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An Elective in Clinical Radiopharmacy

NUCLEAR MEDICINE
GUY'S AND ST THOMAS' NHS FOUNDATION TRUST
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Content

- My background
- Why I choose a radiopharmacy elective
- How I organised the placement
- What the placement consisted of
- THP-PSMA mini project
- What I gained from the elective

My Background

- BSc Medicinal and Biological Chemistry (with industrial experience)
- Year industrial placement at GSK, Worthing as a Process Microbiologist

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Why I chose Radiopharmacy

- Previous placement in sterile pharmaceutical manufacturing
- Previous experience with MHRA and FDA audit process
- Completed pharmacology module at university

- Interest in the production of radiopharmaceuticals
- Links to biochemistry
- Experience the clinical aspect of radiopharmacy

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How I organised the placement

- Contacted the trainee representative for Clinical Pharmaceutical Sciences (found on www.nshcs.hee.nhs.uk).
- Referred to the Clinical Scientist (Scott Edmonds) at Guy's Hospital, who had previously completed the STP.
- Scott organised an elective which would give me an overview of the Radiopharmacy department, which would include the QA, production, QC and patient experience of Radiopharmacy.
- Scott also organised a project for me.

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Any funding required?

- No!
- Fortunate to have a Clinical Scientist organise my elective who had completed the STP.
- Tried to be as flexible as possible, to fit around their working schedule.
- Stayed local.

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What the placement consisted of

- Early starts!

- GMP for radiopharmaceutical products
- Radioisotope production of ^{99}Tc-m and ^{68}Ga
- ^{68}Ga-PSMA QC project

Particles

	Maximum permitted number of particles per m^3 equal to or greater than the tabulated size			
	At rest		In operation	
Grade	**0.5 µm**	**5.0µm**	**0.5 µm**	**5.0µm**
A	3 520	20	3 520	20
B	3 520	29	352 000	2 900
C	352 000	2 900	3 520 000	29 000
D	3 520 000	29 000	Not defined	Not defined

Microbes/ cfu

	Recommended limits for microbial contamination (a)			
Grade	air sample cfu/m^3	settle plates (diameter 90 mm) cfu/4 hours (b)	contact plates (diameter 55 mm) cfu/plate	glove print 5 fingers cfu/glove
A	< 1	< 1	< 1	< 1
B	10	5	5	5
C	100	50	25	-
D	200	100	50	-

