



NUCLEARFUTURES
Bangor

MEDICAL RADIOISOTOPES IN NORTH WALES – ARTHUR & BANGOR UNIVERSITY

Physics Innovation in the Utilisation of Radio Nuclides:
addressing the UK Challenge
25/07/2024

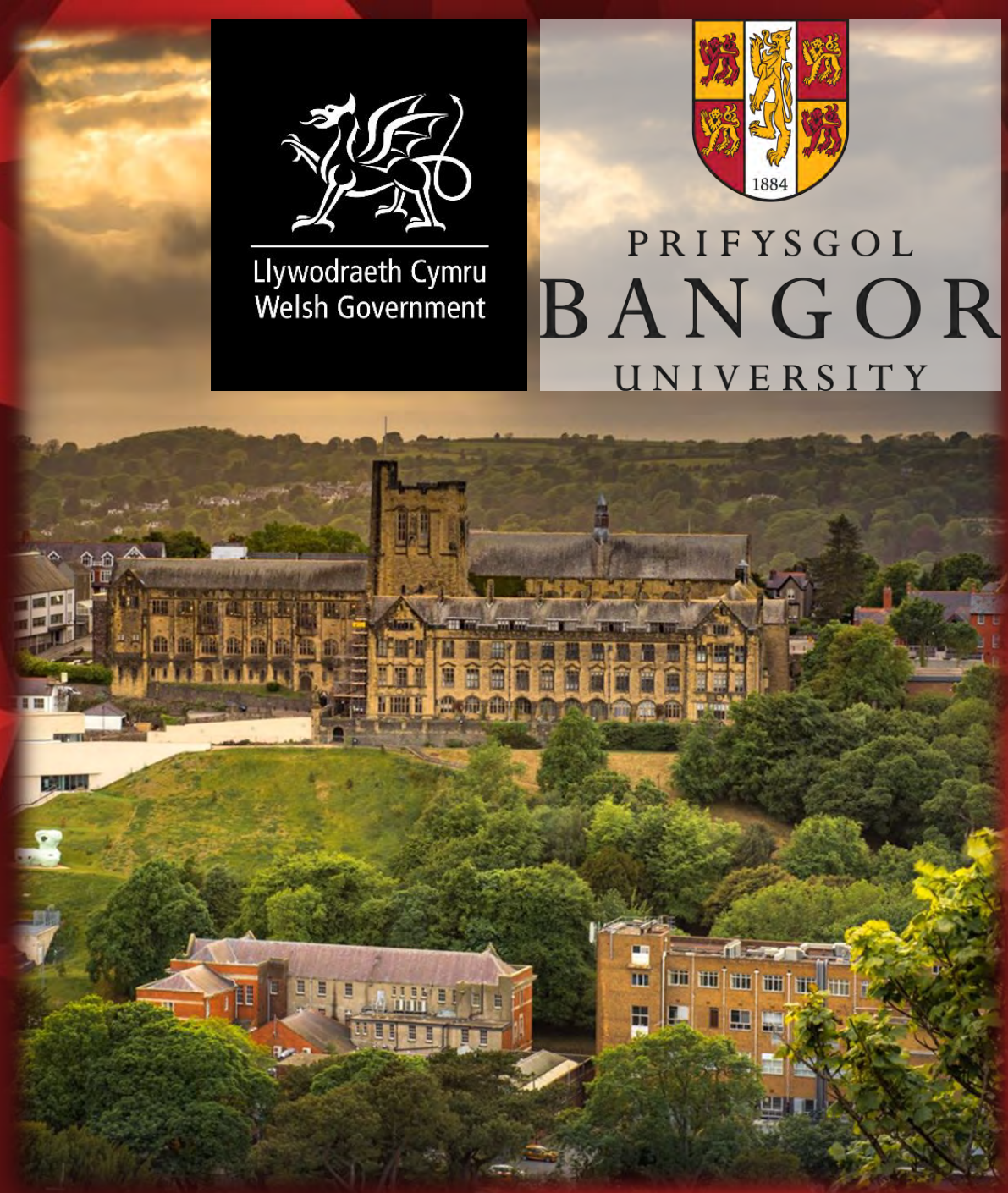
Dr. Luci Gleeson, Prof. Simon Middleburgh, & Dr. Mark D. Ogden



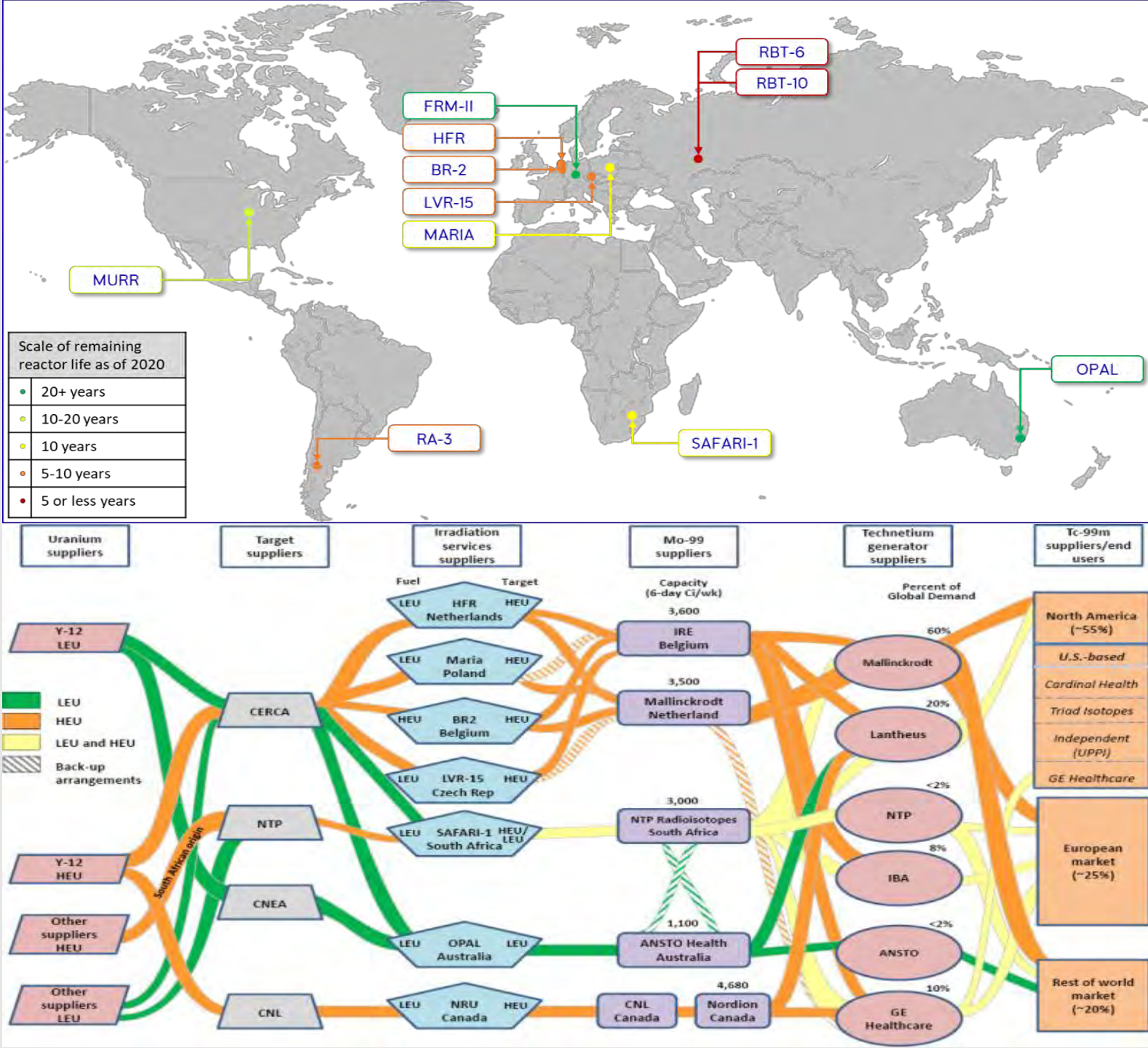
Llywodraeth Cymru
Welsh Government



PRIFYSGOL
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UNIVERSITY



^{99m}Tc is the most commonly used imaging radioisotope in the UK and the most widely used radioisotope for nuclear medicine procedures worldwide (being used in about 80% of all nuclear medicine diagnostics)



BNMS

Global Shortage in Molybdenum availability – BNMS Guidance

updated 4.11.2022

With thanks to Ms Jilly Croasdale, City Hospital, Birmingham, Prof Richard Graham, Royal United Hospital Bath, Prof Sobhan Vinjamuri, Royal Liverpool University Hospital, Dr Stewart Redman, Royal United Hospital Bath, Ms Bev Ellis, Manchester University NHS Foundation Trust and Mr Charnie Kalirai, Nottingham University Hospitals Trust

Background:
We have been notified of a global shortage in Molybdenum availability starting from 4th November, primarily caused by a problem restarting the BR2 reactor in Belgium but exacerbated by required maintenance shutdowns and refuelling at other sites. This issue affects both GE and Curium from this Friday onwards. For the week beginning 7th November, generators will either be cancelled or if sent, at significantly lower activity. This is likely to be the case for the week beginning 14th November as well. There is a provisional date for resolution by 21st November, but this is not yet confirmed.

