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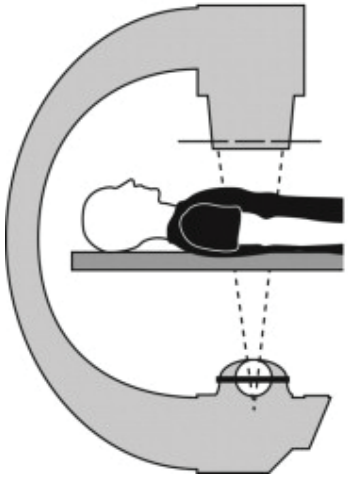
Extravasation of radionuclides: recognising the danger and managing the consequences

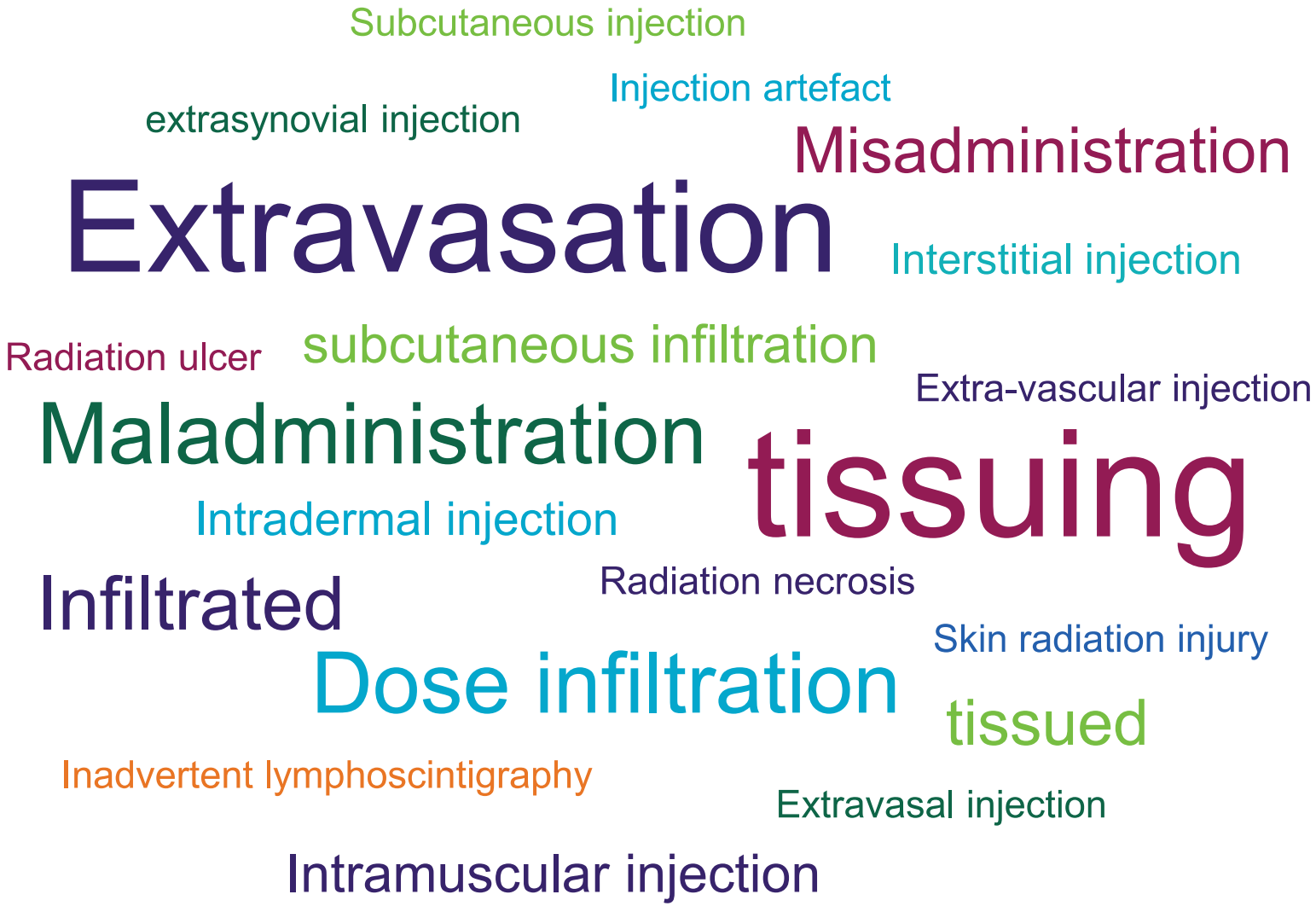
Tamar Willson

Deterministic damage in imaging

- Long procedures in interventional radiology (IR)
  - Can get high skin doses (>~5 Gy)
  - depilation / burns / necrosis
  - High (>~5 Gy) skin doses followed up



- What about nuclear medicine?
  - No deterministic effects if activity dispersed
  - What if it is tissued?


