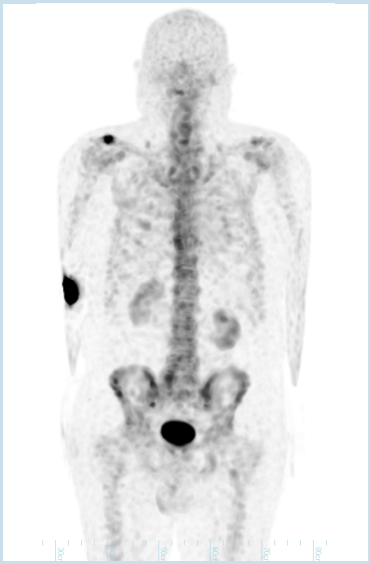
We estimate that 1 cm^3 of the patient's arm tissue received an unintended absorbed dose exposure of 1.3 Sv.



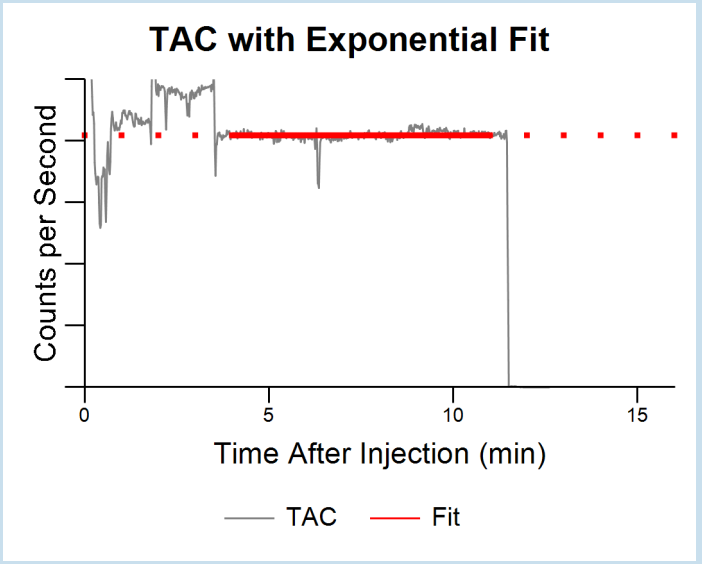
Report generated May 18, 2020

Scan #16380

Absorbed Dose: 31.3 Gy



Isotope	Tc-99m
Injection Method	Manual
Injection Location	R Antecubital
Injected Activity	26.20 mCi
Radiotracer Volume	0.50 mL
Saline Flush Volume	0.0 mL
Imaging Time	201.0 min
% Extravasation	50 %
Initial Activity	13.10 mCi
Imaging Time Activity	8.90 mCi
Reabsorption Rate	∞ min
Dose Calculation Volume	1.00 cm^3
Dose Rate	6.0 mGy/mCi-min
Total Absorbed Dose	31.3 Gy

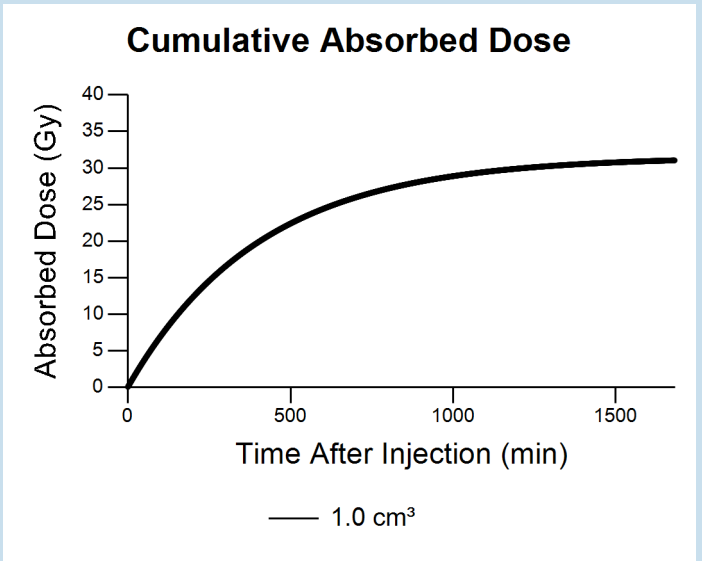


For a bone scan, the patient was injected in the right antecubital with 26.2 mCi of Tc-99m. Lucerno's Lara® System identified the presence of excess radiotracer near the injection site.

