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November 12, 2019

Michael Layton, Director
Division of Materials, Safety, Security, State and Tribal Programs
Office of Nuclear Material Safety and Safeguards
Nuclear Regulatory Commission

Dear Michael,

On Wednesday, October 30, 2019, Dr. Said Daibes of the NRC phoned the Lucerno office. Dr. Daibes mentioned that he was reviewing the eight dosimetry cases which we provided to the NRC in our request dated October 9, 2019. Dr Daibes asked for references that support the dosimetry methodology that was used for these cases. I have attached a thorough description of the dosimetry method used to calculate the equivalent dose to the patients' tissue, as well as the references that support this method. These references include textbooks, peer-reviewed literature, ACMUI transcripts, and previously reported NRC medical events.

This attachment also reviews three alternative dosimetry methods (two of which are published) and provides the resulting dosimetry calculations for the eight cases. Please be aware that the dosimetry calculations included in our October 9 request are more accurate than these alternative methods. Accuracy is improved by making use of dynamic information not available in the other three methods. Later this month we will submit a description of this method to a major medical physics journal for peer-review.

Since our October request, we have become aware of another infiltrated patient. We are also including this patient's data in this communication for your review. In this case, an autoinjector was used in the injection process. In our experience, an autoinjector uses a larger saline flush volume than manual injections. As you will see in the attached case, using a larger flush volume increases the volume of the exposed tissue and thus dilutes the infiltrated activity.

Now that we have a documented dosimetry method, we have begun to analyze other infiltrated cases from our database of over 17,000 injections. As we complete these analyses, and those of newly infiltrated patients, we will provide case reports in groups of ten for the NRC's consideration.

Thank you for your continued interest in this matter.

Sincerely,

DocuSigned by:
Ron Lattanze
0C2FCDBE78A7435...

Ron Lattanze
Chief Executive Officer

Enclosures:

LUCERNO DYNAMICS, LLC
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1. A Novel Method of Calculating Equivalent Dose to Tissue in Cases of Radiopharmaceutical Extravasation
2. Infiltrated Patient Case Report

cc:
Andrea Kock
Chris Einberg
Lisa Dimmick
Said Daibes
Kellee Jamerson
Donna-Beth Howe

A Novel Method of Calculating Equivalent Dose to Tissue in Cases of Radiopharmaceutical Extravasation

Background

On the most basic level, equivalent dose for gamma and beta sources is calculated as the total absorbed energy divided by the mass of the absorber. When calculating internal radiation doses from administered radiopharmaceuticals, one must account for the ways in which the distribution of activity changes over time. The process for doing this was formalized by the Medical Internal Radiation Dose Committee (MIRD) and uses standardized models of human anatomy and biokinetics(*1*).

Extravasation of radiopharmaceuticals can result in high concentrations of activity remaining within extravascular tissue near the injection site. This activity can expose the tissue to significant dose over time(*2-9*). While no published use of the MIRD method for extravasations was identified, two general methods were found.

The first method, proposed by Shapiro et al., is described as a worst case estimate and assumes the entire injection is extravasated into tissue with a minimal volume*(7)*. This method assumes no movement or reabsorption of the activity over time—it decays entirely *in situ*.

A second approach improves upon the first by estimating the biological clearance of the radiopharmaceutical. When a radiopharmaceutical is extravasated into the interstitial space, the body will begin clearing it through the capillaries of both the venous and lymphatic systems. The speed at which this happens depends on the concentration gradient between interstitial fluid and blood as well as the degree of vascularization in the local area. Visser and de Jong report that the clearance process typically has a half-time of 2 hours, but can be up to 8 or 10 hours based on vascularization(*10*). Studies have confirmed this time frame by intentionally extravasating compounds and then monitoring the rate of clearance over time(*11-15*). While use of an assumed clearance rate can improve dose estimation accuracy, the method still assumes complete extravasation within an unchanging volume.

A third method seems obvious, but was not found in published literature. First, measure the extravasation activity and volume with static nuclear imaging. Secondly, for dosimetry calculations, assume volume was constant and activity changed only due to radioactive decay.
Considering the above methods, each would result in a flawed estimate of the tissue dose for individual patients. In order to accurately estimate dose for a particular patient, information is needed about the ways in which both the activity and its volume changed over time. Unfortunately, it is difficult to quantify these processes using static images(*7,13-15*). To estimate the clearance rate, Visser and de Jong suggest using serial images of the injection site or continuous measurement with a scintillation counter or radiation monitor(*10*). Use of this technique was found in the literature(*3,5,8,16-18*).