Subcutaneous injection
Injection artefact
extrasynovial injection
Misadministration
Extravasation
Interstitial injection
Radiation ulcer
subcutaneous infiltration
Extra-vascular injection
Maladministration
tissuing
Intradermal injection
Radiation necrosis
Infiltrated
Skin radiation injury
Dose infiltration
tissued
Inadvertent lymphoscintigraphy
Extravasal injection
Intramuscular injection

Tissuing: it happens

- ~0.05% manual injections in CT are tissued [1]
  - (study defined tissuing as >10 ml extravased)

1. Shaqdan K, Aran S, Thrall J, Abujudeh H. Incidence of contrast medium extravasation for CT and MRI in a large academic medical centre: A report on 502,391 injections. Clin Radiol. 2014

Tissuing: it happens

Risk factors:

- Small vein size
- Poor vein condition
- Large catheter size relative to vein
- Multiple venipuncture sites
- Catheter unstable/ poorly secured
- Patient activity
- Use of an infusion pump/ power injector
- Clots
- lymphedema

[2]: Doellman D, Hadaway L, Bowe-Geddes LA, Franklin M, Ledonne J, Donnell LP, et al. Infiltration and Extravasation: Update on prevention and management. Art Sci Infus Nurs. 2009;32(4):203–11.

Tissuing a radionuclide therapy

Case study from the literature [3]:

- 1200 MBq ^{90}Y Zevalin
- No immediate evidence of extravasation
- 10 ml NaCl solution flush: Extravasation noted
- 1 day post exposure: erythema over ~100cm^2
- 6 days post exposure: referred for surgical advice
- Lipoaspiration/ washing considered, but even if all washed out, most of the dose has already been delivered (+ could make things worse)

[3]: Baus A, Keilani C, Bich CS, Entine F, Brachet M, Duhamel P, 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. Ann Chir Plast Esthet. 2017;

Case study: Tissued ^{90}Y Zevalin

- 26 days post exposure: discharged from hospital
- ‘Lost to follow up’, until 5 months later
- Worsening lesions on the arm

[3]: Baus A, Keilani C, Bich CS, Entine F, Brachet M, Duhamel P, 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. Ann Chir Plast Esthet. 2017;

Injury images ahead

(and they get worse)

Case study: Tissued ^{90}Y Zevalin

- Range of motion restricted, cannot extend past 140 degrees

Case study: Tissued ^{90}Y Zevalin

Figure 4 Pre-operative view of the left elbow, necrosis is identified by the black shape.

Case study: Tissued ^{90}Y Zevalin

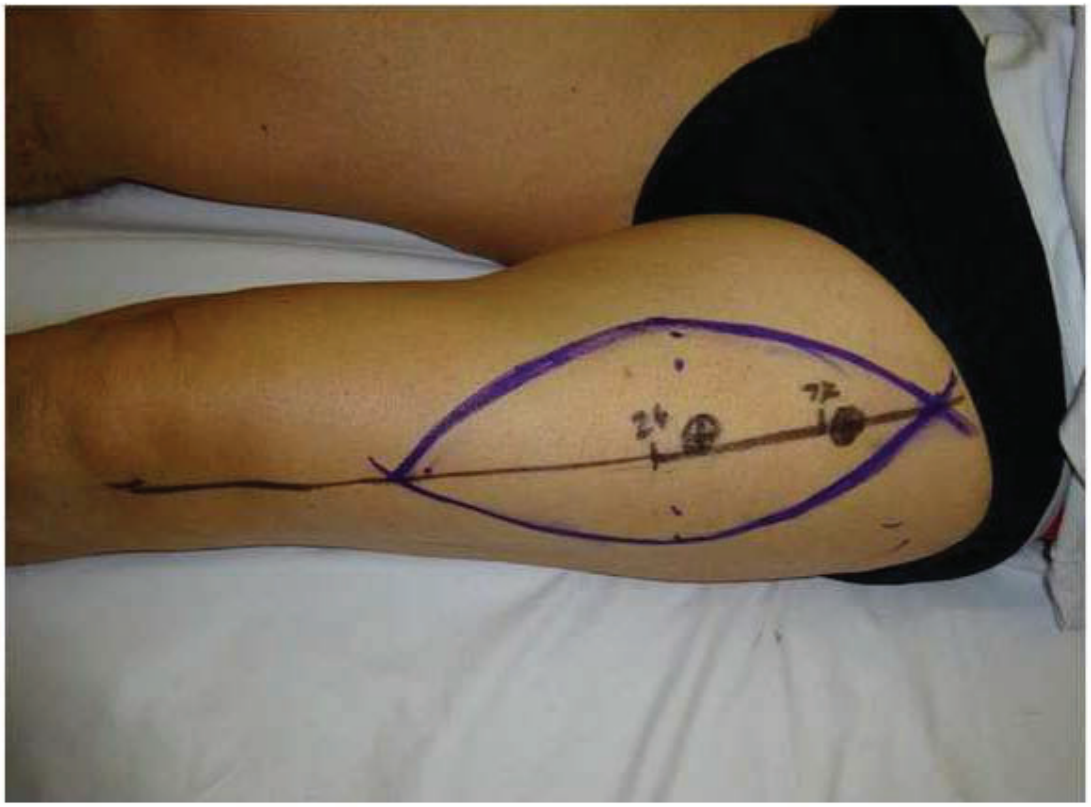


Figure 5 Preoperative marking of a antero-lateral thigh free flap in the left thigh with the perforans branches identification.