The resulting SPECT images were found to be of "no diagnostic value" by the nuclear medicine physician. A repeat imaging study was performed 2 days later.

No activity quantification could be made from the SPECT images and the infiltrated tissue was partially outside of the imaging view. The visible portion of the infiltration at imaging time was measured to be 9.17 cm^3, but we conservatively estimated its true volume to be 30 cm^3. Time-activity curve data indicated that reabsorption was essentially nonexistent.

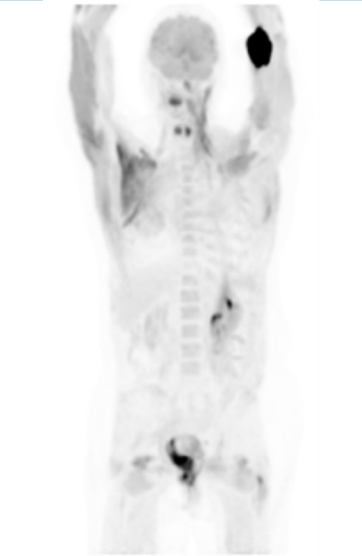
This injection was a "straight stick" procedure with no saline flush after the radiotracer injection. When no flush is performed, initial infiltration volumes are very small. We used 1cm^3 as the minimum initial volume.



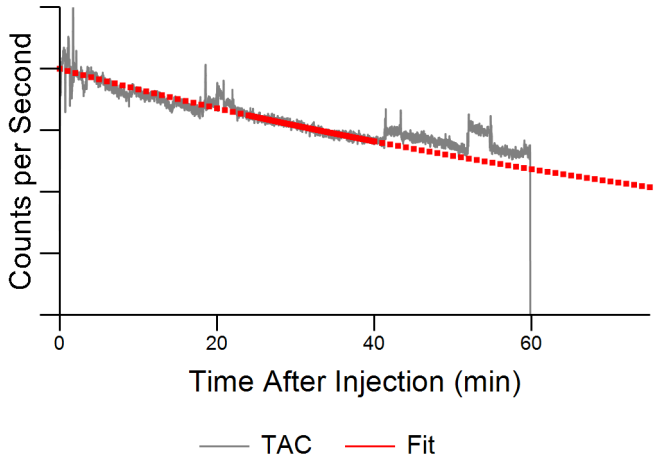
Report generated May 18, 2020

Scan #16448

Absorbed Dose: 0.1 to 1.1 Gy



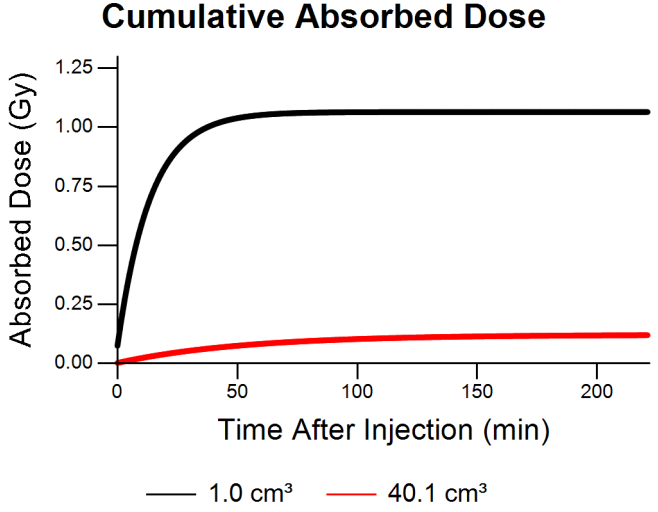
Isotope	F-18
Injection Method	Autoinjector
Injection Location	L Antecubital
Injected Activity	10.01 mCi
Radiotracer Volume	1.50 mL
Saline Flush Volume	40.0 mL
Imaging Time	62.0 min
% Extravasation	9 %
Initial Activity	0.93 mCi
Imaging Time Activity	0.54 mCi
Reabsorption Rate	79.4 min
Dose Calculation Volume	1.00 to 40.14 cm^3
Dose Rate	80.5 to 2.4 mGy/mCi-min
Total Absorbed Dose	1.1 to 0.1 Gy



Using an auto-injector, the patient was injected in the left antecubital with 10.01 mCi of FDG. The auto-injector performed a saline flush of 40 mL. Neither the technologist nor the auto-injector reported anything abnormal about the injection. No repeat of the imaging study was ordered in response to this infiltrated injection.