Scintillation Counters to Assess Activity at the Injection Site

The Lara®* System is designed to measure residual activity at the injection site to provide feedback as to injection quality. The system consists of topically applied scintillation detectors that record incident radiation in counts per second. In the current commercial design, each detector contains only one scintillation crystal and is not able to directly quantify the amount of activity present. However, the change in detector output over time is relative to changes in the local activity(*19*). Future detector designs will quantify activity over time.
For an ideal intravenous injection, the time-activity curve (TAC) produced by Lara shows an initial bolus spike from the injection-arm detector followed by an immediate reduction to a level consistent with that measured by the reference-arm detector. This would indicate that the injected radiopharmaceutical is systemic and there is low probability of residual activity at the injection site.

In the case of an extravasation that leaves significant activity near the injection site, the output for the injection arm detector will remain elevated. As the extravasated activity is reabsorbed, detector output will decrease accordingly. This relationship between detector output and the presence of residual activity near the injection site has been clinically validated using dynamic imaging(*20*). See Figure 1 for examples of TACs from both ideal and non-ideal injections.

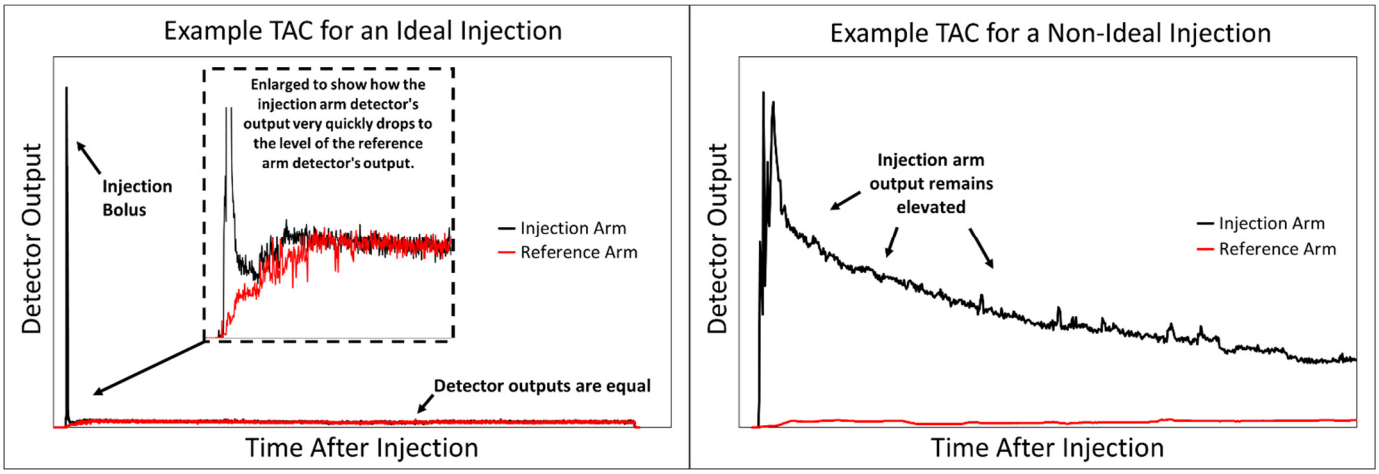

Figure 1. Example TACs for both an ideal and non-ideal injection.

* Lara is a registered trademark of Lucerno Dynamics, LLC

Novel Method

With the availability of time-activity data for the injection site, one can address the shortcomings of the existing extravasation dosimetry methods. Overall, the steps in this novel method are:

1. Calculate the rate (in minutes) of activity clearance using injection site TAC data.
2. Measure the imaging time extravasation activity (in mCi) using static images.
3. Use the activity clearance rate to calculate the initial extravasation activity (in mCi) and percent extravasation.
4. Estimate the initial extravasation volume (in mL) based on injected volumes and percent extravasation.
5. Using images of the extravasation at the time of imaging, measure the activity (in mCi) within this estimated initial extravasation volume.
6. Interpolate between initial and imaging time activities to find activity (in mCi) over time in the initial extravasation volume.
7. Calculate the dose rate per mCi (in Sv/mCi-min) within the initial extravasation volume.
8. Multiply activity (in mCi) and dose rate (Sv/mCi-min) over time to get dose (in Sv/min), and then integrate to find total dose (in Sv) to the initial extravasation volume.

This document describes the method in detail and also demonstrate its use with examples of clinical extravasations. For each of the example cases, topical scintillation detectors were used to monitor the injection and the injection site was also included in the imaging field of view.

Table 1 details the specifics of each example case.