Case study: Tissued ^{90}Y Zevalin

Figure 6 Debridement of the erythematous and necrosis wound. Respect of the tendinous, vascular and nervous structures (median nerve is identified by siliconed silastic® and the black shape) in the bending area.

Case study: Tissued ^{90}Y Zevalin

Figure 7 Covering of the cutaneous defect.

Case study: Tissued ^{90}Y Zevalin

Figure 8 Complete recovery of a passive and active extension and disappearance of nervous disorders.

Case study: Tissued ^{90}Y Zevalin

- ~86% of activity tissued
- Estimated dose ~43 Gy
- Method of dose estimation not explained

Injury images over

(mostly)

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What about diagnostic radionuclides?

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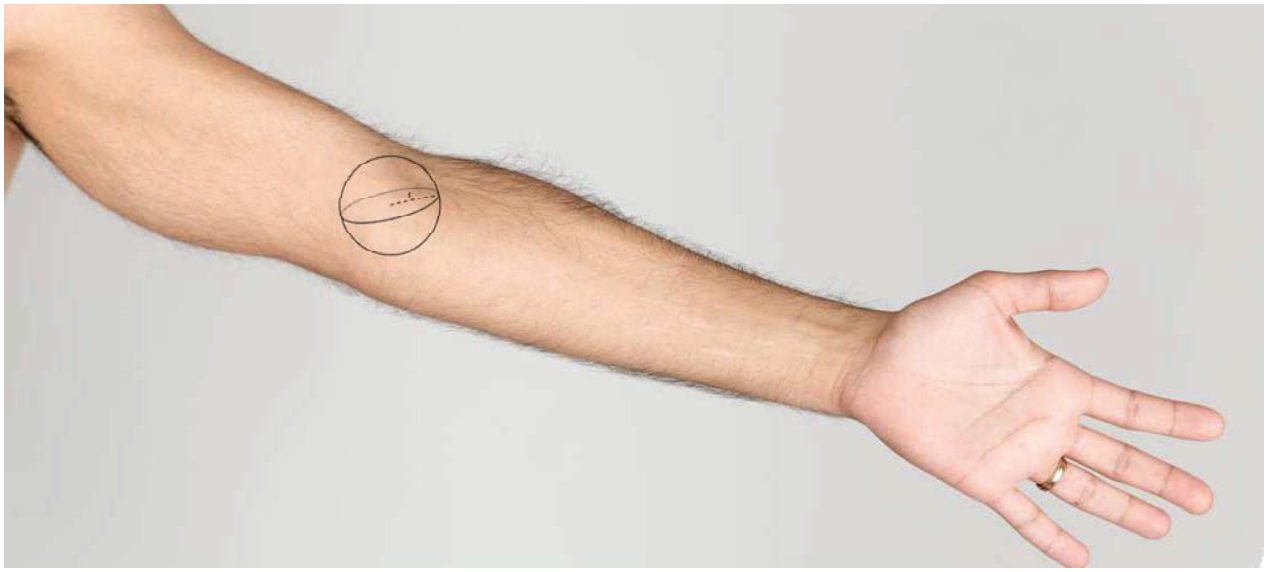
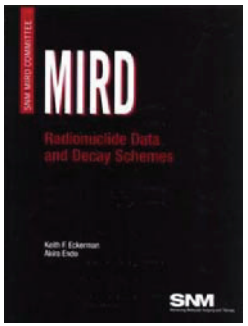
How can we calculate the dose?

$$Dose[Gy] = \frac{Energy\ deposited\ [J]}{Mass\ [kg]}$$



How can we calculate the dose?