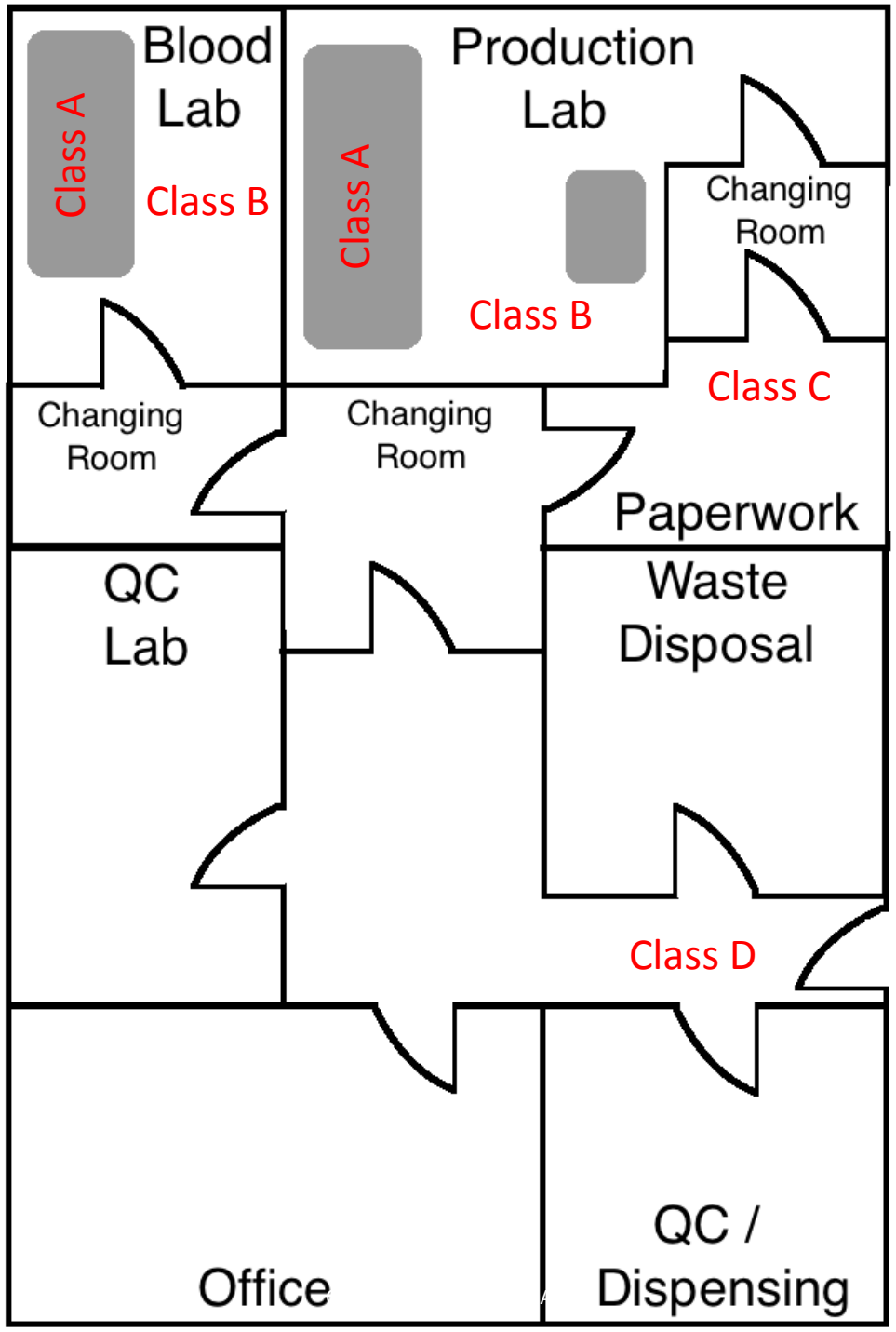
Microbial / particle monitoring

Isolators

LAF

Aseptic techniques

Strict cleaning routine