Case ID	Radio-pharmaceutical	Injected Activity (mCi)	Radiopharmaceutical Volume (mL)	Saline Flush Volume (mL)	Imaging Time After Injection (min)
14547	18F-FDG	10.22	1.5	30	62
15170	18F-FDG	9.99	4.0	41	62
16074	18F-FDG	17.65	2.6	0	67
16031R	18F-FDG	4.82	0.9	0	56
16031L	18F-FDG	4.82	0.9	20	56
11490	18F-FDG	13.72	1.5	10	57
15771	Tc99m-MDP	25.38	1.0	10	214
15819	Tc99m-MDP	27.40	1.5	0	247
16380	Tc99m-MDP	26.20	0.5	0	201

Table 1. Details of each example case of extravasation.

Step 1: Calculate the Rate of Activity Reabsorption

In order to calculate the rate of clearance, use a least-squares fit of an exponential function to the latter portion of the TAC data (Figure 2). Because the TAC is pre-corrected for radioactive decay, its shape represents the relative change in activity near the injection site. As the body clears extravasated activity back into the venous or lymphatic systems, the measured activity at the injection site will decrease.

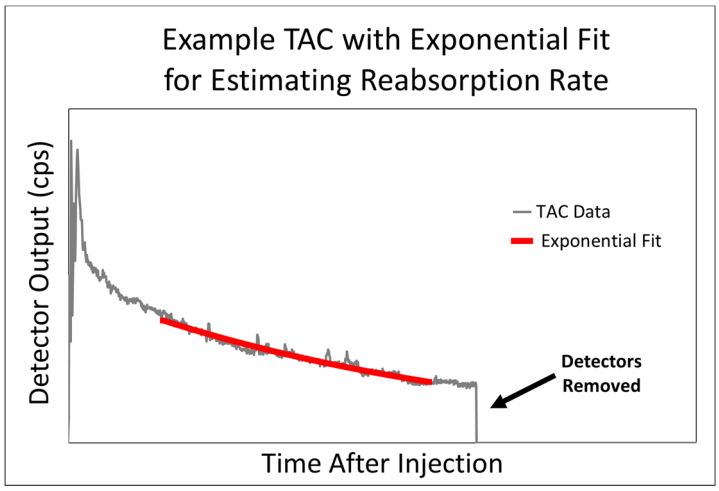

Figure 2. Graph of an exponential fit to the injection arm TAC. Detector data is corrected for radioactive decay prior to curve fitting. For clarity, the reference arm detector output is not shown.

	Example Case ID								
	14547	15170	16074	16031R	16031L	11490	15771	15819	16380
Clearance Rate Half-time (min)	55.9	27.6	64.7	63.5	197.5	61.4	100.5	81.7	n/a*
Imaging Time Total Extravasation Activity (mCi)									
Initial Extravasation Activity (mCi)									
Initial Extravasation Tissue Volume (cm^3)									
Activity Within the Initial Volume at Imaging Time (mCi)									
Dose Rate (mSv/mCi-min)									
Total Equivalent Tissue Dose (Sv)									

* Note that the TAC for example case 16380 was flat, so no reabsorption was used.

Step 2: Measure the Imaging Time Extravasation Activity Using Static Images

Because the scintillation detectors are not able to absolutely quantify the injection site activity, the TAC data must be scaled to units of mCi. Measurements from the static images are used for this.

All PET images used were obtained using a Siemens Biograph mCT 20 scanner with software version SVG60A. Images were reconstructed and corrected for scatter, decay, and attenuation per the hospital's standard imaging protocol. The center's diagnostic radiology physician created volumes of interest for calculation of activity. A threshold of 10% of SUV_{MAX} was used to segment the extravasation.

All SPECT images were obtained with a Siemens Encore 2 scanner and were reconstructed and corrected according to the center's standard imaging protocol. For SPECT, image quantification was not possible, so activities equating to extravasations of 10% and 50% were used for these cases. For case #16380, the nuclear medicine physician noted that, based on the image quality, he would estimate at least 50% of the activity was extravasated.

Figure 3 shows an example VOI and calculation of extravasation activity.