$$Energy\ deposited = Energy\ per\ decay \times No.of\ decays$$

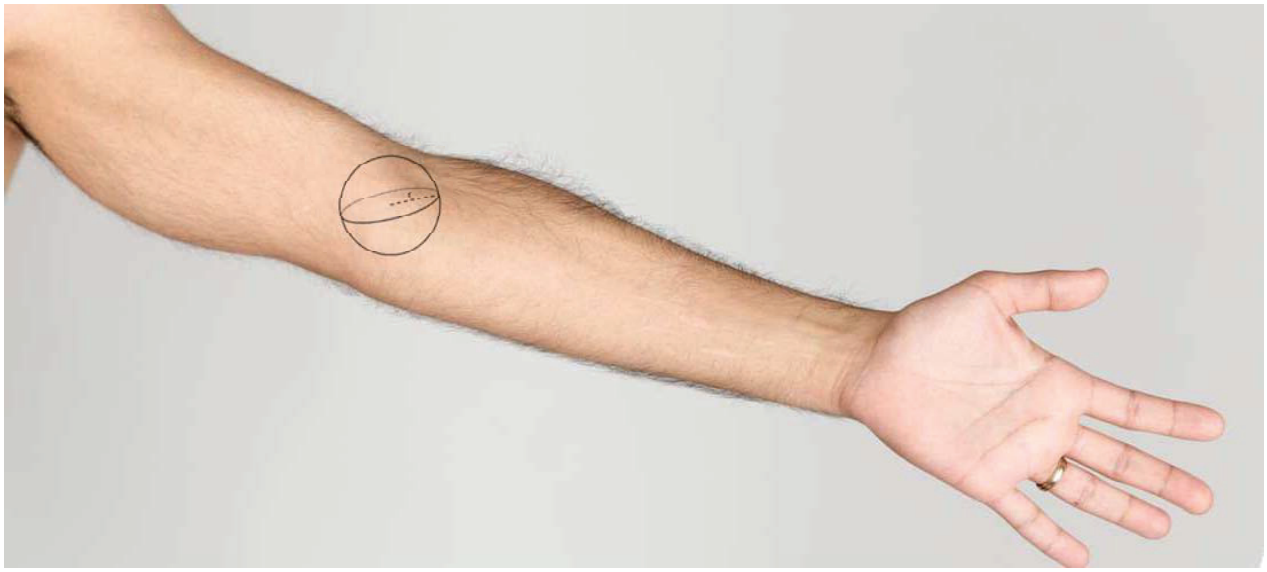


from activity

- Energy per decay from MIRD tables (β, internal conversion and auger only)
  - Assume these are absorbed within volume.
  - Neglect γ and X-rays
- No. of decays: Assume activity is fixed, then it is = $\frac{Activity}{\lambda}$

How can we calculate the dose?

$$Dose[Gy] = \frac{Energy\ deposited\ [J]}{Mass\ [kg]}$$



Arm image by Genusfotografen (genusfotografen.se) & Wikimedia Sverige (wikimedia.se), CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=50355953

How can we calculate the dose?

How to estimate the mass?

- Assume tissue is water-equivalent, and the injection is not self-attenuating
- 5 g [4]
- Area of red patch × 1 cm [5]
- 1 ml [6]
- ~volume of injection [7]

[4]: Castronovo FP, Mckusick KA, Strauss HW. The infiltrated radiopharmaceutical injection: Dosimetric considerations.
[5]: Williams G, Palmer MR, Parker JA, Joyce R. Extravazation of Therapeutic Yttrium-90-Ibritumomab Tiuxetan (Zevalin ®): A Case Report. Vol. 21, CANCER BIOTHERAPY & RADIOPHARMACEUTICALS. 2006.
[6]: Hoop B. The Inifitrated Radiopharmaceutical Injection: Risk Considerations. J Nucl Med [Internet]. 1991;890–1. Available from: http://jnm.snmjournals.org/site/misc/permission.xhtml
[7]: Shapiro B, Pillay M, Cox PH. Dosimetric consequences of interstitial extravasation following IV administration of a radiopharmaceutical. Eur J Nucl Med. 1987;12(10):522–3.

How can we calculate the dose?

- Using volume of injection:

Nuclide	Activity /MBq	Injection volume /ml	Dose /Gy
^{18}F	370	0.3	470
^{68}Ga	200	4	35
^{99m}Tc	800	0.5	130
^{111}In	220	1.1	390
^{123}I	190	2.5	23