Equipment validation

Strict radiation policy

Staff monitoring

Product monitoring

Clear gowning procedure

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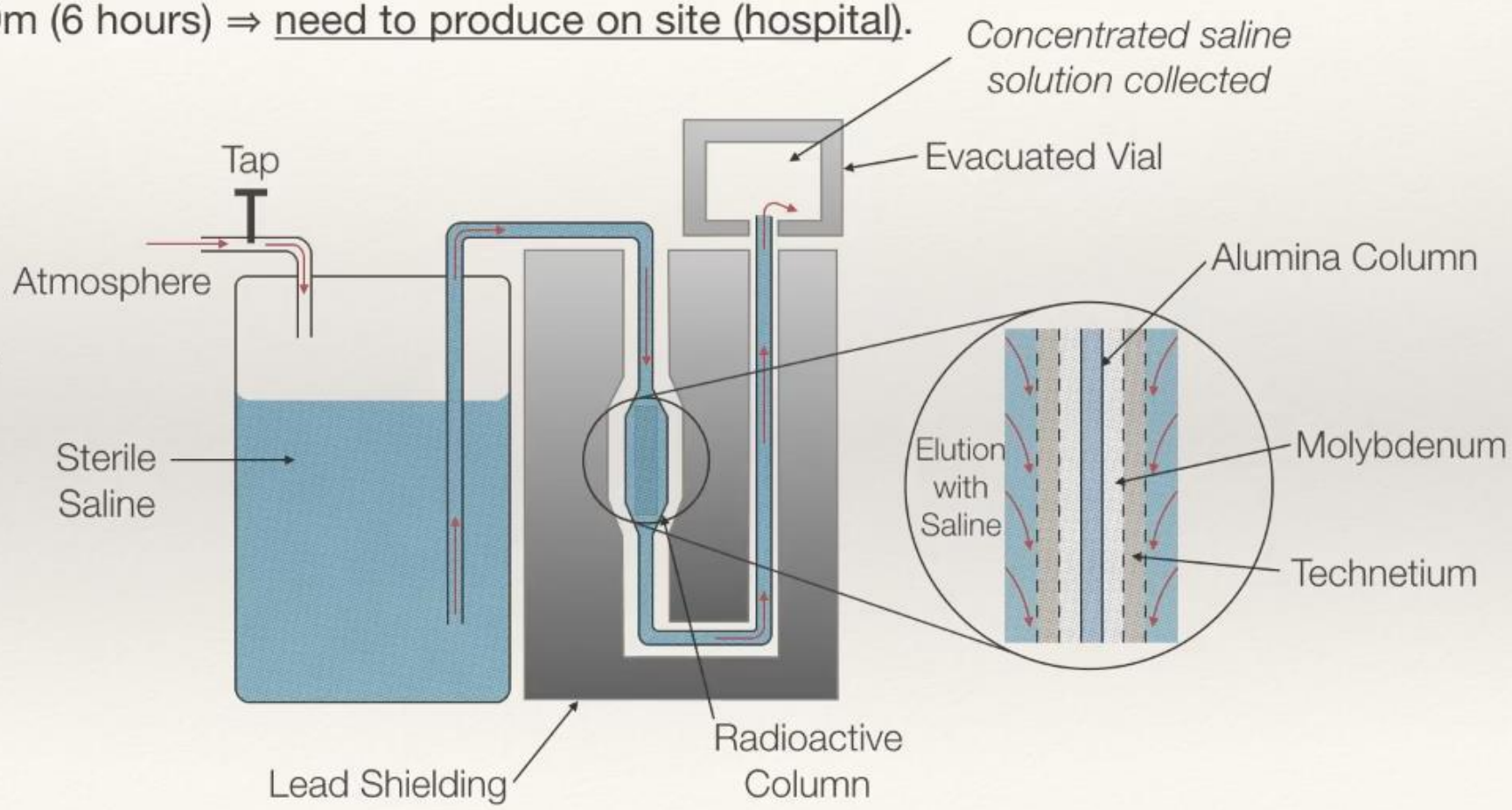
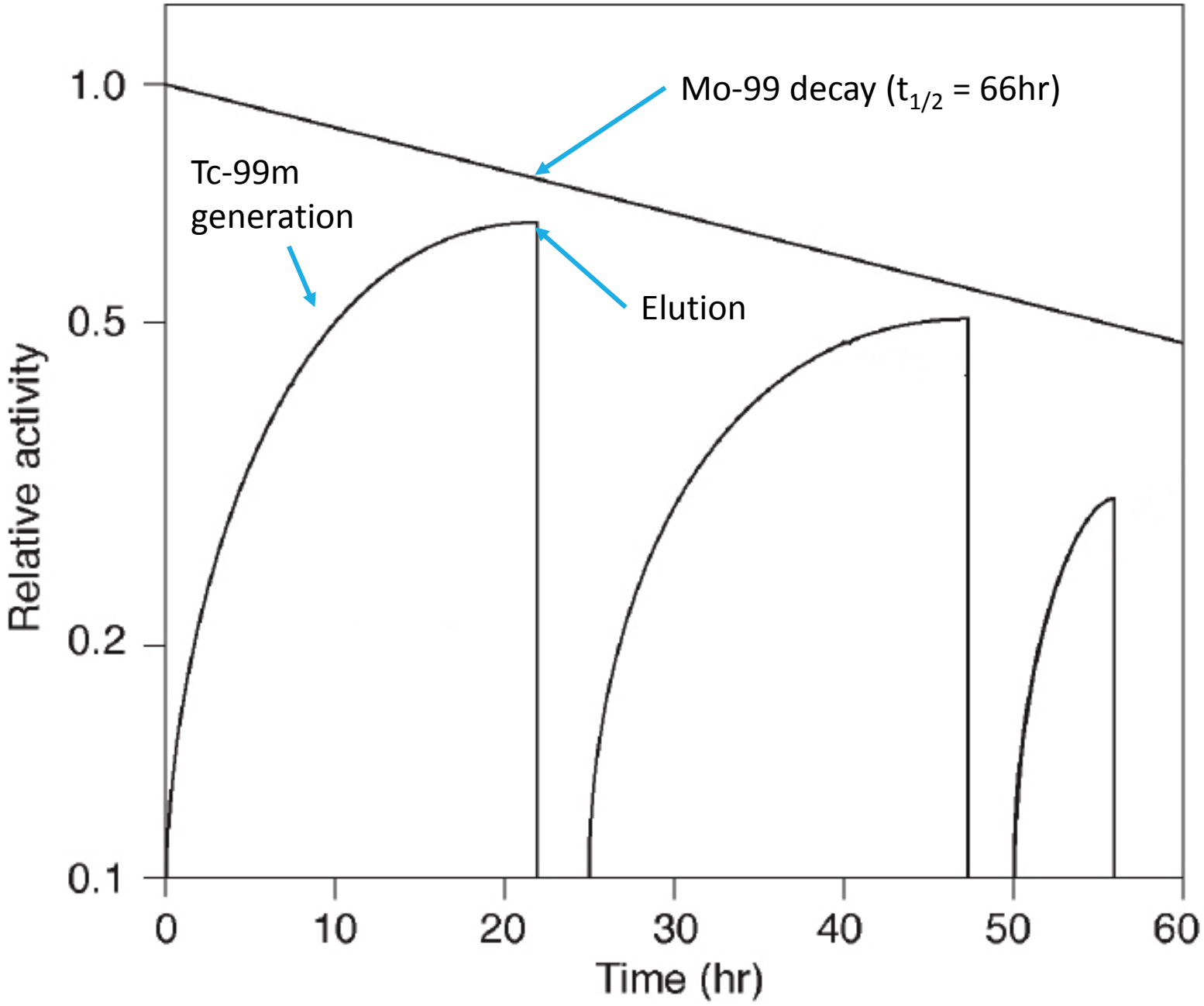
Technetium-99m Generator