Using PET-measured infiltration activity at imaging time and the time-activity curve data, we estimate that 9% of the injected activity was infiltrated.

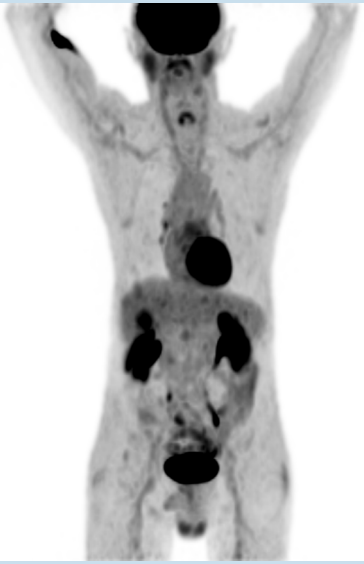
Not knowing how much of the saline flush may have been infiltrated as well, we used 1 cm^3 as a minimum initial infiltrated volume and 40.1 cm3 as a maximum. We estimate that the absorbed dose exposure to this patient's arm tissue was between 0.1 Sv and 1.1 Sv.



Report generated May 18, 2020

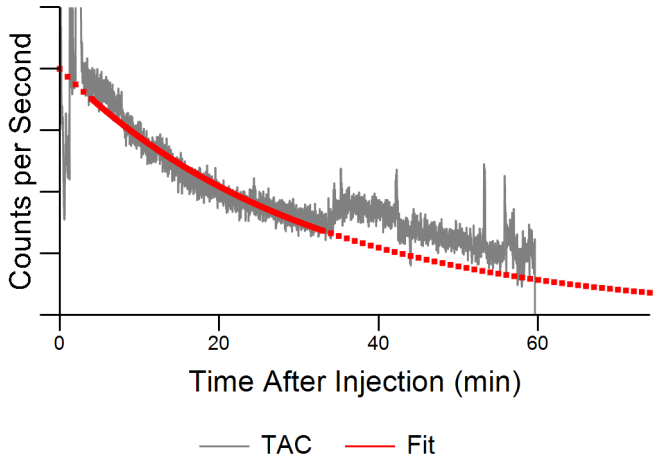
Scan #17889

Absorbed Dose: 0.5 to 2.8 Gy



Isotope	F-18
Injection Method	Manual
Injection Location	R Antecubital
Injected Activity	9.80 mCi
Radiotracer Volume	1.00 mL
Saline Flush Volume	10.0 mL
Imaging Time	71.0 min
% Extravasation	27 %
Initial Activity	2.65 mCi
Imaging Time Activity	0.17 mCi
Reabsorption Rate	21.4 min
Dose Calculation Volume	1.00 to 11.00 cm^3
Dose Rate	84.4 to 8.7 mGy/mCi-min
Total Absorbed Dose	2.8 to 0.5 Gy

TAC with Exponential Fit

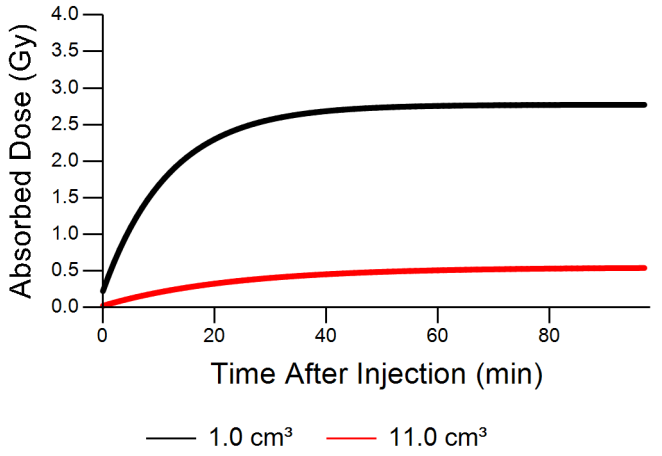


An 80 year old male presented with a history of bladder carcinoma that had metastasized to the liver. Initial follow-up imaging was determined to be relatively non-diagnostic in quality due to a significant extravasation observed on imaging and external injection monitoring.

The extravasated injection consisted of 9.8 mCi of 18F-FDG in the right antecubital using an IV. The absorbed dose to the injection site tissue was estimated to be 0.55 to 2.77 Sv.