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The mass matters…

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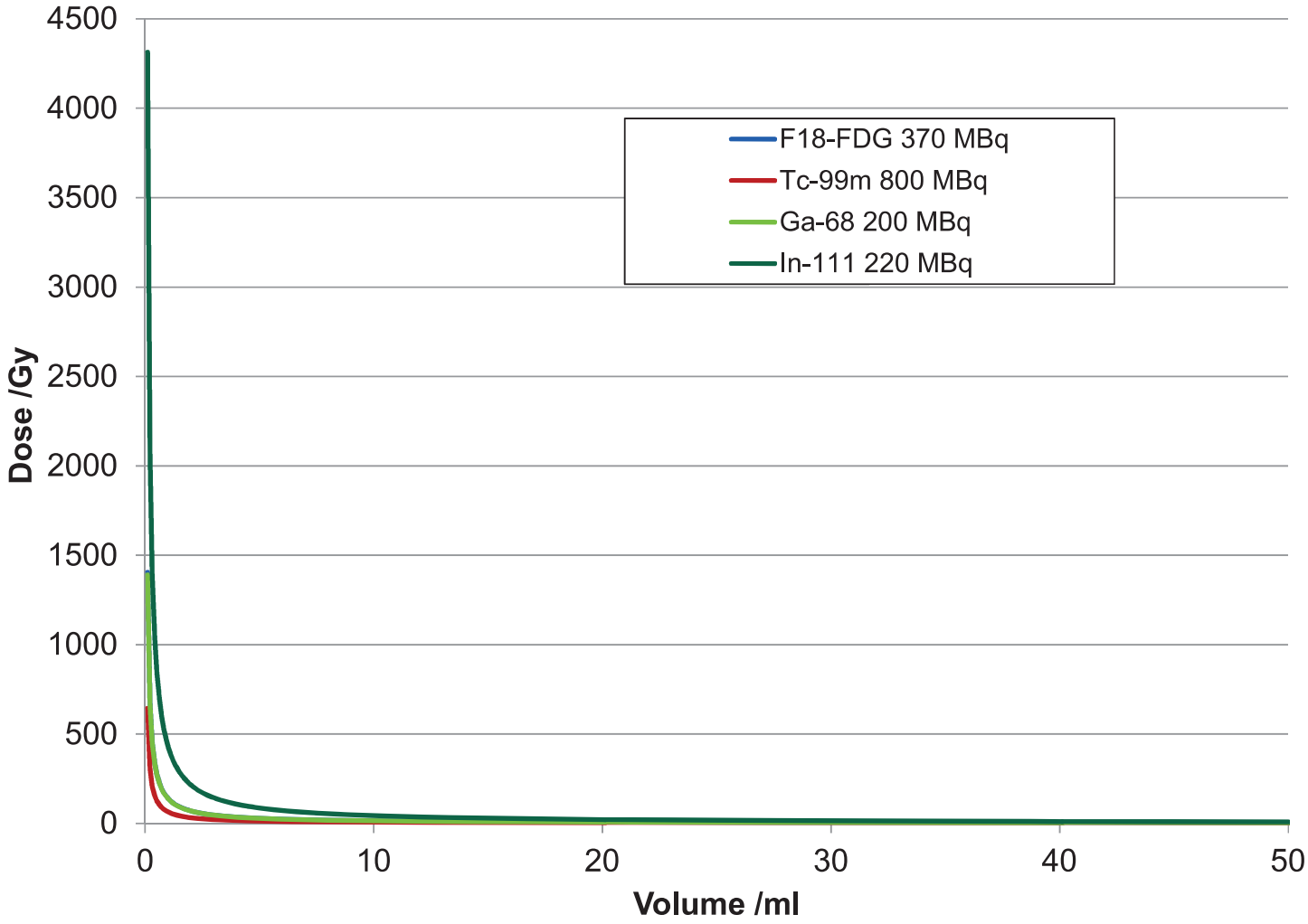
Dose Volume relationship for fixed totally tissued administration



