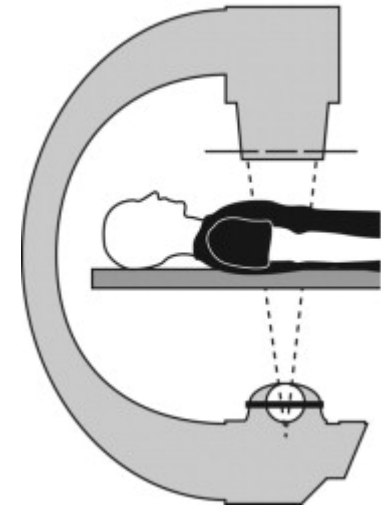


# Extravasation of radionuclides: recognising the danger and managing the consequences

Tamar Willson

# Deterministic damage in imaging

- Long procedures in interventional radiology (IR)
  - Can get high skin doses ( $> \sim 5$  Gy)
  - depilation / burns / necrosis
  - High ( $> \sim 5$  Gy) skin doses followed up
- What about nuclear medicine?
  - No deterministic effects if activity dispersed
  - What if it is tissue?



Subcutaneous injection  
extrasynovial injection  
Injection artefact  
Misadministration  
**Extravasation**  
Interstitial injection

Radiation ulcer  
subcutaneous infiltration  
Extra-vascular injection  
**Maladministration**  
Intradermal injection  
**tissuing**

Infiltrated  
Radiation necrosis  
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 extravasated)

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  $^{90}\text{Y}$  Zevalin
- No immediate evidence of extravasation
- 10 ml NaCl solution flush: Extravasation noted
- 1 day post exposure: erythema over  $\sim 100\text{cm}^2$
- 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 $^{90}\text{Y}$ 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 $^{90}\text{Y}$ Zevalin



- Range of motion restricted, cannot extend past 140 degrees

# Case study: Tissued $^{90}\text{Y}$ Zevalin



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

# Case study: Tissued $^{90}\text{Y}$ Zevalin



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

# Case study: Tissued $^{90}\text{Y}$ 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<sup>®</sup> and the black shape) in the bending area.

# Case study: Tissued $^{90}\text{Y}$ Zevalin



Figure 7 Covering of the cutaneous defect.

# Case study: Tissued $^{90}\text{Y}$ Zevalin



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

# Case study: Tissued $^{90}\text{Y}$ Zevalin

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

**Injury images over**

(mostly)



# What about diagnostic radionuclides?

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# How can we calculate the dose?

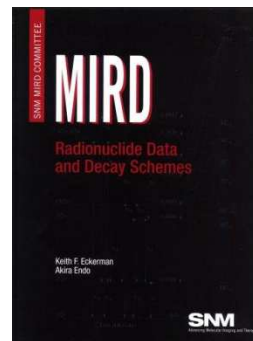
$$Dose [Gy] = \frac{\text{Energy deposited [J]}}{\text{Mass [kg]}}$$



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?

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



from activity

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

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# How can we calculate the dose?

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



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  $\times$  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. Extravasation of Therapeutic Yttrium-90-Ibritumomab Tiuxetan (Zevalin®): A Case Report. Vol. 21, CANCER BIOTHERAPY & RADIOPHARMACEUTICALS. 2006.

[6]: Hoop B. The Infiltrated 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?