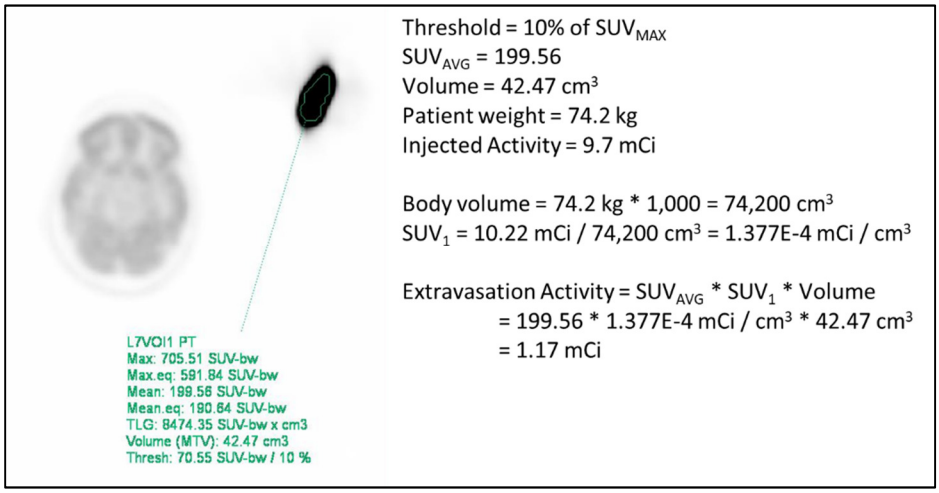

Figure 3. Example screenshot of PET image VOI and calculation of activity using SUV measurement.

	Example Case ID								
	14547	15170	16074	16031R	16031L	11490	15771	15819	16380
Clearance Rate Half-time (min)	55.9	27.6	64.7	63.5	197.5	61.4	100.5	81.7	n/a
Imaging Time Total Extravasation Activity (mCi)	5.2	1.6	0.3	0.2	0.08	4.6	0.4 1.9	0.2 1.0	8.9
Initial Extravasation Activity (mCi)									
Initial Extravasation Tissue Volume (cm^3)									
Activity Within the Initial Volume at Imaging Time (mCi)									
Dose Rate (mSv/mCi-min)									
Total Equivalent Tissue Dose (Sv)									

Step 3: Calculate the Initial Extravasation Activity and Percent Extravasation

Knowing the extravasated activity at imaging time (step 2) and the rate or reabsorption (step 1) allows for calculation of the amount of activity that was initially extravasated. First, the TAC curve fit is scaled so that it passes through the total extravasation activity measurement found with static images in step 2. Then, the curve fit y-intercept indicates the extravasation activity at time zero. Figure 4 shows an example of this extrapolation. Initial activity divided by injected activity provides percent extravasation.

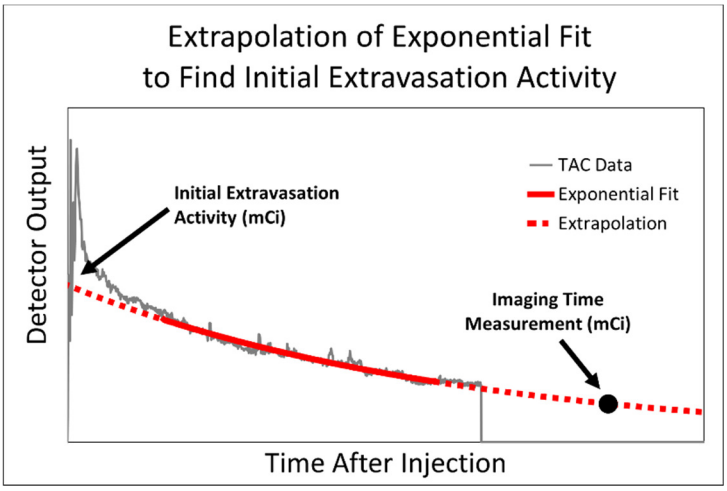

Figure 4. Graph showing extrapolation of the exponential fit to pass through the activity measured on static images. Then, the y-intercept indicates the initial extravasation activity.

	Example Case ID								
	14547	15170	16074	16031R	16031L	11490	15771	15819	16380
Clearance Rate Half-time (min)	55.9	27.6	64.7	63.5	197.5	61.4	100.5	81.7	n/a
Imaging Time Total Extravasation Activity (mCi)	5.2	1.6	0.3	0.2	0.08	4.6	0.4 1.9	0.2 1.0	8.9
Initial Extravasation Activity (mCi)	10.2	7.7	0.7	0.4	0.1	12.6	2.5 12.7	2.7 13.7	13.1
Initial Extravasation Tissue Volume (cm^3)									
Activity Within the Initial Volume at Imaging Time (mCi)									
Dose Rate (mSv/mCi-min)									
Total Equivalent Tissue Dose (Sv)									

Step 4: Estimate the Initial Extravasation Volume Based on Injected Volumes and Percent Extravasation

This method uses two approaches to estimate the initial extravasation volume:

1) twice the injected radiopharmaceutical volume(*7*), scaled by percent extravasation, and
2) the injected radiopharmaceutical volume scaled by percent extravasation plus the flush volume, if any(*3*).

Extravasation of the saline flush would result in immediate dilution of the activity and a reduction in the resulting dose to tissue(*9*). Insight into the volume of saline flush that may have been extravasated is not available, though. This method bounds the dose calculations by assuming either none or all of the saline is extravasated. If no flush was performed, only the volume of the radiopharmaceutical is used (approach 1).