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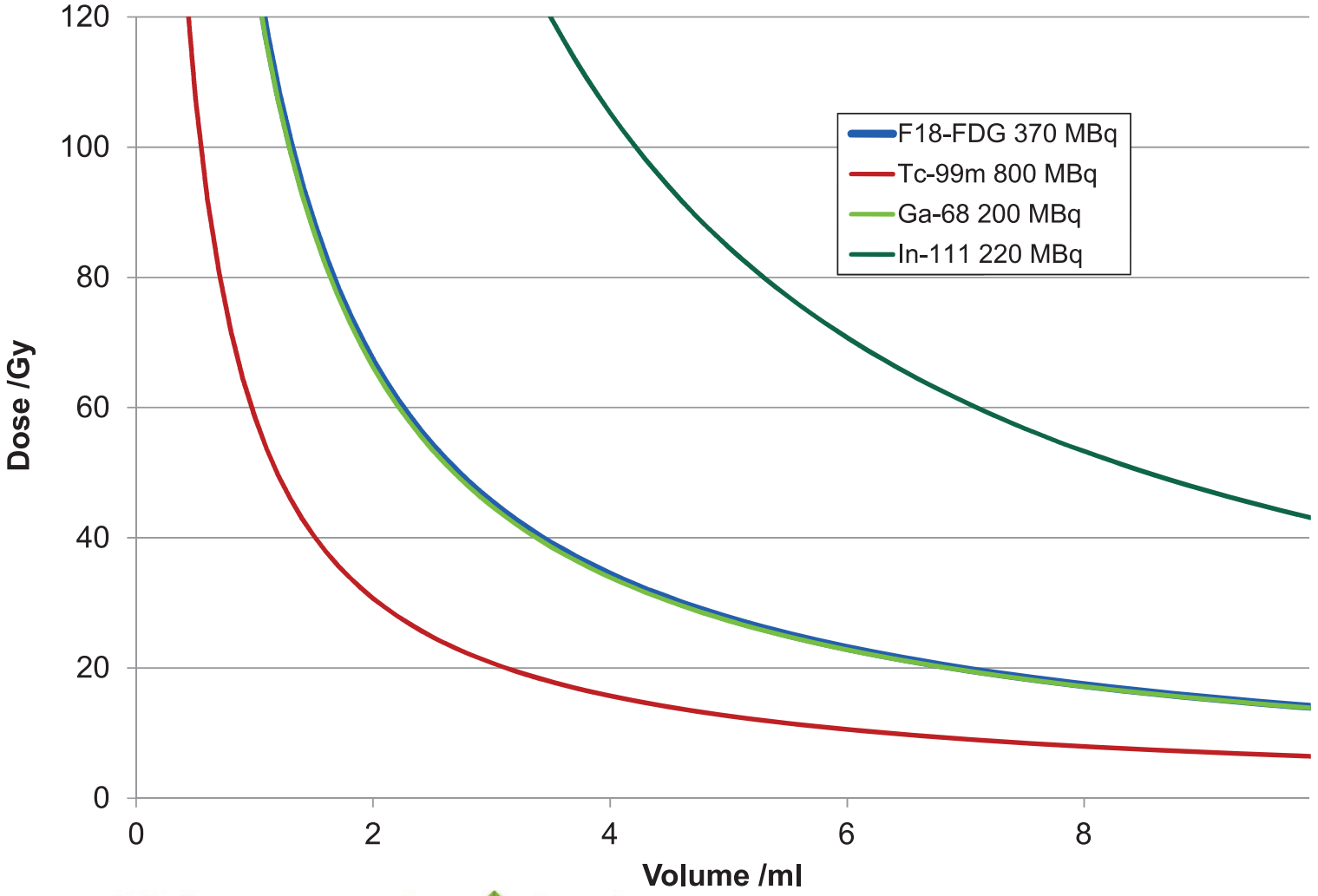
Dose Volume relationship for fixed totally tissued administration



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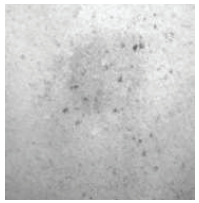
possibilities: 370 MBq ^{18}F-FDG

~7.6 mGy
whole body dose



~70 cm^3
transient
erythema

~9-14 cm^3
prolonged
erythema,
dermal atrophy

~5 cm^3 necrosis

Fully distributed
Normal scan

Tissued in larger
volume

Tissued in small
volume

Skin dose images: Balter S, Hopewell JW, Miller DL, Wagner LK, Zelefsky MJ. Fluoroscopically guided interventional procedures : a review of radiation effects on patients' skin and hair. Radiology. 2010;254(2):326–42.

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What is a meaningful dose?

Instead of calculating

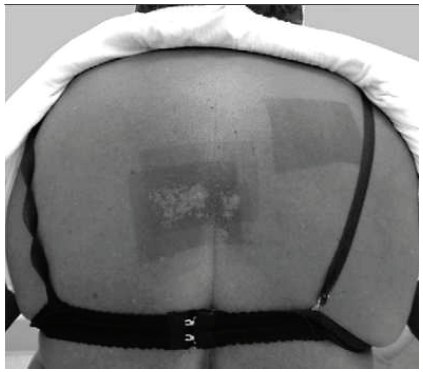
- Maximum dose delivered to the volume

why not

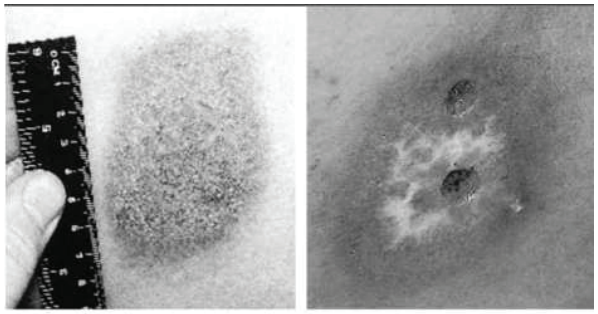
- Maximum volume ‘treated’ to a dose

<~5 Gy

~10 Gy



~10+ Gy



2 months 5 months

~20 Gy

Nuclide	Activity/ MBq	Volume (ml) treated to dose			
		2 Gy	10 Gy	15 Gy	25 Gy
^{18}F	370	70	14	9	5
^{68}Ga	200	70	14	9	6
^{99m}Tc	800	32	6	4.3	2.6
^{111}In	220	216	43	29	17
^{123}I	190	29	5.7	3.8	2.3

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Tissuing a diagnostic injection

- Diagnostic administrations can theoretically give high doses
- This model is a worst case scenario (totally tissued, totally fixed activity)
- Nevertheless, it indicates the potential for deterministic damage
- Delayed effect → patients may not connect adverse reactions to a tissued administration