Impact:

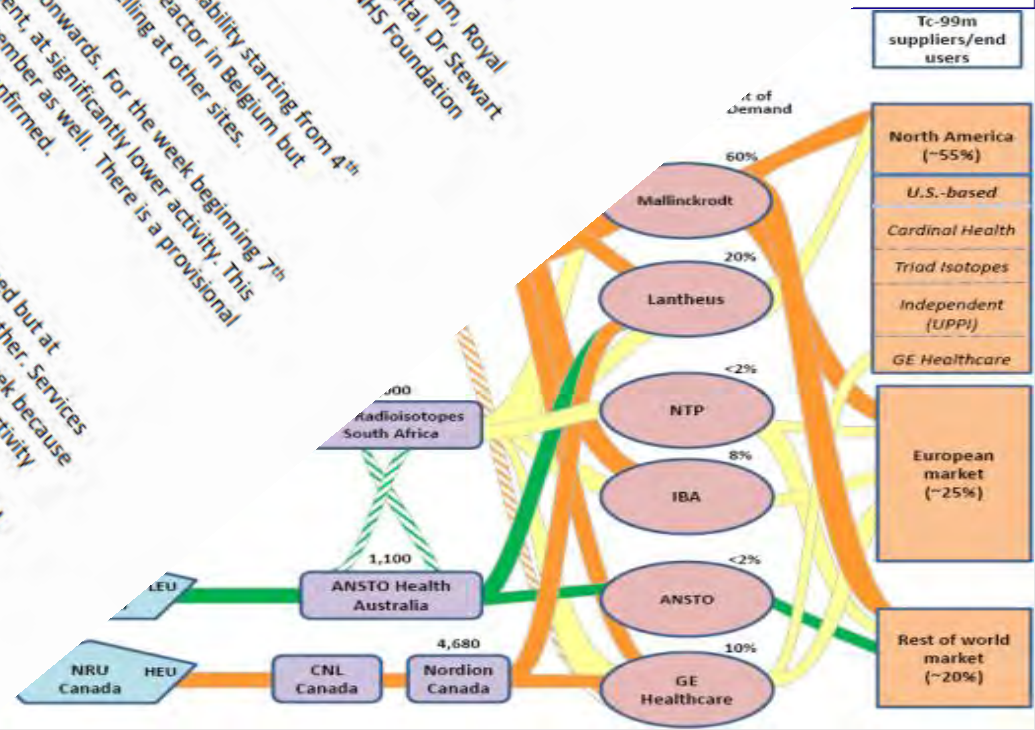
- Week Commencing 7th November: Some generators may be shipped but at significantly lower than usual activities. Many will be cancelled altogether. Services may be able to operate more or less as normal in the early part of the week because of residual capacity in older generators. However, as the week progresses, activity levels will be significantly down
- Week commencing 14th November: **Generators production will be severely limited, which will mean generator deliveries will be cancelled altogether or generator size reduced. Capacity will be significantly reduced.**
- Week commencing 21st November: The situation remains uncertain, as generator suppliers will not know until 14th November whether the BR2 reactor will be operational.

There will then be 2 scenarios:

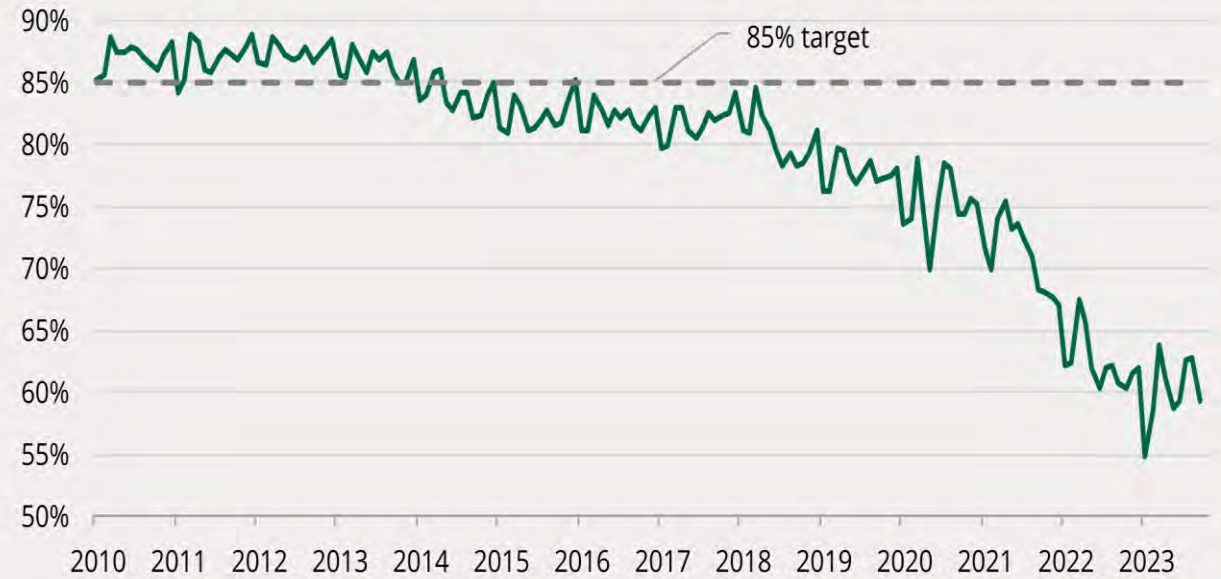
- BR2 Reactor restarts and Generators will be produced and shipped
- BR2 reactor does not restart. Other reactors will be used but may not be immediately available and capacity may be lower than usual.

This situation will impact on many of our patients, some of whom will be on the 2 Week Wait pathway. It is important that this situation is escalated up to senior NHS Trust management as a matter of priority.

There is also a possible impact on I-131 availability, although we have been informed that 131 sodium iodide capsules for treatment of hyperthyroidism are not present



^{99m}Tc is the most common radioisotope in the UK and is used for a wide range of nuclear medicine procedures worldwide (being used in 80% of all nuclear medicine diagnostic procedures).

[illegible]



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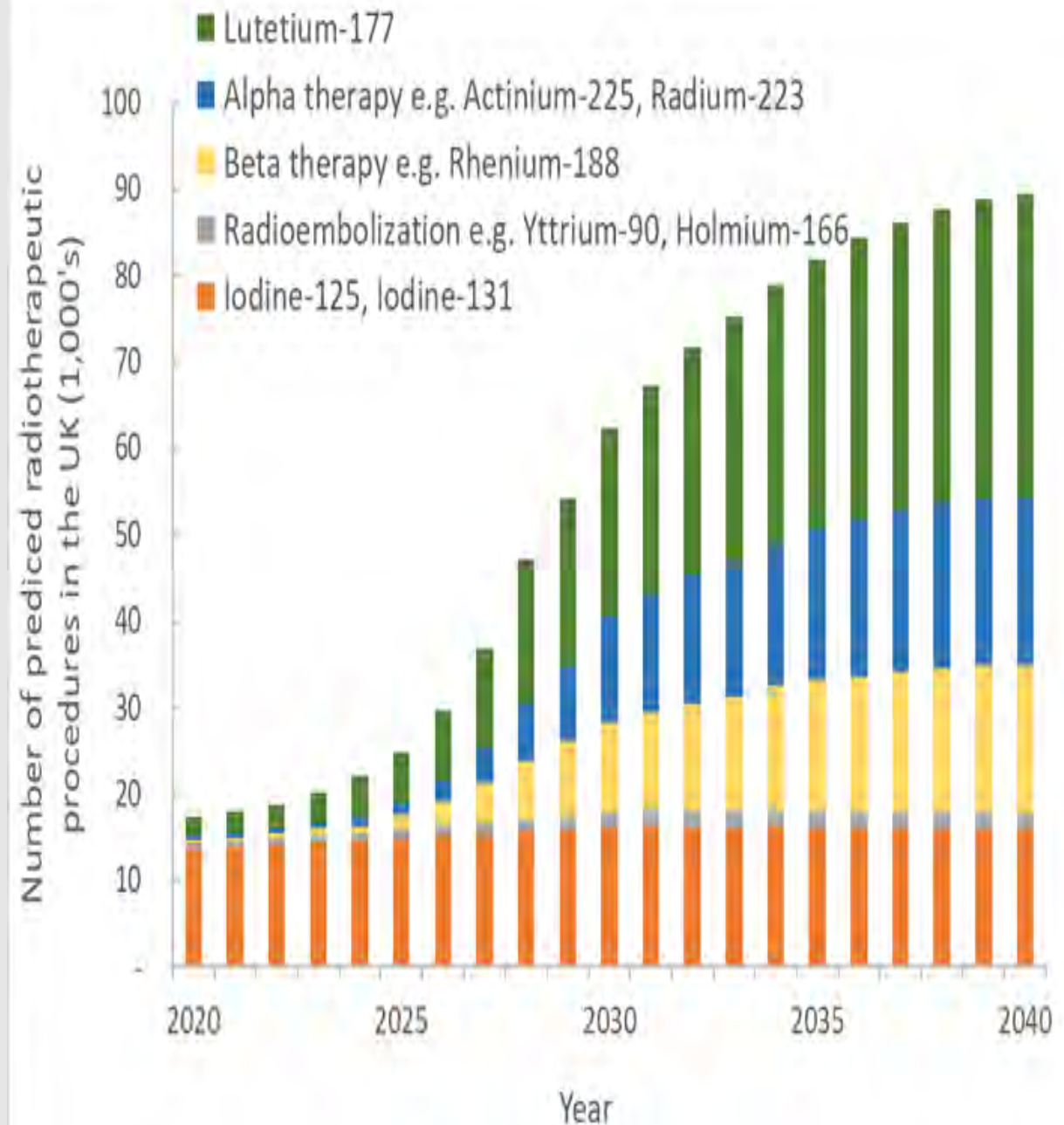
NIHR | Innovation
Observatory