PET/CT scanning was repeated the following day. The repeat imaging confirmed disease progression and identified additional uptake not seen in the prior extravasated scan-including an upper liver lesion, increased hilar node activity, and prostate uptake. Quantitative results showed an average increase in SUVmax of approximately 25%.

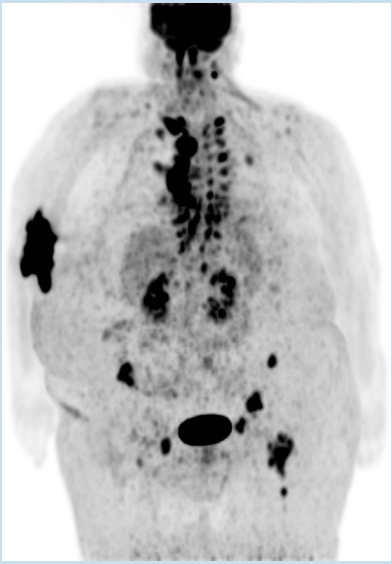
Cumulative Absorbed Dose



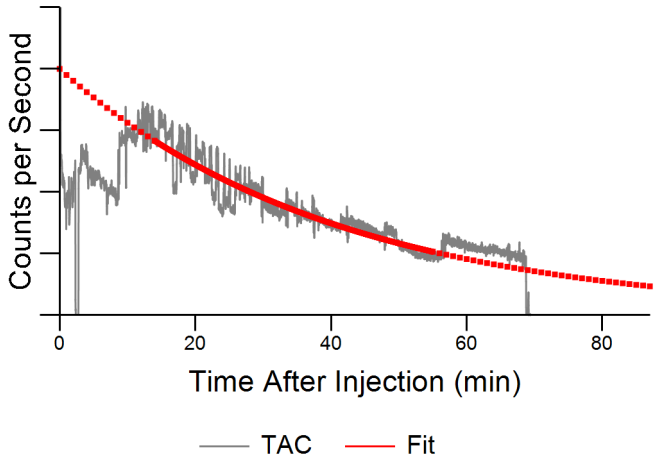
Report generated May 18, 2020

Scan #17967

Absorbed Dose: 1.9 to 6.5 Gy



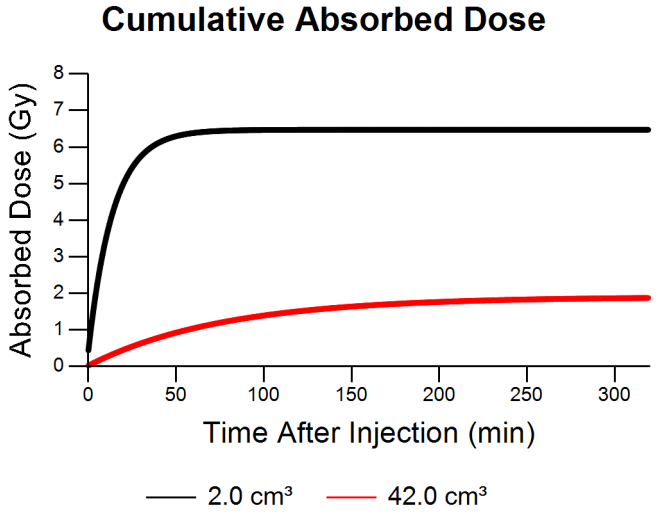
Isotope	F-18
Injection Method	Manual
Injection Location	R Antecubital
Injected Activity	10.10 mCi
Radiotracer Volume	1.00 mL
Saline Flush Volume	40.0 mL
Imaging Time	76.0 min
% Extravasation	100 %
Initial Activity	10.10 mCi
Imaging Time Activity	3.75 mCi
Reabsorption Rate	28.1 min
Dose Calculation Volume	2.00 to 42.00 cm^3
Dose Rate	43.7 to 2.4 mGy/mCi-min
Total Absorbed Dose	6.5 to 1.9 Gy



A 61 year old female presented with a history of breast cancer and malignant right pleural effusion. Follow up imaging identified possible bone involvement and additional PET/CT imaging was ordered. The restaging PET/CT injection was deemed non-diagnostic due to identification of a significant infiltration based on Lara TACs and a large area of activity observed in the arm of the patient.

From the extravasated 18F-FDG injection, arm tissue was estimated to have recieved between 1.96 and 6.47 Sv of absorbed dose.