Going forward

- Local database of tissued administrations
- In the future, we can
  - estimate incidence %
  - calculate doses
  - audit patient notes for adverse reactions
- After data has been gathered → create protocol for following up tissued injections
  - Possibly similar to protocol in IR

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End

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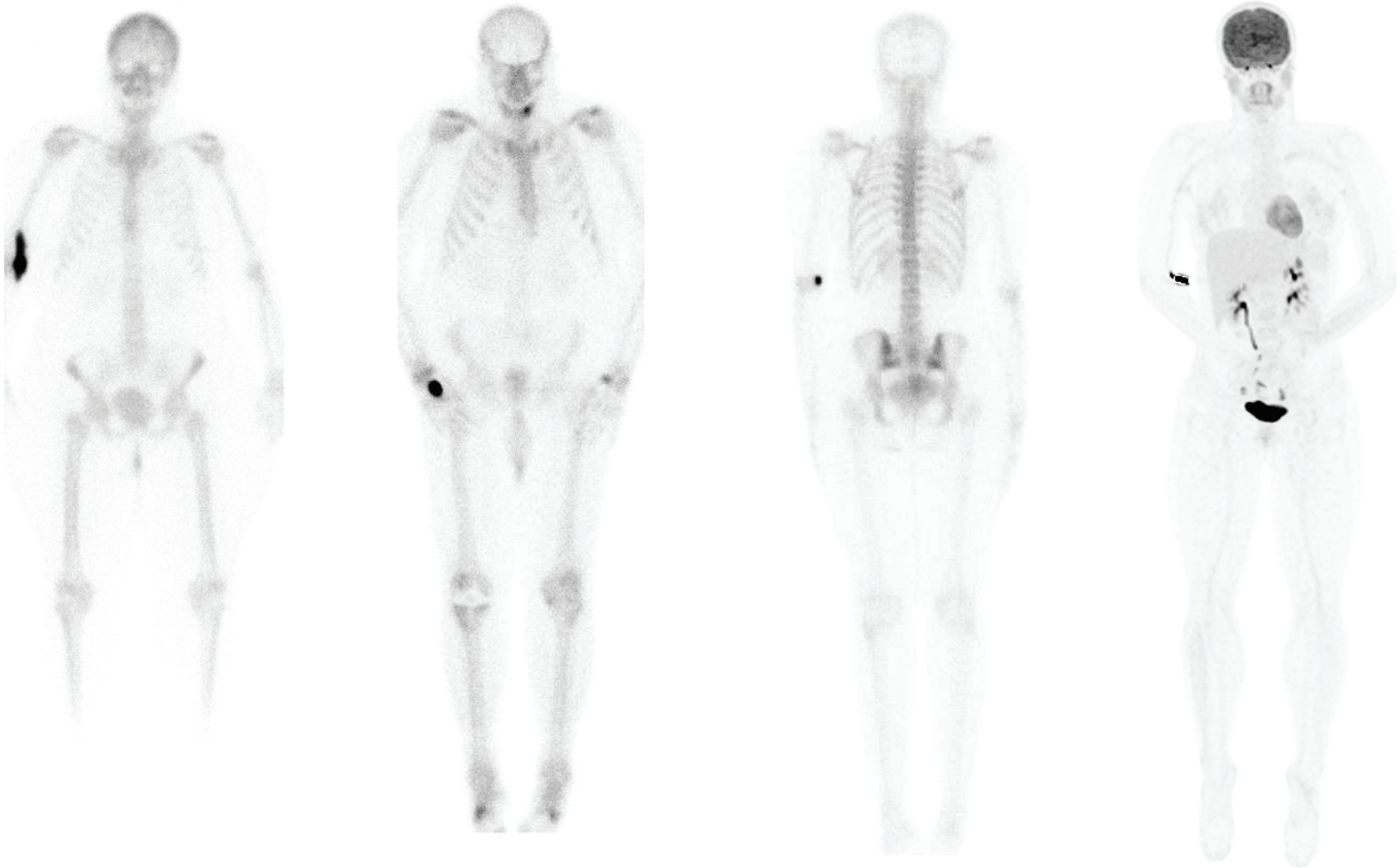
So far…



Strategies following tissued dose

Various strategies from the literature

- Try to draw it back out
- Warm up the site (promote reabsorption)
- Elevate the limb
- Massage
- Squeezing a stress ball
- If a radiation ulcer develops: surgical resection, antibiotics, topical steroids
- Amifostine: experimental but potentially radioprotective

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Eur J Nucl Med Mol Imaging (2017) 44:1234–1243
DOI 10.1007/s00259-017-3675-7

CrossMark

REVIEW ARTICLE

Consequences of radiopharmaceutical extravasation and therapeutic interventions: a systematic review

Jochem van der Pol[1] · Stefan Vöö[1] · Jan Bucerius[1,2] · Felix M. Mottaghy[1,2]