Horizon Scanning Report: Horizon scan and landscape analysis of innovations in therapeutic radioligand technologies

Authors: Sarah Khan, Anjum Jahan, Sonia Garcia Gonzalez Moral, Andrew Mkwashi

Date: February 2024



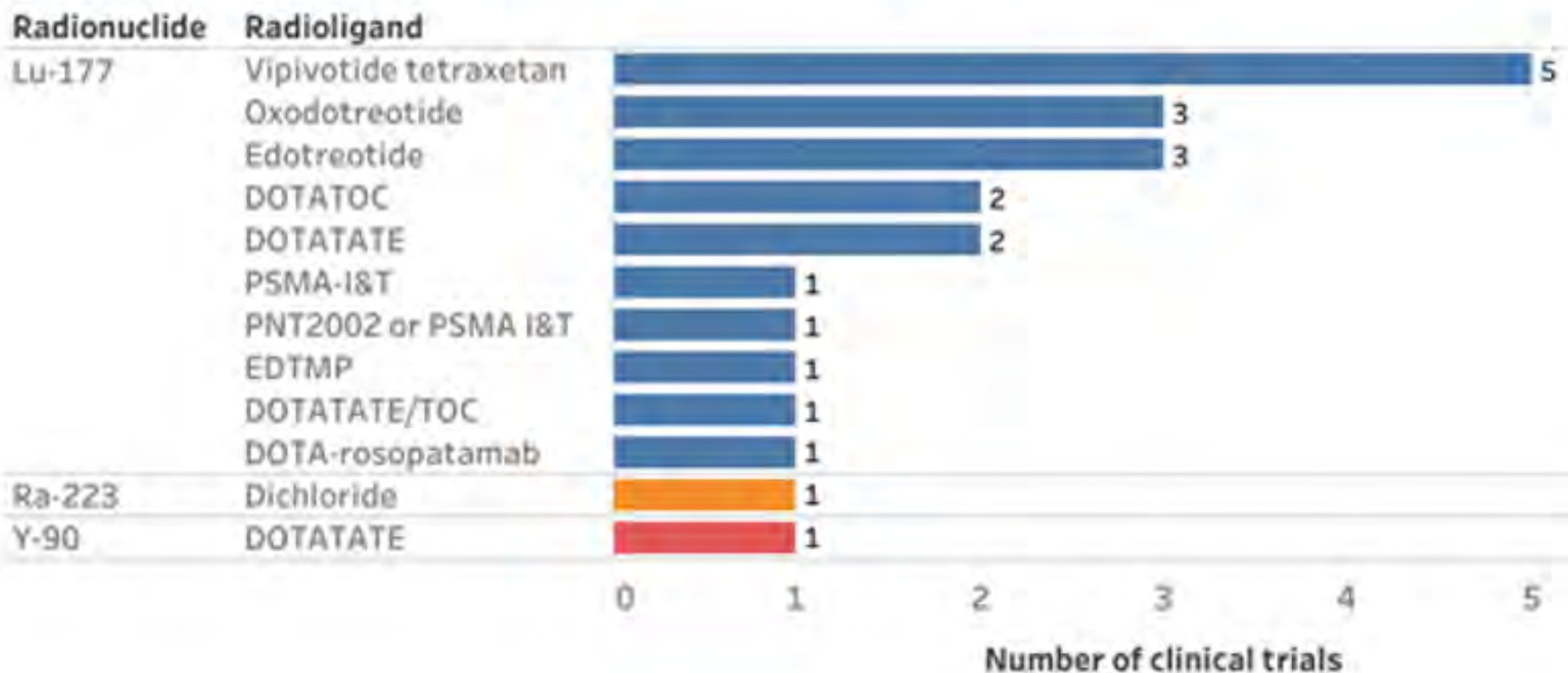
Horizon Scanning Report: analysis of innovations in technologies

Authors: Sarah Khan, Anjum Jahan, Sonia Garcia

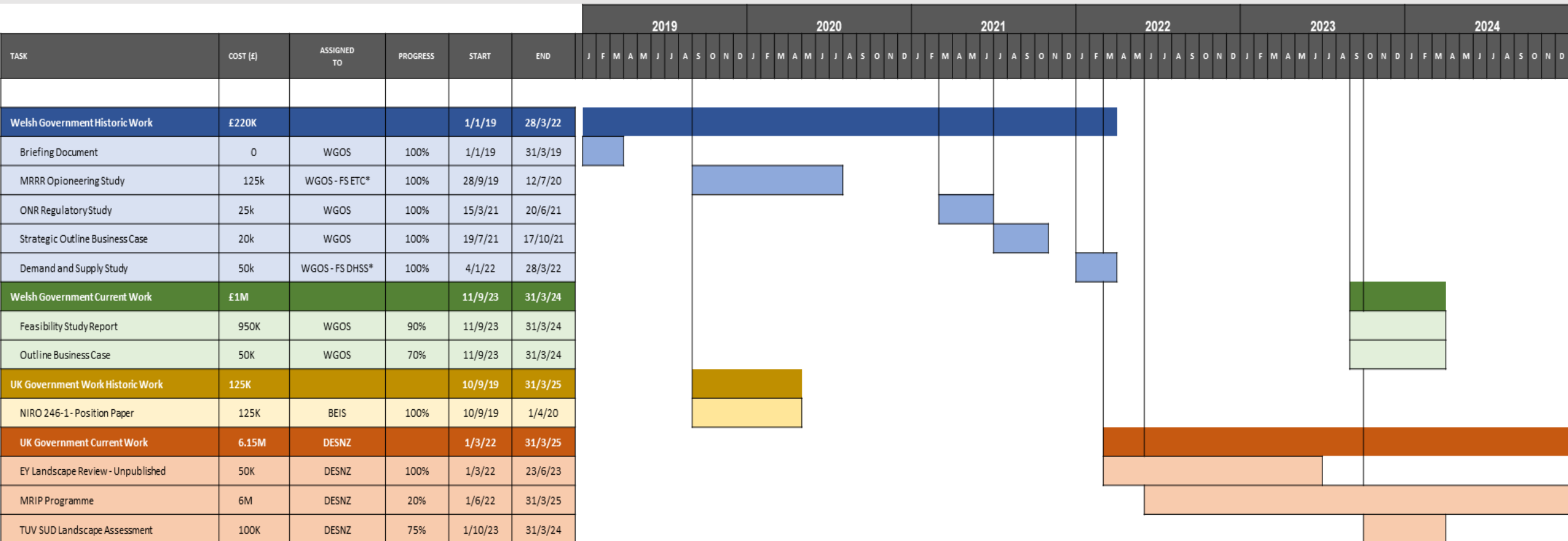
Date: February 2024

■ Lutetium-177
■ Alpha therapy e.g. Actinium-225, Radium-223

Volume of ongoing trial activity for therapeutic radioligands



Our scan shows that while there is substantial interest in therapeutic radioligand technologies, there is limited ongoing late-stage clinical development. Additionally, this is limited to a few therapeutic radioligand technologies radiolabelled with Lu177, Ra223, and Y90, mainly for prostate cancer and NETs.