In extravasation dosimetry, the true affected tissue volume is uncertain. Arguments have been made that very small tissue volumes can always lead to high equivalent dose calculations(*21*). In cases when an extravasated radiopharmaceutical was not followed with a saline flush, this novel method uses a minimum tissue volume of 1 cm^3 to assuage concerns of small tissue volumes when the estimated radiopharmaceutical volume in the initial extravasation is less than 1 mL. While using a minimum volume of 1 cm^3 in these cases could vastly underestimate true equivalent dose to the smaller volumes of tissue, it provides a consistent minimum volume for calculation and comparison. Additionally, from a review of NRC records, this 1 cm^3 volume appears consistent with previously reported medical events(*22,23*).

	Example Case ID								
	14547	15170	16074	16031R	16031L	11490	15771	15819	16380
Clearance Rate Half-time (min)	55.9	27.6	64.7	63.5	197.5	61.4	100.5	81.7	n/a
Imaging Time Total Extravasation Activity (mCi)	5.2	1.6	0.3	0.2	0.08	4.6	0.4 1.9	0.2 1.0	8.9
Initial Extravasation Activity (mCi)	10.2	7.7	0.7	0.4	0.1	12.6	2.5 12.7	2.7 13.7	13.1
Initial Extravasation Tissue Volume (cm^3)	3.0 31.5	6.2 44.1	1.0	1.0	1.0 20.0	2.8 11.4	1.0 10.5	1.0	1.0
Activity Within the Initial Volume at Imaging Time (mCi)									
Dose Rate (mSv/mCi-min)									
Total Equivalent Tissue Dose (Sv)									

Step 5: Using Static Images, Measure the Activity Within the Initial Extravasation Volume

Values are now known for the initial extravasation activity (step 3) and volume (step 4). In order to simplify calculations, this method analyzes dose within only the initial extravasation tissue volume. This volume represents the tissue that would be exposed to the highest concentration of activity for the longest period of time. A measurement of imaging time activity within only this volume is needed. It should be noted that tissue surrounding the initial extravasation tissue volume is also being exposed to activity that is not being captured in this calculation. Additionally, source activity outside of this tissue volume will contribute dose that is not accounted for in this method.

Create a spherical VOI within the static images that has a volume equal to the initial extravasation volume and location centered around the voxel with highest activity (SUV_{MAX}). This location is assumed to be the site of initial extravasation because activity will tend to spread outward and away from its initial location over time(*24,25*). Calculate the activity within the VOI with the method used in step 2.

Step 6: Interpolate Initial and Imaging Time Activities to Find Activity Over Time in the Initial Extravasation Volume

The values for activity within the initial extravasation volume at time zero as well as within the same volume at the time of imaging are used to perform a curve fit of activity within the initial extravasation volume over time. The method assumes the activity changes as an exponential. The specific rate of change will be patient- and radiopharmaceutical-specific(*24*).

	Example Case ID								
	14547	15170	16074	16031R	16031L	11490	15771	15819	16380
Clearance Rate Half-time (min)	55.9	27.6	64.7	63.5	197.5	61.4	100.5	81.7	n/a
Imaging Time Total Extravasation Activity (mCi)	5.2	1.6	0.3	0.2	0.08	4.6	0.4 1.9	0.2 1.0	8.9
Initial Extravasation Activity (mCi)	10.2	7.7	0.7	0.4	0.1	12.6	2.5 12.7	2.7 13.7	13.1
Initial Extravasation Tissue Volume (cm^3)	3.0 31.5	6.2 44.1	1.0	1.0	1.0 20.0	2.8 11.4	1.0 10.5	1.0	1.0
Activity Within the Initial Volume at Imaging Time (mCi)	0.5 3.2	0.5 1.7	0.04	0.06	0.01 0.06	4.4 4.6	0.35 0.38	0.2	1.8 8.9
Dose Rate (mSv/mCi-min)									
Total Equivalent Tissue Dose (Sv)									

Step 7: Calculate the Dose Rate Per mCi for the Initial Extravasation Volume

The curve fit from step 6 describes the activity within the initial extravasation volume over time. Conversion factors for this volume of tissue are needed to calculate dose.

The IDAC-dose 2.1 software(*26*) can calculate self-dose to spheres made of various materials. Dose per minute for 1 mCi of activity within the initial extravasation volume is found using a material of "muscle." Figure 5 shows a screenshot of the software being used. Since the dose rate is a function of volume, cases that include a saline flush will have two dose rates – with and without saline. The resulting dose factors are used to convert activity over time to dose over time.