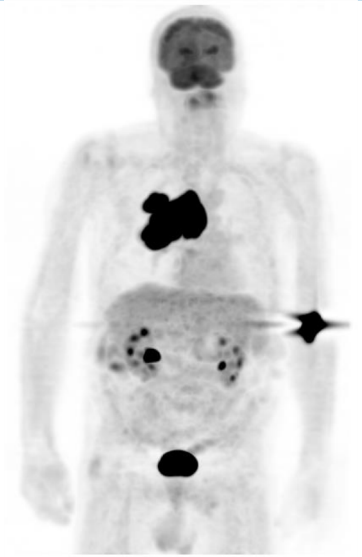
Repeat PET/CT imaging was ordered and the patient was imaged five days later. Follow up imaging showed diffuse metastatic disease with bone involvement and confirmed further disease progression.



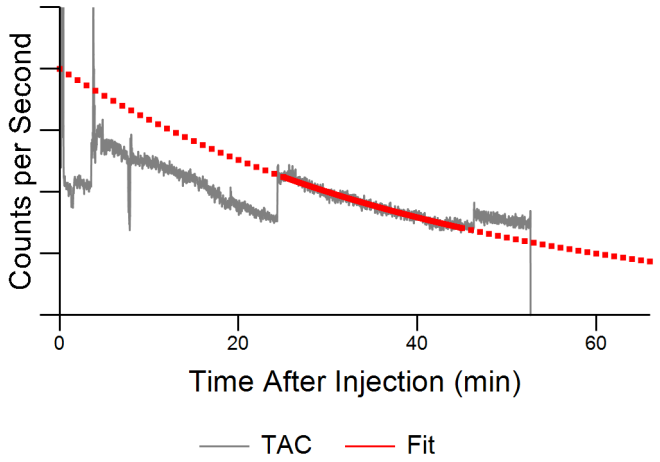
Report generated May 18, 2020

Scan #18642

Absorbed Dose: 4.3 to 6.6 Gy



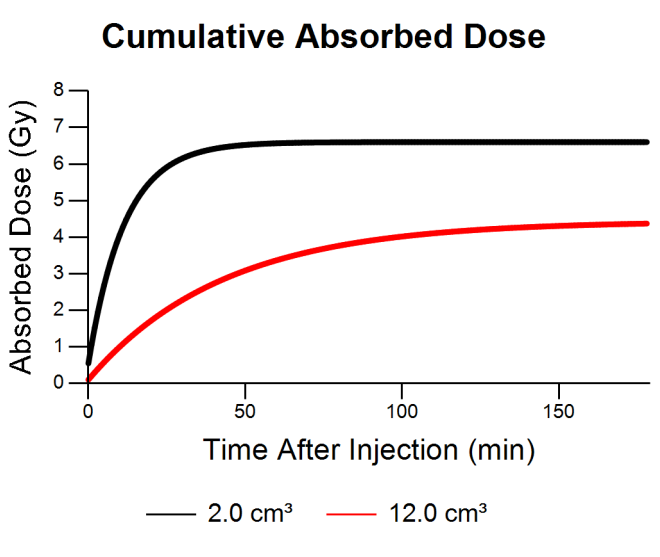
Isotope	F-18
Injection Method	Manual
Injection Location	L Antecubital
Injected Activity	12.82 mCi
Radiotracer Volume	1.02 mL
Saline Flush Volume	10.0 mL
Imaging Time	60.0 min
% Extravasation	100 %
Initial Activity	12.82 mCi
Imaging Time Activity	4.07 mCi
Reabsorption Rate	30.0 min
Dose Calculation Volume	2.04 to 12.04 cm^3
Dose Rate	42.9 to 8.0 mGy/mCi-min
Total Absorbed Dose	6.6 to 4.3 Gy



The patient was injected in the left antecubital fossa with 12.82 mCi of 18F-FDG consisting of 1.02 mL. The injection was followed by 10 mL of saline flush.

The time-activity curve indicated likely presence of residual activity at the injection site. After 60 minutes of uptake, PET imaging was performed and confirmed significant radioactivity in the left antecubital.