*FS ETC – Funding Source Economy Treasury and Constitution

*FS DHSS – Funding Source Department of Health and Social Services



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BRIEFING NOTE: MEDICAL RADIOISOTOPES AND RESEARCH REACTOR

TRAWSFYNYDD SITE



WELSH GOVERNMENT OFFICE FOR SCIENCE

MARCH 2019 – Draft Version 6

CONFIDENTIAL

GRESS	START	END
	1/1/19	28/3/22
0%	1/1/19	31/3/19



MEDICAL RADIOISOTOPE RESEARCH REACTOR OPTIONEERING STUDY WELSH GOVERNMENT OFFICE OF SCIENCE

Date: JULY 2020
Your Reference: C246/2019/2020
Our Reference: EDN5970857910
Material Description: MRRR OPTIONEERING STUDY FINAL REPORT

OFFICIAL SENSITIVE
COMMERCIAL SENSITIVE – WELSH GOVERNMENT
DATA NOT RATED FOR EXPORT CONTROL

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A Study into the Regulation of a Medical Isotope Production Facility on or near the Trawsfynydd Nuclear Licensed Site

Professor Laurence G Williams OBE FREng

Professor Lynda M Warren OBE FLSW

Reviewed by David Smeathan for the Welsh Govern

Bangor 10 Jun

2021															20
J	J	A	S	O	N	D	J	F	M	A	M	J			



Medical Radionuclide Demand and Supply Over the Next 20 Years

Executive Summary

A study into the impact on the UK of the future changes in the supply and demand of medical radionuclides produced nuclear reactors

Professor Laurence G Williams OBE FREng

Dr Lee J. Evtits

Bangor 14 April 2022

ARTHUR

(Advanced Radioisotope Technology for Heath Utility Reactor)

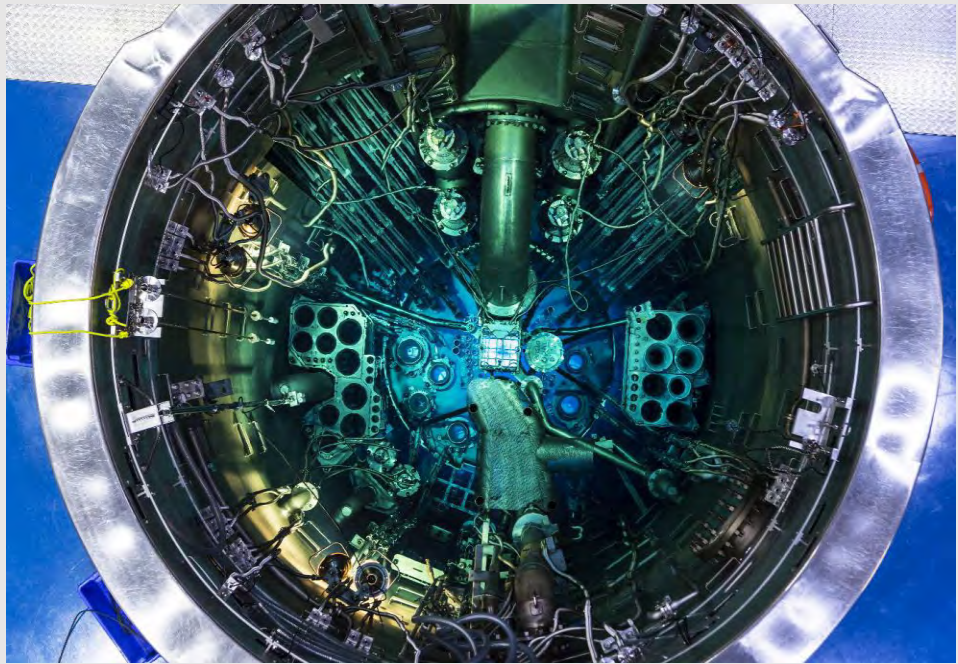
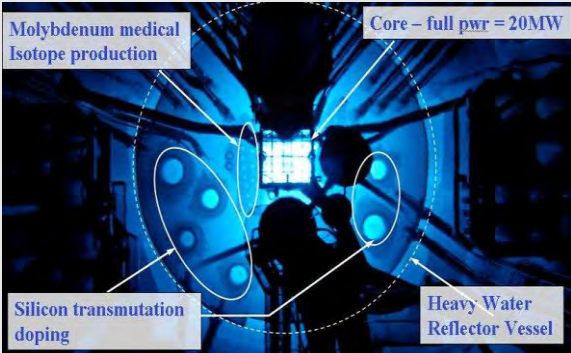
The Strategic Case

*FS ETC – Funding

*FS DHSS – Funding

Constitution
and Social Services





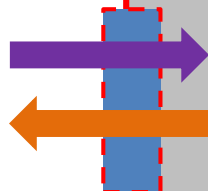
Technology Family	Description	Example	Total Score	Notes
A	Fuel plate type assemblies	OPAL (20MWth)	32	
B	Very compact high flux reactor	FRM-II (20MWth)	23	Discounted due to reliance on HEU fuels
C	Concentric fuel elements in the assembly – conventional design for irradiation channels	LVR-15 (10MWth)	26	Discounted due to complexity of fuel
D	Concentric fuel elements in the assembly – complex design of irradiation channels	BR2 (100MWth)	24	Discounted due to reliance on HEU fuels
E	Concentric fuel elements in the assembly – advance design	JHR (100MWth)	13	Discounted due to reliance on HEU fuels
F	Fuel Rod Assemblies	HANARO (30MWth)	26	Discounted due to safety concerns





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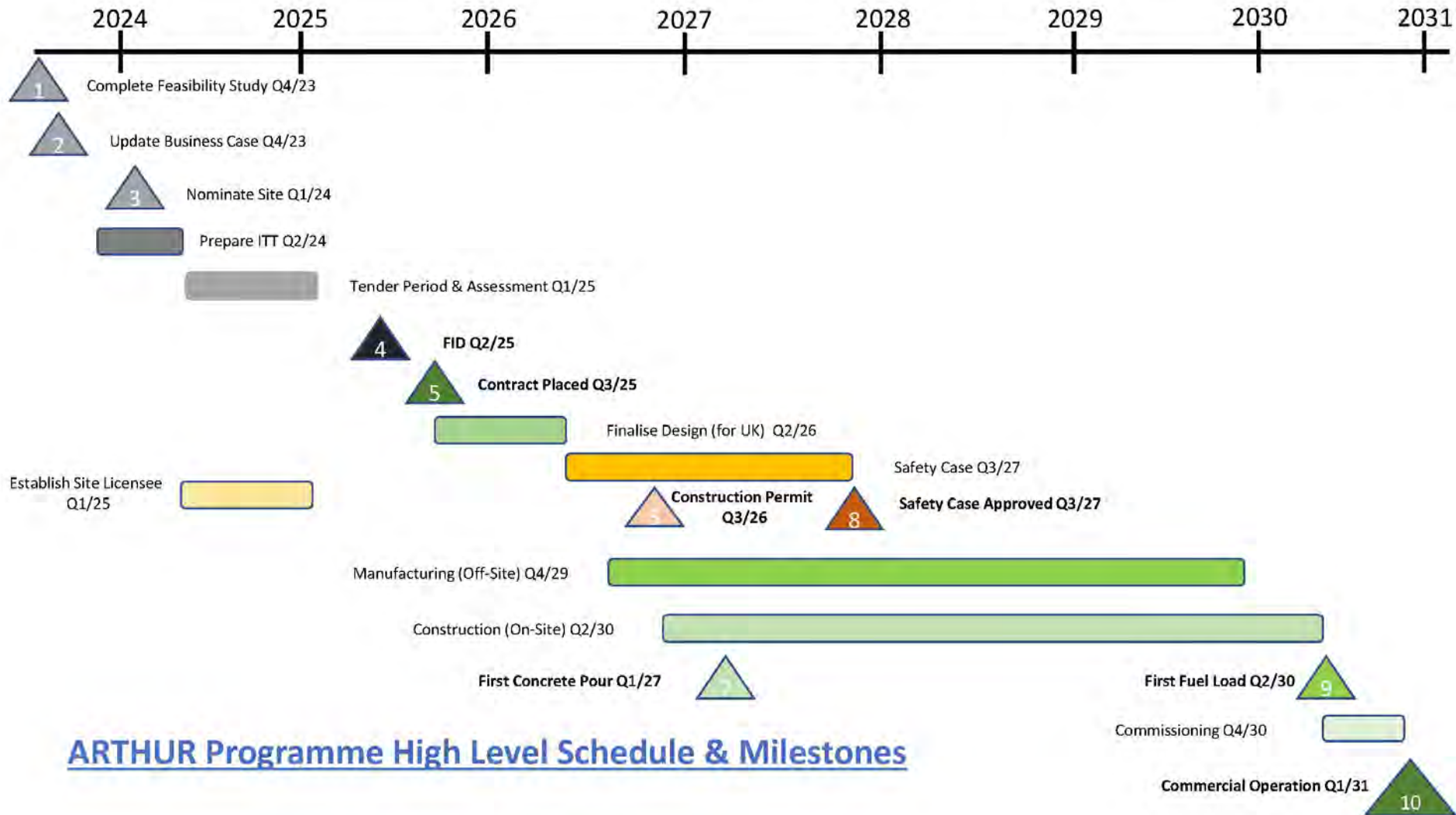