- Short half life of Tc-99m (6 hours) ⇒ need to produce on site (hospital).
- Lead shields operators from gamma (Tc) and beta$^-$ (Mo).
- Vial is evacuated; atmospheric pressure will force saline through generator.



https://youtu.be/uLNazQthGkc


Mo-99 decay ($t_{1/2}$ = 66hr)
Tc-99m
generation
Elution
Relative activity
1.0
0.5
0.2
0.1
0
10
20
30
40
50
60
Time (hr)

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^{68}Ga-PSMA QC project

- Prostate cancer is the second most common cancer and major cause of morbidity and mortality.
- Radiopharmaceuticals have assisted with staging and investigation of metastasis.
- However previous imaging methods associated with poor sensitivity.

- New kit chelates ^{68}Ga using THP, which is linked to prostate specific membrane antigen (PSMA).
- Improved sensitivity and specificity.
- Easy to make.

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^{68}Ga-PSMA QC project

- Project aim: to determine a QC protocol and the stability of THP-PSMA kit.
  - Determine appropriate iTLC method (iTLC required as quick and easy).
  - Confirm manufacturers stability claims.
  - Confirm product compliant with EU endotoxin concentrations.
  - Confirm product at safe pH for IV administration, for up to 4-hours after manufacture.

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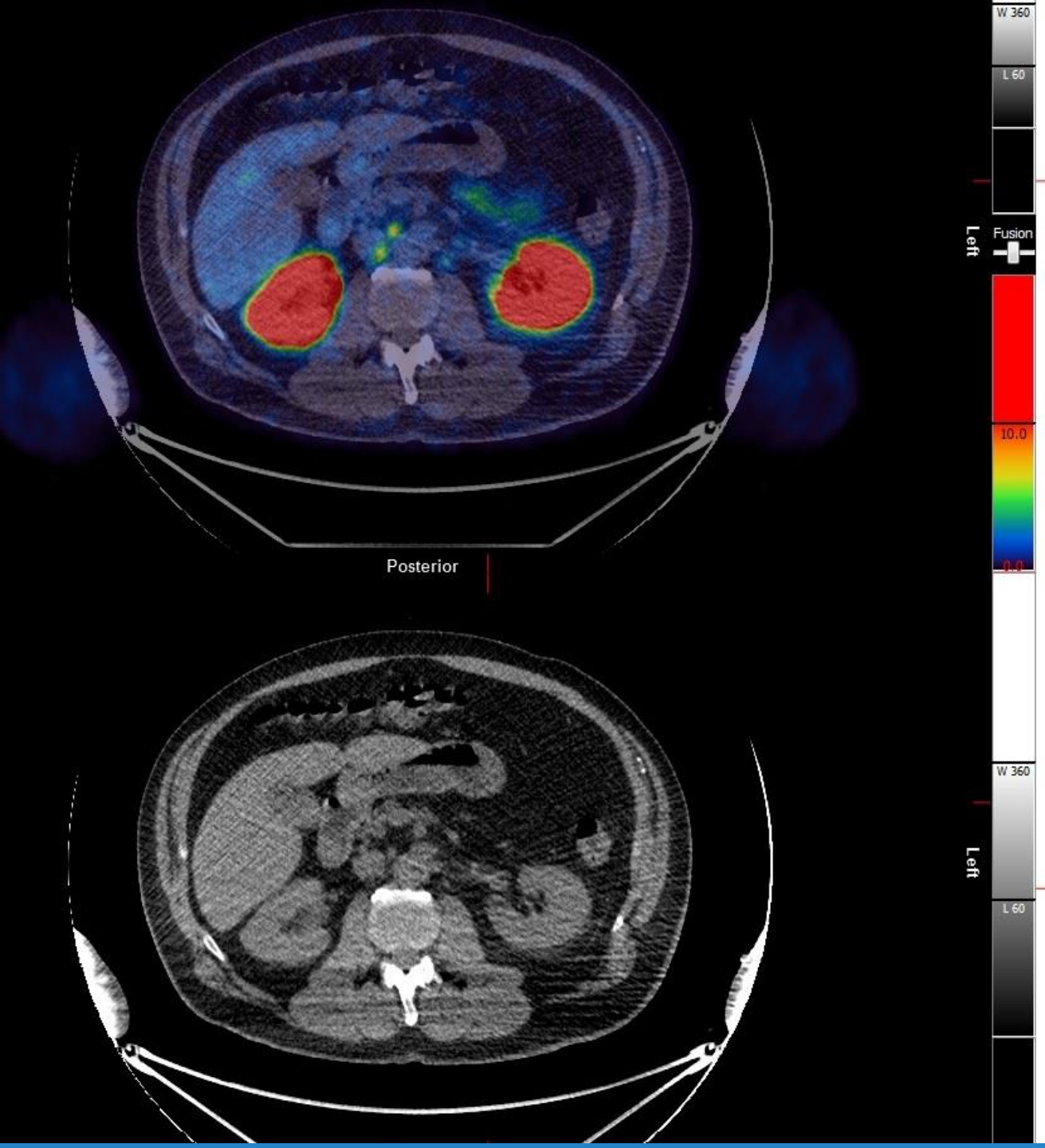
^{68}Ga-PSMA QC project