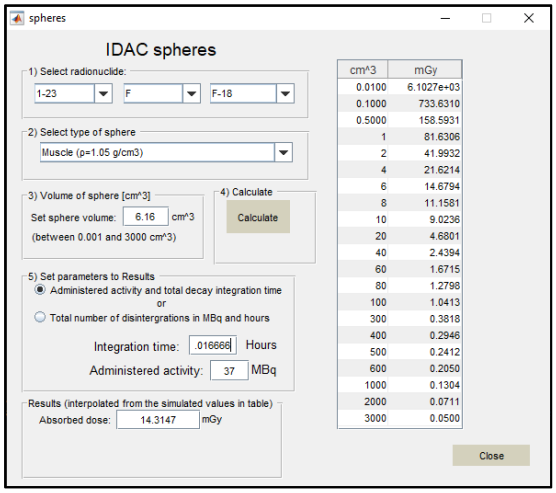

Figure 5. Screenshot of IDAC-dose 2.1 software used to calculate dose rates.4

	Example Case ID								
	14547	15170	16074	16031R	16031L	11490	15771	15819	16380
Clearance Rate Half-time (min)	55.9	27.6	64.7	63.5	197.5	61.4	100.5	81.7	n/a
Imaging Time Total Extravasation Activity (mCi)	5.2	1.6	0.3	0.2	0.08	4.6	0.4 1.9	0.2 1.0	8.9
Initial Extravasation Activity (mCi)	10.2	7.7	0.7	0.4	0.1	12.6	2.5 12.7	2.7 13.7	13.1
Initial Extravasation Tissue Volume (cm^3)	3.0 31.5	6.2 44.1	1.0	1.0	1.0 20.0	2.8 11.4	1.0 10.5	1.0	1.0
Activity Within the Initial Volume at Imaging Time (mCi)	0.5 3.2	0.5 1.7	0.04	0.06	0.01 0.06	4.4 4.6	0.35 0.38	0.2	1.8 8.9
Dose Rate (mSv/mCi-min)	28.5 3.1	14.4 2.2	80.5	80.5	80.5 4.7	30.8 8.1	5.9 0.7	5.9	5.9
Total Equivalent Tissue Dose (Sv)									

The dose rate for Tc99m is lower than that of F18 because it does not emit positrons. However, the resulting equivalent dose to tissue from Tc99m-MDP can be higher than that of F18-FDG because Tc99m-MDP:

- ▶ uses higher administered activities
- ▶ has a longer half-life
- ▶ is not routinely flushed with saline
- ▶ tends to reabsorb more slowly

Step 8: Multiply Activity and Dose Rate Over Time, Then Integrate to Find Total Dose to the Initial Extravasation Volume

In this step, multiply the activity over time found in step 6 with the dose factors found in step 7 to calculate dose over time. Then integrate the dose over time to find total equivalent dose to the initial extravasation volume. Values are calculated with and without saline flush as applicable.

Figure 6 shows an example of the results of this step.

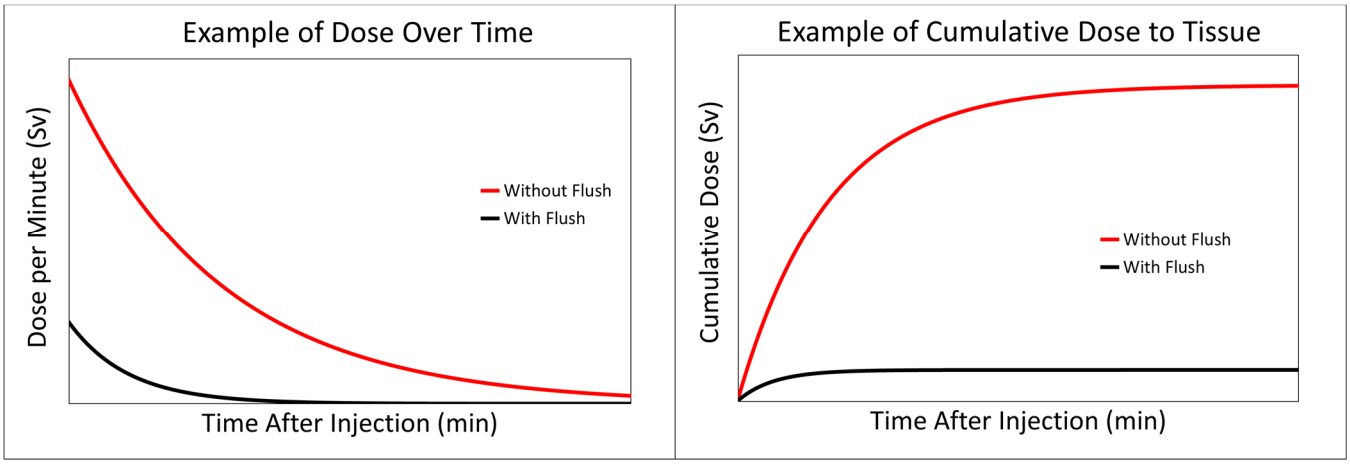

Figure 6. Example graphs of tissue dose over time as well as cumulative dose.