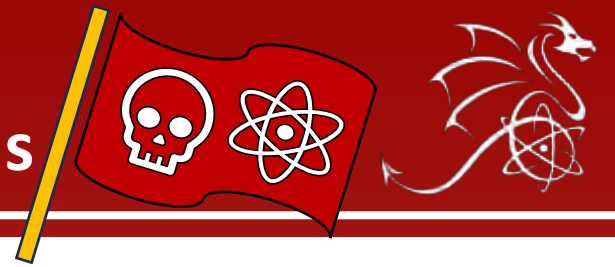
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Bangor University Centre for Cancer Abatement through Nuclear and Exploration of Emerging Radiopharmaceuticals



EQUIPMENT TO BUILD
BUCANEER



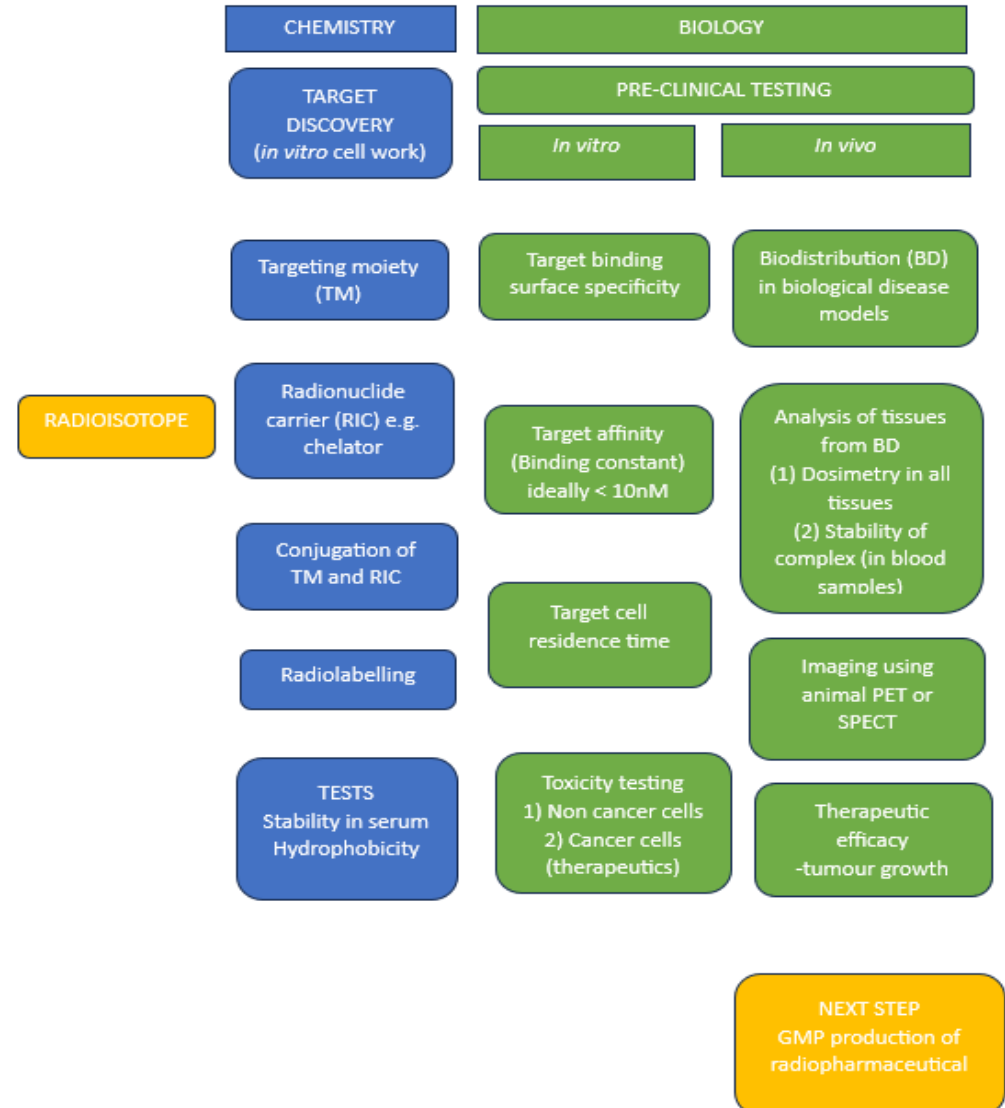
RESEARCH USING
BUCANEER



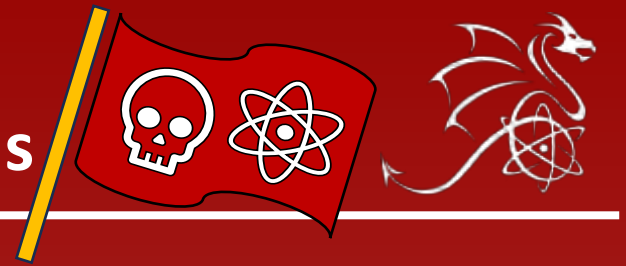
TEACHING IN BUCANEER



- ***BUCANEER***



Bangor University Centre for Cancer Abatement through Nuclear and Exploration of Emerging Radiopharmaceuticals



EQUIPMENT TO BUILD
BUCANEER



RESEARCH USING
BUCANEER



TEACHING IN BUCANEER



Supporting
ARTHUR

- *BUCANEER*

Target manufacture

- Avoiding parasitic absorption
- Optimizing radionuclide production
- Proliferation resistant

Target irradiation

- Reactor
- Cyclotron
- Generator
- Optimizing radionuclide production

Radiopharmaceutical manufacture

- Combined with a drug
- High purity
- Consistent quality
- Scale up of production

Isotope purification

- Removal of co-contaminants
- Concentration of isotope
- Sustainable & cheap
- Proliferation resistant

Target dissolution

- Benign conditions
- Sustainable
- Reduced co-contaminant

Radiopharmaceutical shipping

- Containment
- Safety
- Reduce losses in isotope
- Consistent quality

Radiopharmaceutical preparation

- Controlled dose
- Mixing with other drugs
- Optimized lifetime
- Easy administration to patient



Diagnostic and
radiotherapy
treatment



Nuclear medicine: medical specialty that uses radioactive tracers (radiopharmaceuticals) to assess bodily functions and to diagnose and treat disease

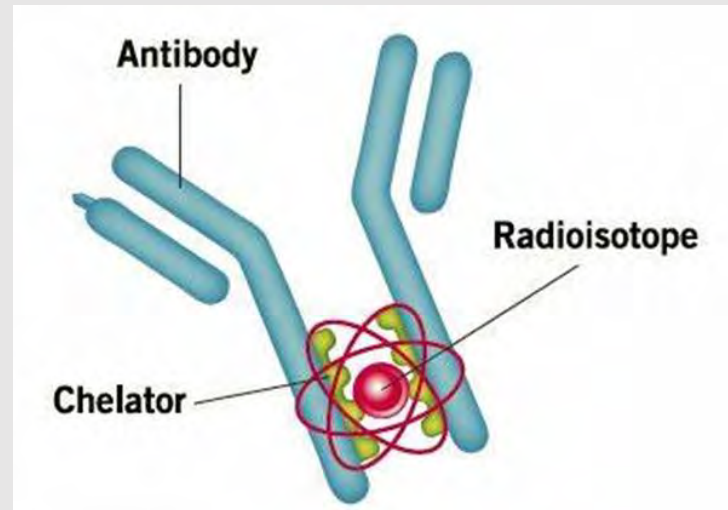
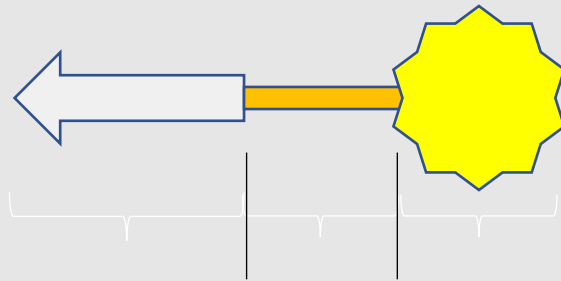
Nuclear medicine imaging: detection of radiation introduced into the body and accumulated in regions of interest often using targeting molecules to which radionuclides are attached

Nuclear medicine therapy: administration of radionuclides/targeted radionuclides to destroy tumour or normal tissue

Radionuclide categories used in nuclear medicine

Emission	Range	LET	Examples (range in tissue)	Use
γ /positron			^{89}Zr , $^{203}\text{Pb}^*$	Imaging
β	Up to 10 mm	low	^{177}Lu (1mm), ^{198}Au , ^{90}Y (10mm)	MRT
α	Up to 100 μm	high	$^{212}\text{Pb}^*$, ^{223}Ra	MRT
Auger electrons	Up to 5 μm	high	^{125}I , ^{89}Zr , ^{111}In	MRT