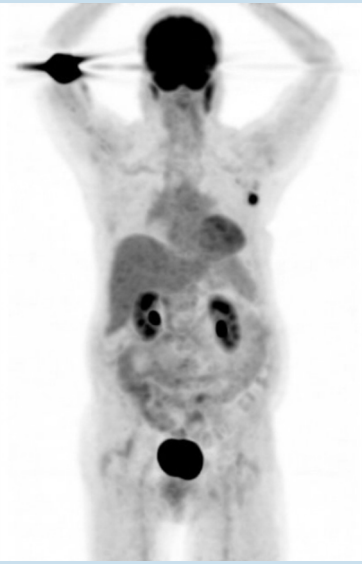
Based on the static PET imaging and time activity curve, initial extravasation severity was estimated to be 100%. For tissue volumes of between 2 and 12 cm3, absorbed dose was calculated as 6.6 and 4.3 Gy.



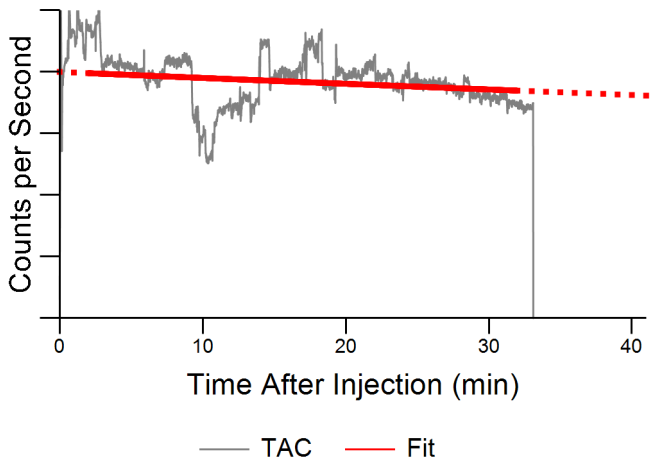
Report generated May 18, 2020

Scan #19110

Absorbed Dose: 0.6 to 1.6 Gy



Isotope	F-18
Injection Method	Manual
Injection Location	R Antecubital
Injected Activity	14.77 mCi
Radiotracer Volume	1.50 mL
Saline Flush Volume	20.0 mL
Imaging Time	65.0 min
% Extravasation	11 %
Initial Activity	1.62 mCi
Imaging Time Activity	0.91 mCi
Reabsorption Rate	281.7 min
Dose Calculation Volume	1.00 to 21.00 cm^3
Dose Rate	84.4 to 4.7 mGy/mCi-min
Total Absorbed Dose	1.6 to 0.6 Gy

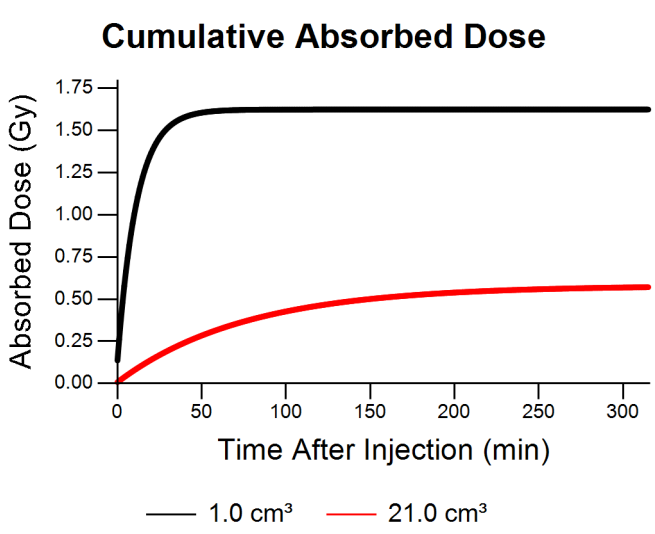


While undergoing PET/CT imaging with 18F-FDG, the patient was injected in the right antecubital with 14.77 mCi in a volume of approximately 1.5 mL. The injection was followed by a flush of 20 mL of saline.

Following the injection, the nuclear medicine technologist reported "No complaints of discomfort during injection."

Lara system output indicated a potential infiltration of the injection, which was confirmed by imaging the injection site. Based on the TAC, approximately 11% of the injected radioactivity is believed to have been infiltrated. Biological clearance was minimal. Absorbed tissue dose is estimated to be between 0.6 Gy and 1.6 Gy.

The patient was called back for repeated PET/CT imaging two days later. The repeated procedure was not infiltrated and indicated that the infiltrated imaging study understated target lesion SUV measurements by 20%.



Report generated May 18, 2020