	Example Case ID								
	14547	15170	16074	16031R	16031L	11490	15771	15819	16380
Clearance Rate Half-time (min)	55.9	27.6	64.7	63.5	197.5	61.4	100.5	81.7	n/a
Imaging Time Total Extravasation Activity (mCi)	5.2	1.6	0.3	0.2	0.08	4.6	0.4 1.9	0.2 1.0	8.9
Initial Extravasation Activity (mCi)	10.2	7.7	0.7	0.4	0.1	12.6	2.5 12.7	2.7 13.7	13.1
Initial Extravasation Tissue Volume (cm^3)	3.0 31.5	6.2 44.1	1.0	1.0	1.0 20.0	2.8 11.4	1.0 10.5	1.0	1.0
Activity Within the Initial Volume at Imaging Time (mCi)	0.5 3.2	0.5 1.7	0.04	0.06	0.01 0.06	4.4 4.6	0.35 0.38	0.2	1.8 8.9
Dose Rate (mSv/mCi-min)	28.5 3.1	14.4 2.2	80.5	80.5	80.5 4.7	30.8 8.1	5.9 0.7	5.9	5.9
Total Equivalent Tissue Dose (Sv)	6.0 1.7	2.6 0.7	1.3	1.0	0.18 0.05	21.4 5.8	4.5 0.2	7.5 1.5	31.3

Conclusion

This paper describes a novel method of calculating equivalent dose to tissue in the case of radiopharmaceutical extravasation. Use of the method is demonstrated for several clinical cases of extravasation of 18F-FDG and Tc99m-MDP.

This method differs from existing methods by estimating the ways in which both the extravasation activity and its volume change over time. Inclusion of this dynamic information results in a more accurate estimation of equivalent dose to the initially extravasated tissue volume. Table 2 details the novel method's results compared to the existing methods.

	Equivalent Dose to Extravasated Tissue (Sv)			
Case ID	Existing Method 1*	Existing Method 2**	Naïve Method***	Novel Method
14547	3.3 - 70.1	2.6 - 24.2	0.6	1.7 - 6.0
15170	2.3 - 25.7	1.8 - 9.3	0.4	0.7 - 2.6
16074	69.3	24.6	0.1	1.3
16031R	55.1	18.5	0.4	1.0
16031L	2.4 - 55.1	1.8 - 18.5	0.03	0.05 - 0.18
11490	12.3 - 94.1	9.1 - 32.5	3.2	5.8 - 21.4
15771	6.2 - 68.5	2.1 - 10.3	0.1	0.2 - 4.5
15819	49.3	7.70	0.04	1.5 - 7.5
16380	141.4	20.3	1.5	31.3

Table 2. Comparison of different methods of extravasation dosimetry.

* Existing method 1 assumes that the entire injection is extravasated into a volume of tissue equal to its injection volume. Furthermore, it assumes no reabsorption and no movement of the radiopharmaceutical. Dose was calculated with and without saline flush.

** Existing method 2 assumes a reabsorption half-time of 120 minutes and 100% extravasation into a volume equal to twice the injected radiopharmaceutical volume or the injected radiopharmaceutical volume plus the saline flush volume.

*** The naïve method uses activity and volume from static images and accounts for physical decay, but assumes no reabsorption. Note that evidence of this method was not found in the literature.

Results of the novel method presented here are within the overall range of values found with other methods, but the spread of its estimates is less.

Practitioners familiar with nuclear medicine imaging would likely reject existing method 1 as implausible because the assumption of 100% extravasation with no reabsorption is easily refuted by the static images. If all activity decays within tissue at the injection site, then no image could be constructed.

Neither existing method 2 nor the naïve method accurately account for the ways in which the extravasation can change over time. Existing method 2 assumes reabsorption with a half-time of 120 minutes, however, the example cases presented here show that 18F-FDG reabsorbs with a half-time of 78 minutes on average. An assumed reabsorption half-time of 120 minutes would over-estimate the tissue dose in most of these examples. Of the three cases using Tc99m-MDP, two reabsorbed faster than 120-minutes while the third showed very slow reabsorption. Existing method 2 fails to consider that reabsorption can be patient- and radiopharmaceutical-specific.