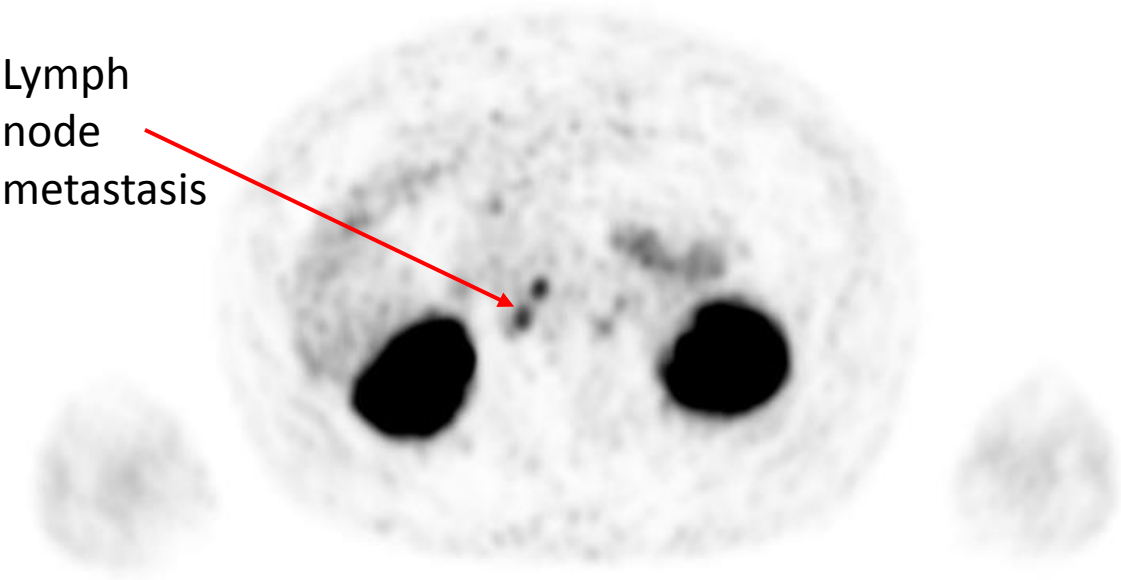
- Results:
  - Product endotoxin concentrations <87.5 EU/dose (lower than 175 EU/dose recommendations).
  - pH ~6.

  - Citrate buffer separated free ^{68}Ga from ^{68}Ga-colloid and ^{68}Ga-THP-PSMA.
  - Ammonium acetate:methanol (30:70 v/v) separated ^{68}Ga-colloid from free and ^{68}Ga-THP-PSMA.
  - iTLC using these reagents allowed quick QC check of the sample.

  - Showed the product was stable for minimum of 3-hours. Required HPLC to confirm longer than this.



Lymph node metastasis



Prostate

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What I gained from the elective

- An overview of the radiopharmaceutical production process.
- The strict regulations that accompany production (GMP, aseptic techniques, GLP, etc.).
- Gained an insight in the use of radioisotopes for diagnosing and monitoring disease.
- The difficulties of working in a Grade B zone and organising the production of various hospitals' radiopharmaceuticals.

- Networked, met some great people and had FUN!

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Thanks!

- Thanks to Scott Edmonds and Victoria Gibson for arranging my elective and supporting me through the six weeks.

- Please contact Scott.Edmonds@gstt.nhs.uk if you wish to enquire regarding an elective.

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^{68}Ga-PSMA QC project

Method	Ga-68 added direct to kit vial	Additional reagents added to kit vial	Labelling pH	Heat	Purification	Time to final product (min)
Conventional semi-automated synthesis	NO	YES	4.0 to 5.0	YES	YES	45 to 60
Conventional two-step kit	YES/NO	YES	4.0 to 5.0	YES	NO	20 to 30
Galli™ one-step kit	YES	NO	3 to 7.5	NO	NO	1 to 5

Kit/Trade Name	Description
DMSA / Renocis	Static renal imaging
DTPA / Technescan DTPA	Renal imaging. Aerosol form can be used for lung ventilation too.
HIDA (Mebrofenin) / Choledíam	Hepatobilliary
HM-PAO (Exametazime)	White blood cell labelling.
Sulesomab / Leukoscan	Inflammation imaging
MAA (Macroaggregated albumin) /LyoMAA	Lung perfusion
MAG3 (Tiatide)	Dynamic renal imaging.
MDP (Medronate) / Daximage	Bone imaging.
MIBI / Sestamibi	Cardiac or parathyroid imaging.
Rhenium Sulphide / Nanocis	Lymphoscint
Nanocolloid (Human albumin colloid) / Nanocoll	Lymph bone marrow.
TFM (Tetrofosmin) / Myoview	Cardiac imaging.
Tin Colloid / Hepatate	Lacrimal liver/spleen imaging, as well as GI bleeds.
TcO_4 / Pertechenetate	MUGA, Mechels, salivary, thyroid, GI bleed lacrimal.