*theragnostic pair



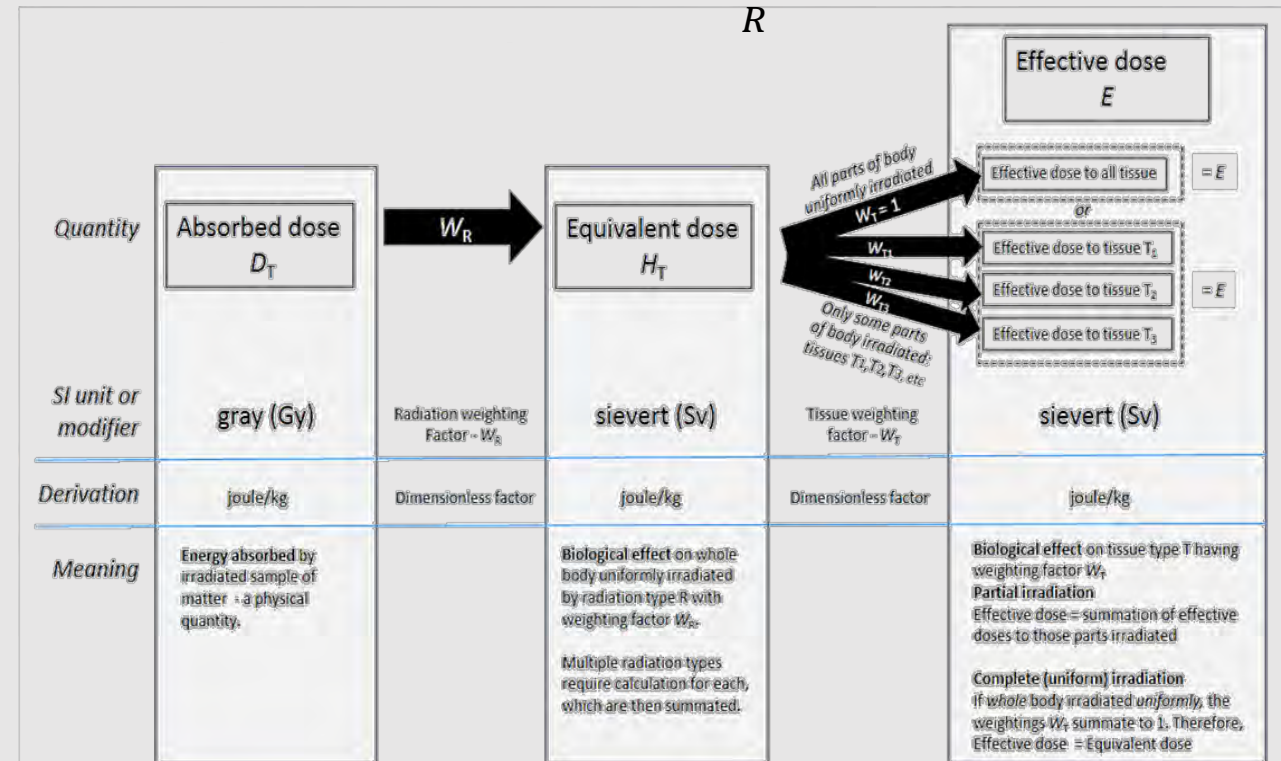
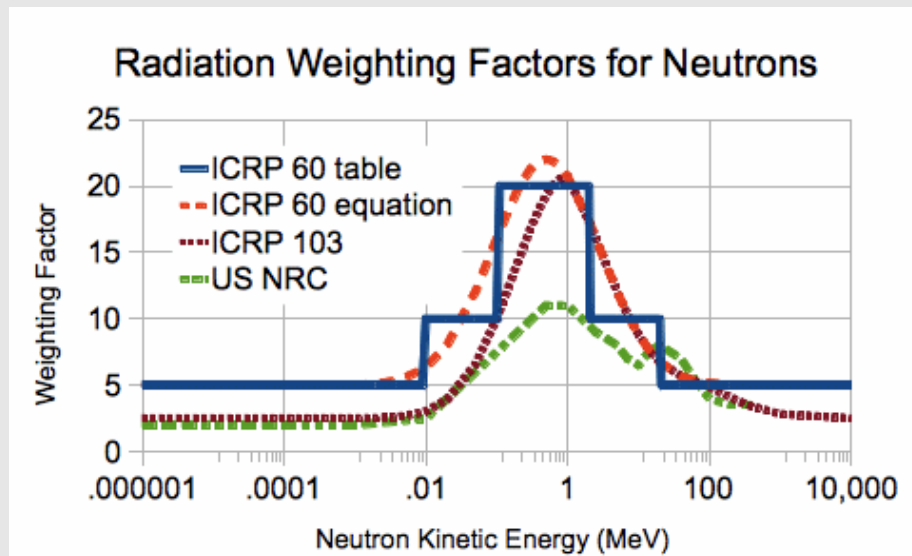
Advantages

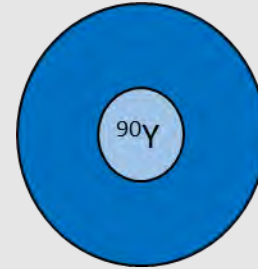
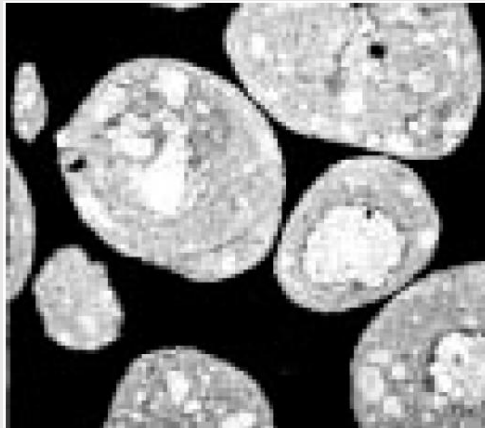
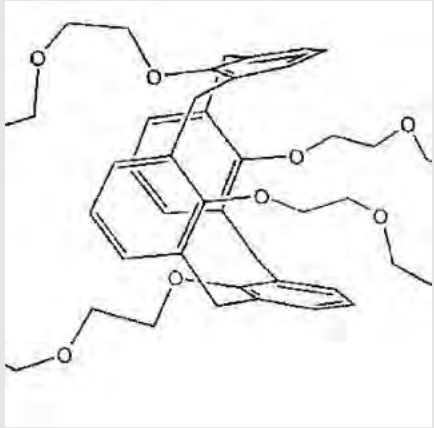
- 1) Systemic – treats primary and metastasis
- 2) Low normal tissue dose (c.f. EBRT)
- 3) Easy to administer

Emission	Range	LET	Examples (range in tissue)	Use
β	Up to 10 mm	low	^{177}Lu (1mm), ^{198}Au , ^{90}Y (10mm)	MRT
α	Up to 100 μm	high	$^{212}\text{Pb}^*$, ^{223}Ra	MRT

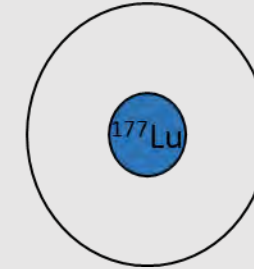


$$H_T = \sum_R W_R \times D_{T,R}$$

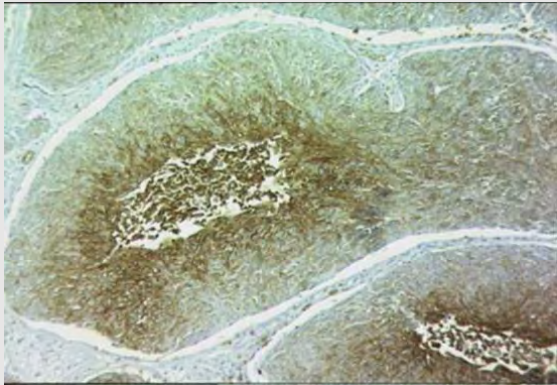




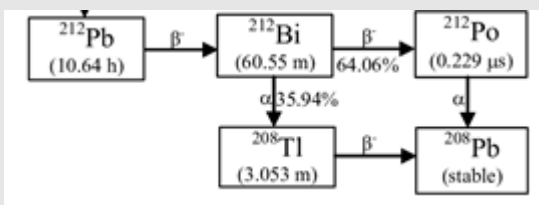
^{90}Y - high energy beta
- most dose
deposited mm from atom