Extravasation dosimetry is dependent on the specific circumstances of each event. An estimate of biological clearance is needed in order to accurately calculate tissue dose. Topical scintillation detectors

can provide feedback to clinicians to ensure that when extravasations do occur, they can include the injection site in the static imaging FOV. Additionally, the dynamic data provided by the detectors can be used to perform more accurate extravasation dosimetry.

This method has been reviewed and is supported by distinguished medical physicists. Their information can be provided upon request. Additionally, the method is being prepared for submission later this month to a medical physics journal for peer-reviewed publication.

References

1. Stabin MG. *Fundamentals of Nuclear Medicine Dosimetry*: Springer; 2008.

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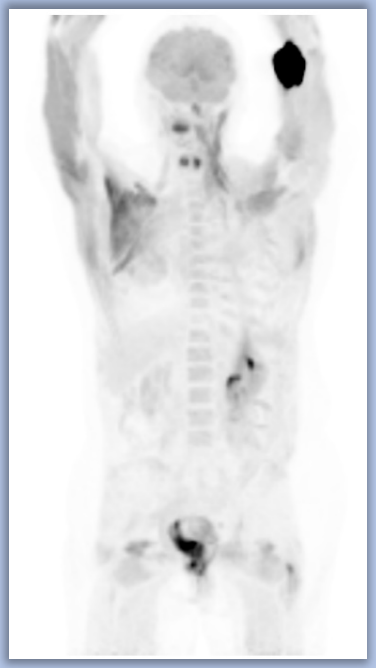
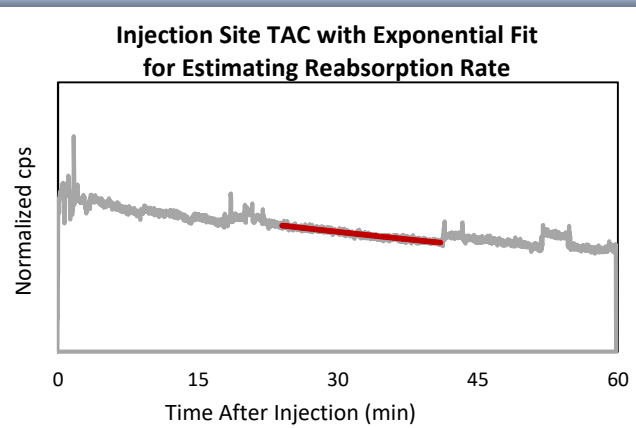
Scan #16448

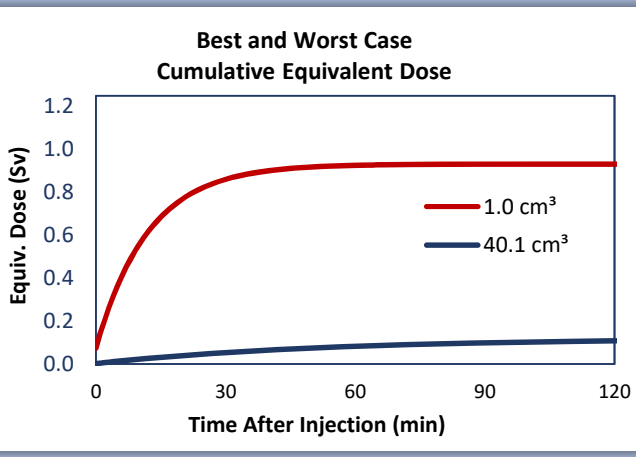
Equivalent Dose: 0.1 to 0.9 Sv



Radioisotope:	F-18	
Physical Half-life	109.77	min
Injection Method	Auto	
Injection Location:	Left Antecubital	
Injected Activity:	10.0	mCi
Radiotracer Volume	1.5	mL
Saline Flush Volume	40	mL
Imaging Time:	62	min
% Infiltration:	9	%
Initial Activity	0.9	mCi
Imaging Time Activity	0.5	mCi
Reabsorption Rate (half-life):	80.6	min

Dose Calculation Volume	1.0 to 40.1	cm^3
Dose Rate	2.4 to 80.5	mSv/mCi-min
Total Equivalent Dose	0.1 to 0.9	Sv





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 cm^3 as a maximum. We estimate that the equivalent dose exposure to this patient's arm tissue was between 0.1 Sv and 0.9 Sv.

- Dose Calculation Volume is twice the infiltrated radiotracer volume or the total flush volume plus the infiltrated radiotracer volume with a minimum volume of 1 cm^3.
- Initial Infiltration amount and reabsorption rate estimates are based on PET measurements and injection site monitoring data from Lara® sensors.
- Volumetric expansion is modeled as a mono-exponential function using initial volumes and PET measurements of volume.
- Dose rates are based on nuclear decay data from ICRP Publication 107 using the IDAC-dose 2.1 software's sphere module.