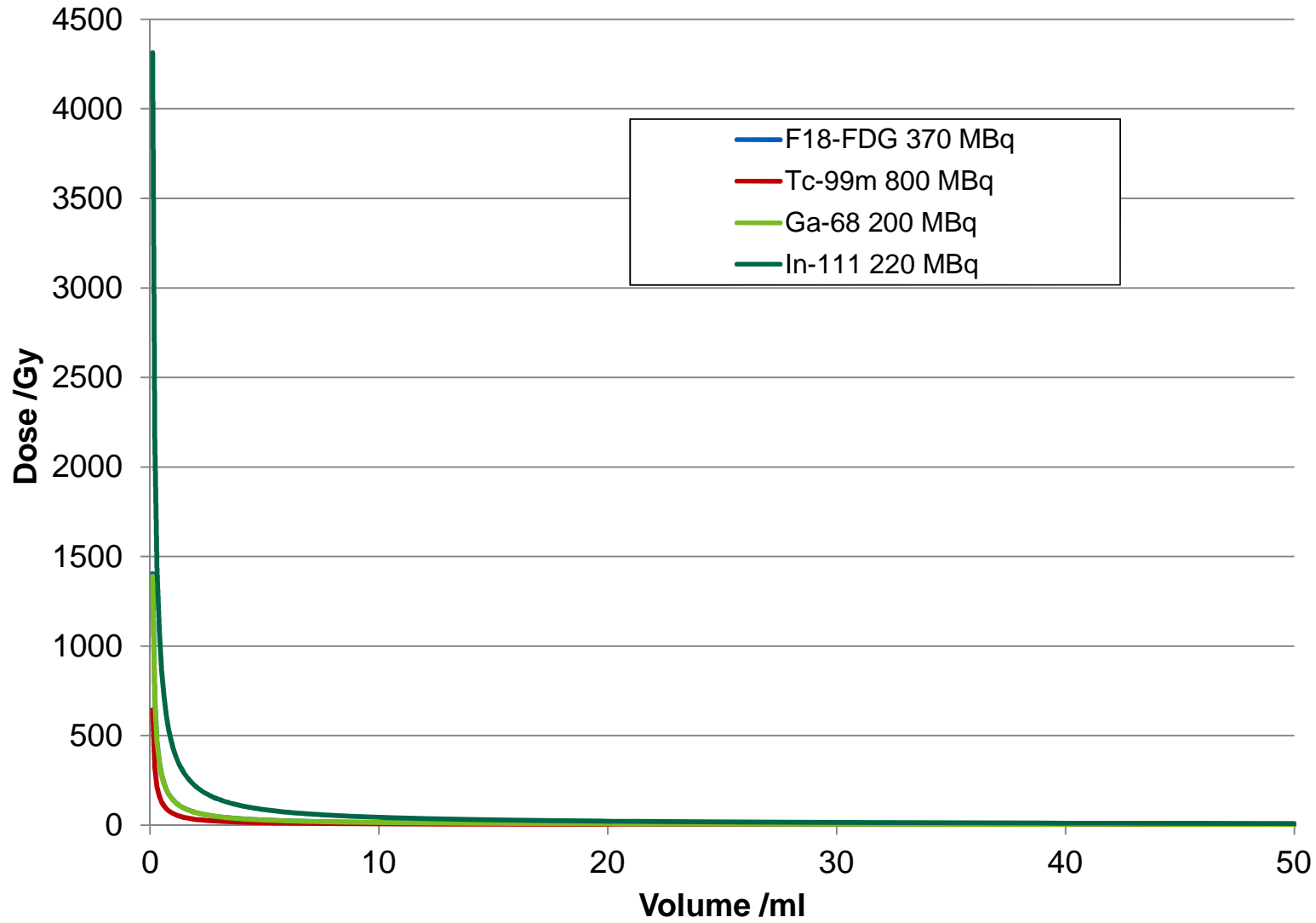
- Using volume of injection:

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

# The mass matters...

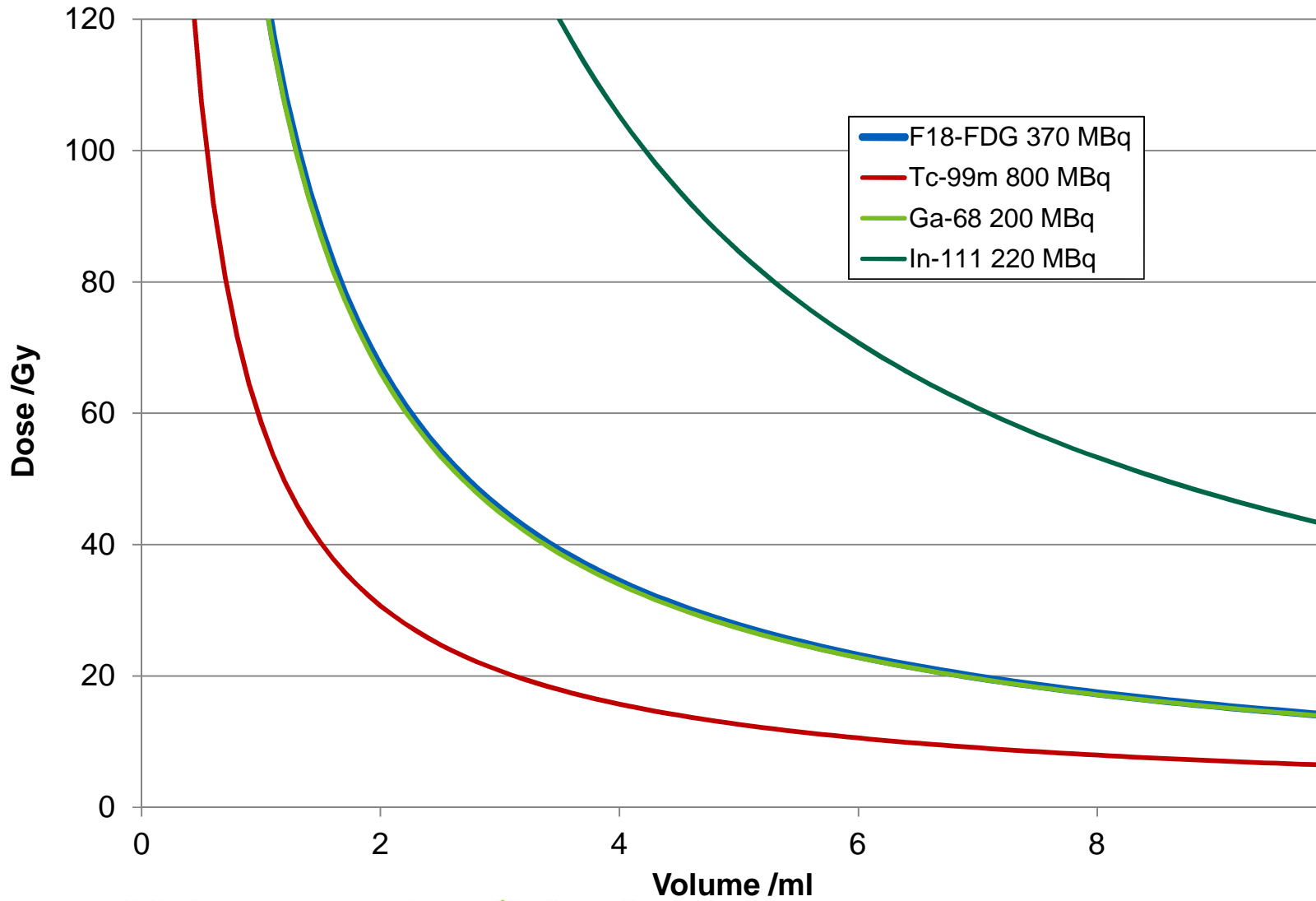
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### Dose Volume relationship for fixed totally tissue administration





### Dose Volume relationship for fixed totally tissue administration



# possibilities: 370 MBq $^{18}\text{F}$ -FDG



~7.6 mGy  
whole body dose

~70 cm<sup>3</sup>  
transient  
erythema



~9-14 cm<sup>3</sup>  
prolonged  
erythema,  
dermal atrophy



~5 cm<sup>3</sup> 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

~20 Gy

2 months

5 months

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

# Tissuing a diagnostic injection

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

# Going forward

- Local database of issued 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 issued injections
  - Possibly similar to protocol in IR

**End**

So far...





# Strategies following tissue 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



# Tissuing Cases: Diagnostic

# Tissuing Cases: Diagnostic

# Dose reaction lessons from IR

<~5 Gy

~10 Gy

~10+ Gy

~20 Gy

2 months

5 months

- 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.