^{177}Lu – low energy beta
emission – most dose
deposited within 1mm

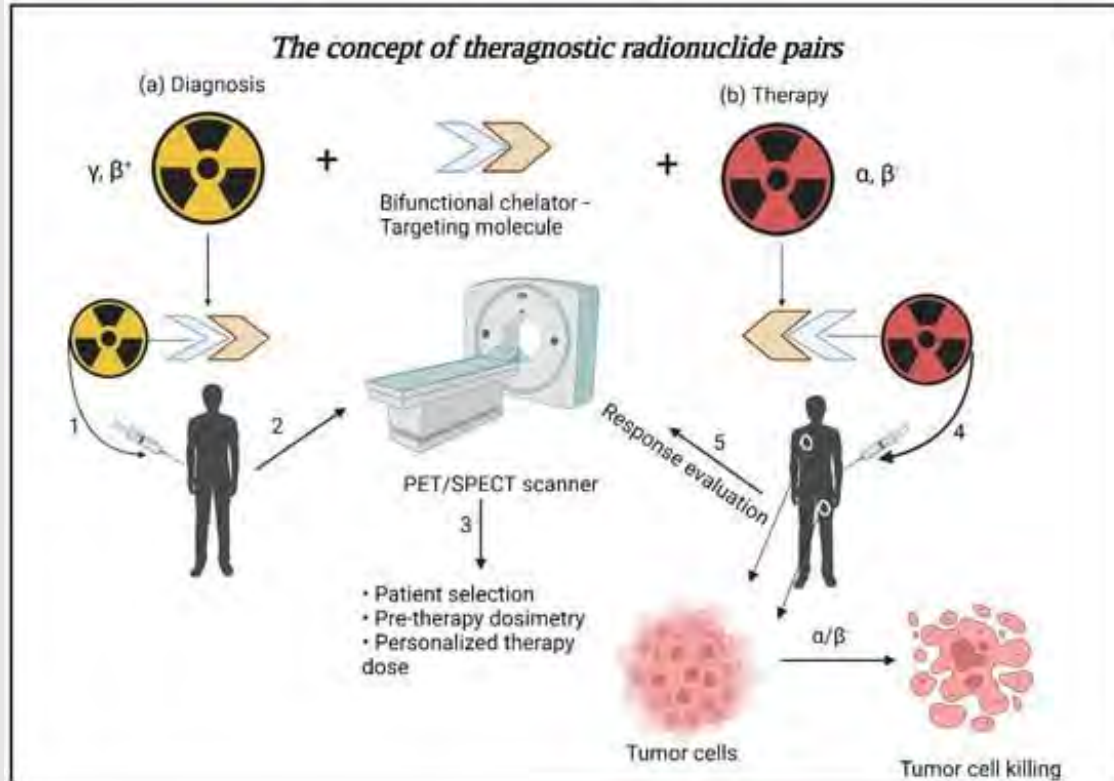


Pimonidazole bladder cancer
Hoskin et al Br J Cancer 2004

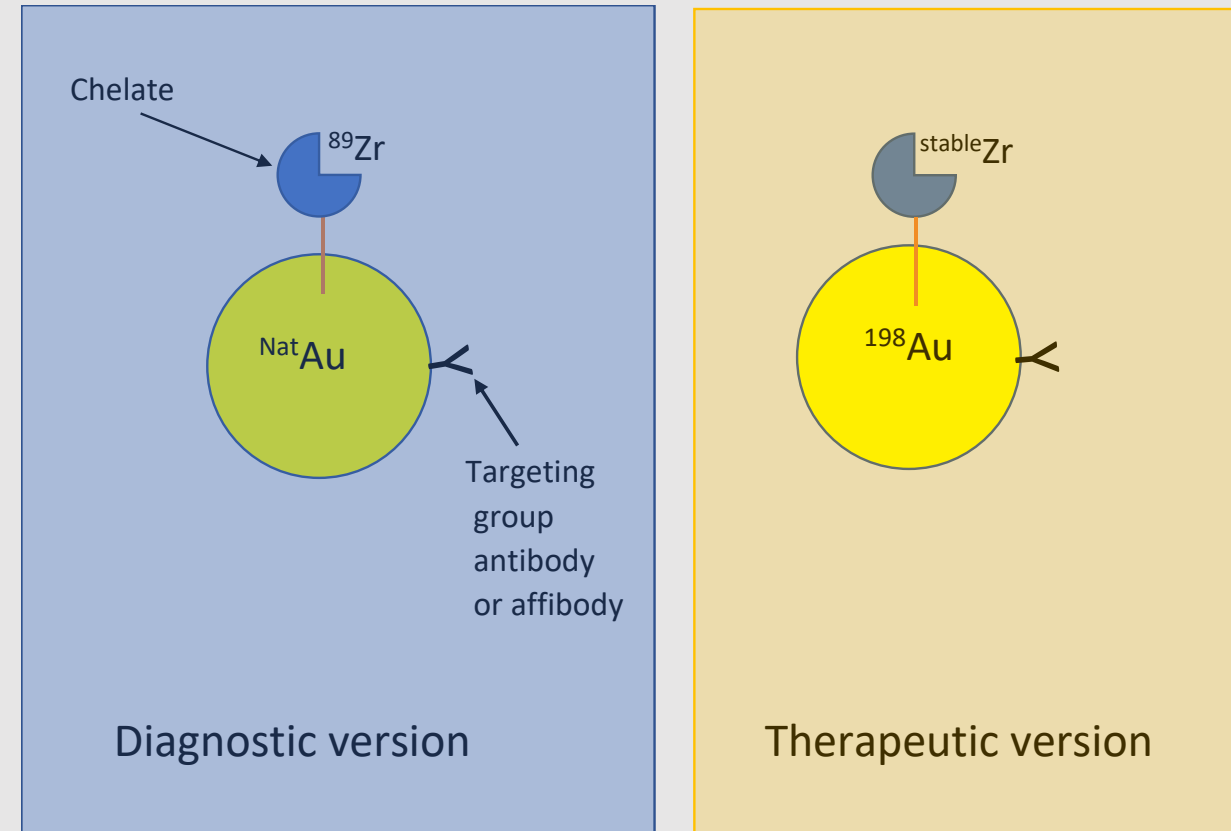


Imaging and treatment

Enables dosimetry prior to delivery of therapeutic radionuclides



Chhabra and Thakur Biomedicines 2022

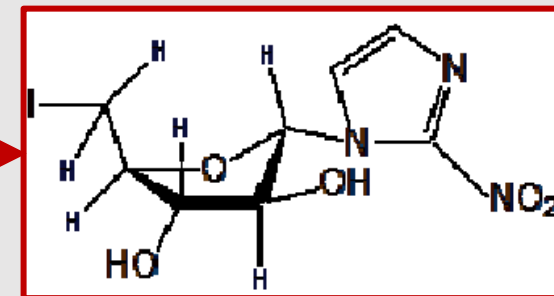
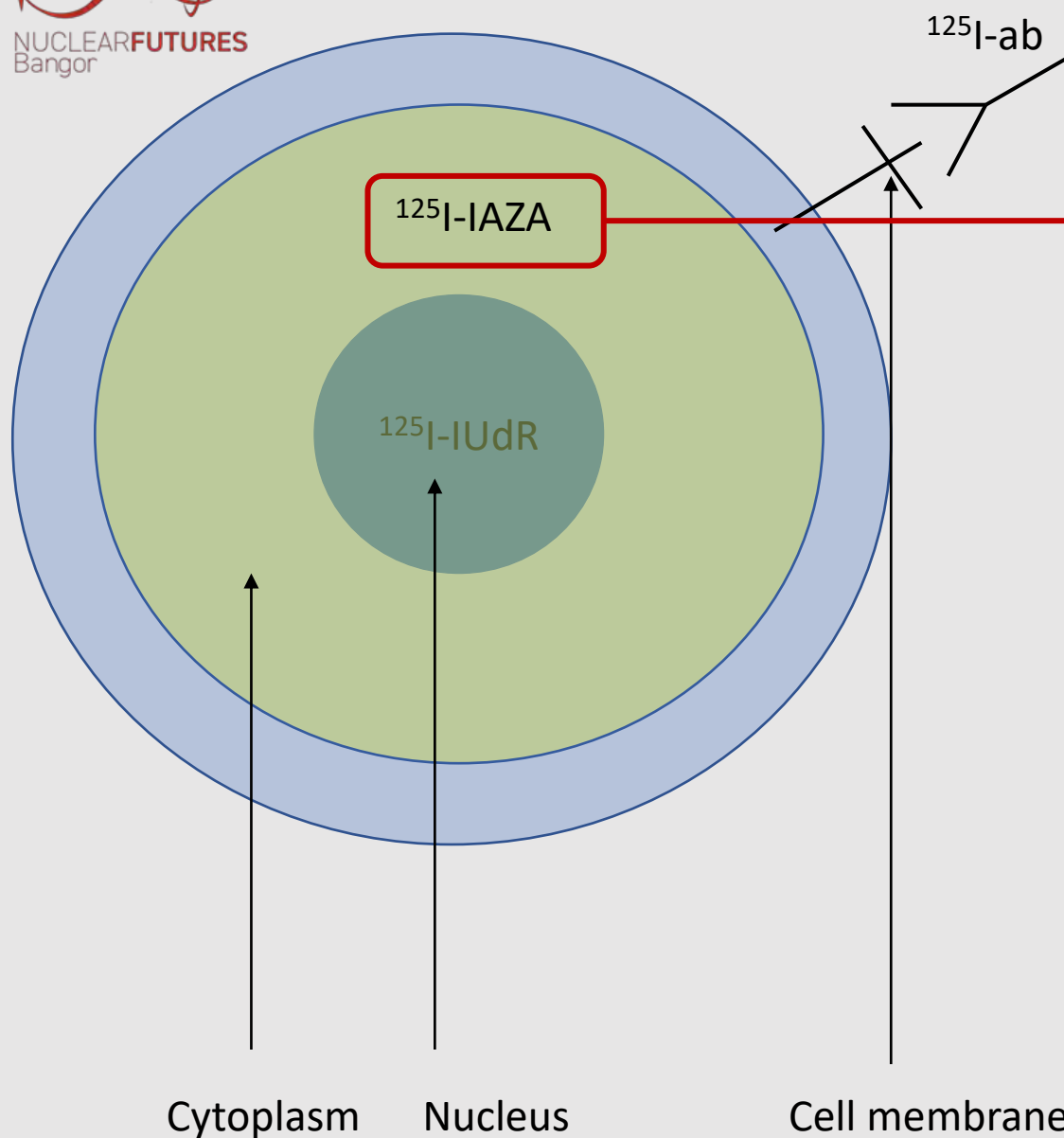