Received: 13 January 2017 / Accepted: 7 March 2017 / Published online: 16 March 2017

Abstract
Purpose Radiopharmaceutical extravasation can potentially lead to severe soft tissue damage, but little is known about incidence, medical consequences, possible interventions, and effectiveness of these. The aims of this study are to estimate the incidence of extravasation of diagnostic and therapeutic radiopharmaceuticals, to evaluate medical consequences, and to evaluate medical treatment applied subsequently to those incidents.
Methods A sensitive and elaborate literature search was performed in Embase and PubMed using the keywords "misadministration", "extravasation", "paravascular infiltration", combined with "tracer", "radionuclide", "radiopharmaceutical", and a list of keywords referring to clinically used tracers (i.e. "Technetium-99m", "Yttrium-90"). Reported data on radiopharmaceutical extravasation and applied interventions was extracted and summarised.
Results Thirty-seven publications reported 3016 cases of diagnostic radiopharmaceutical extravasation, of which three cases reported symptoms after extravasation. Eight publications reported 10 cases of therapeutic tracer extravasation. The most severe symptom was ulceration. Thirty-four differ- do not require specific intervention. Extravasation of therapeutic radiopharmaceuticals can give severe soft tissue lesions. Although not evidence based, surgical intervention should be considered. Furthermore, dispersive intervention, dosimetry and follow up is advised. Pharmaceutical intervention has no place yet in the immediate care of radiopharmaceutical extravasation.

Keywords Extravasation · Dose infiltration · Radiopharmaceuticals · Radiation ulcer

Introduction

High doses of radiation exposure can potentially cause severe tissue damage, such as skin desquamation and necrosis. Extravasation of radionuclides used in nuclear medicine practice results in localized tissue retention of the radiopharmaceutical and subsequently in an unintended extended local radiation exposure. Because of the character of the radiation, extravasation of therapeutic radiopharmaceuticals has the

Tissuing Cases: Diagnostic

used ^{99m}Tc labelled radiopharmaceuticals. Similarly, no cases have been found with any symptoms after extravasation of ^{99m}Tc, ^{123}I, ^{18}F, and ^{68}Ga labelled radiopharmaceuticals.

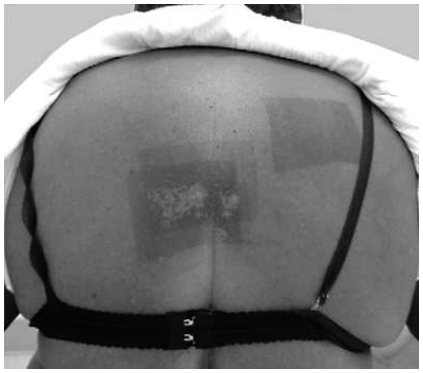
Tissuing Cases: Diagnostic

Total reported cases	Radiopharmaceutical	No. of patients with reported radiation injury	No. of patients with reported follow-up	Most severe injury reported
332	18F-FDG	0	0	
2584	^{99m}Tc bone tracers	0	0	
3	^{99m}Tc-MAA	0	0	
1	^{99m}Tc-DMSA	0	0	
10	^{99m}Tc-DTPA	0	0	
1	^{99m}Tc-HMPAO	0	0	
1	^{99m}Tc-MAG3	0	0	
15	^{99m}Tc-pertechnetate	0	0	
2	^{99m}Tc-sestamibi	0	0	
38	^{99m}Tc-sulfurcolloid	0	0	
16	^{99m}Tc-microspheres	0	0	
1	^{131}I-iodocholesterol	1	1	Erythematous plaque and pruritus.
12	^{201}Tl-thallous chloride	2	2	Radiation ulcer
3016		3	3	

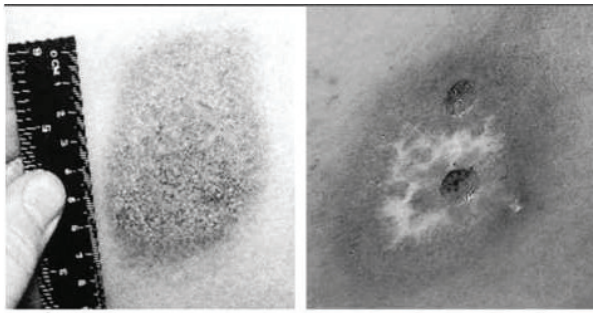
Dose reaction lessons from IR

<~5 Gy

~10 Gy



~10+ Gy



2 months 5 months

~20 Gy

- Dose thresholds are best expressed in terms of a range of doses, rather than a single dose
- It depends on the patient
- Effects are delayed, hours to years
- Medical follow up for high doses

Balter S, Hopewell JW, Miller DL, Wagner LK, Zelefsky MJ. Fluoroscopically guided interventional procedures : a review of radiation effects on patients' skin and hair. Radiology. 2010;254(2):326–42.