Fabrication of gold nanoparticles

^{89}Zr – positron emitter

^{198}Au – β -emitter

Collaboration: Fred Currell DCF University of Manchester
Zeljka Krpetic University of Salford



Short range ($<10\mu\text{m}$)

Very high LET

Is cytotoxic efficacy related to nuclear accumulation?

DESIGN

Cell nucleus ^{125}I -IUdR

Cytoplasm ^{125}I -IAZA

Cell surface ^{125}I -labelled antibody

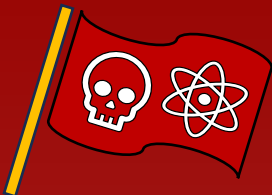
Iodide distribution in cell may be a problem

Ag – high affinity for iodide

Location modification using Ag nanoparticle-membrane

penetrating peptides

BUCCANEER



SMART Grants

CAPITAL equipment
bid – SPEX-SANA +
HPLC

MRC equipment
proposal

Leverhulme
Welsh Government
Royal Commission for the
Exhibition 1851



EQUIPMENT TO BUILD
BUCANEER



RESEARCH USING
BUCANEER

RADIOIODINE
theragnostics

NIMUE

AI & Computing to support
patient tailored MRT

NANOPARTICLE
theragnostics

CANCER Biomarkers for
tailored treatment and care

TEACHING IN BUCANEER

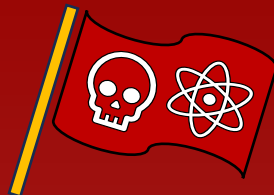
Radiochemistry CPD
modules & labs

Radiochemistry Summer
School

MSc Nuclear
Medicine



BUCCANEER



EQUIPMENT TO BUILD
BUCANEER



SMART Grants

CAPITAL equipment
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RESEARCH USING
BUCANEER

RADIOIODINE
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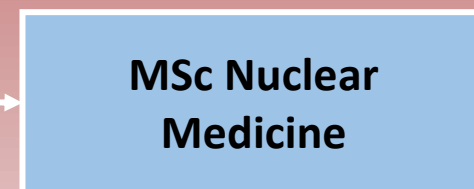
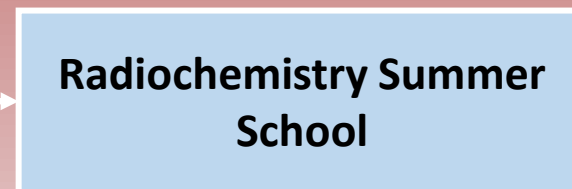
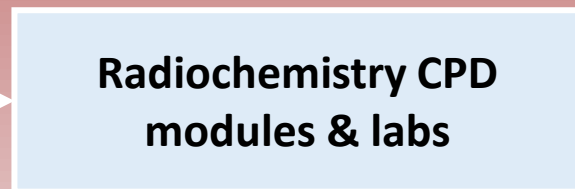
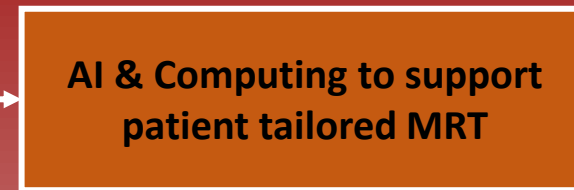
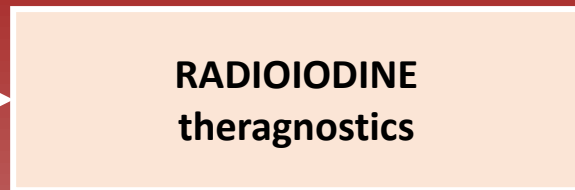
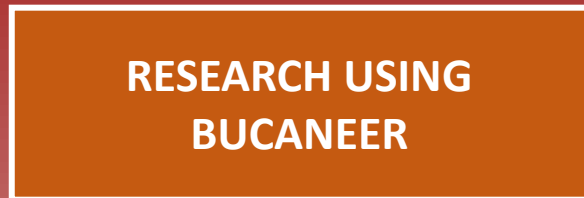
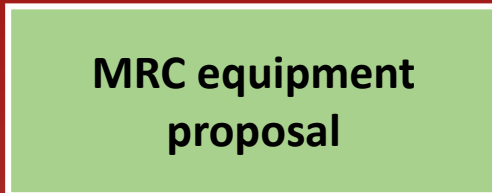
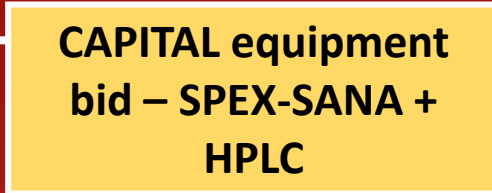
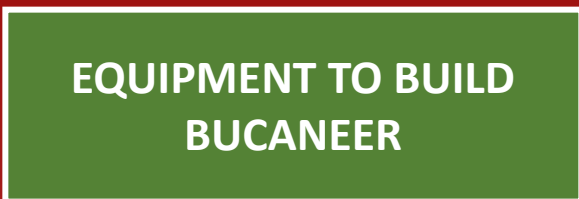
CANCER Biomarkers for
tailored treatment and care

TEACHING IN BUCANEER

Radiochemistry CPD
modules & labs

Radiochemistry Summer
School

MSc Nuclear
Medicine





Nuclear Irradiator for Medical Use and Education [NIMUE] facility



Development of neutron, proton, or helium irradiations of target material.
Collection of tritium from moderator interactions of n?



HOT CELL 1
Post irradiation inspection & characterisation

HOT CELL 2
Target dissolution & analysis
Solution preparation

HOT CELL 3
Training & operational redundancy (waste handling?)

SEPARATIONS LABS

Solution cleanup (Chemistry)
SPEX-SANA or RBR (Engineering)
Recycle & Sustainability
radiometric QA/QC

WASTE TREATMENT LABS

Waste-form development (Chemistry)
HIPing or geopolymers (Engineering)
Primary/secondary waste volume reduction

TARGET MANUFACTURE
characterisation, manufacture & QA/QC development

Informed isotope production for
ARTHUR & Cyclotron facilities

BUCANEER facility

 **IN VIVO**
Cancer cell line testing and efficacy trials

Preparation of radiopharmaceutical precursor

HPLC preparation of pharmaceutical radioisotope

Shipping to collaborators for testing & analysis





New materials testing for fusion and fission applications

Neutron activation analysis to measure trace materials

Support in nuclear forensics applications

Radiotracers for biological research

Radiotracers for environmental and geochemistry research

Fuels research for Space applications – energy and propulsion

Nuclear fuel safety research and post irradiation inspection

Neutron capture therapy research

Material degradation behaviour in radioactive environments

Non-destructive testing of mechanical materials

Semiconductor doping research

Archaeological characterisation

Health physics research

Neutron and radiation metrology research

NIMUE



Production of research quantities of medical theragnostics

Developing isotope production by irradiation of parent elements

Testing of target materials for isotope production

Separation schemes for medical isotopes

Production of new radiopharmaceuticals (with BUCANEER)

Development of new pathways to manufacture and IP

Development of waste treatment options for ARTHUR



Radiochemistry & radioisotope manufacturing training

Hot cell training

Neutronics and materials irradiation training

Supporting the development of ARTHUR



NFI Academics 2022-2024

