GIG CYMRU NHS WALES
Cyd-bwyllgor Comisiynu Joint Commissioning Committee

All Wales Molecular Radiotherapy (MRT) Programme

Strategic Report

All Wales Molecular Radiotherapy Advisory Group

Contents

Executive summary

Molecular Radiotherapy (MRT) is an umbrella term for the use of radioactive pharmaceuticals in the treatment of cancer and some non-malignant conditions. The radioactive nature of these drugs means that there are special requirements for manufacture, transport, storage, administration, and disposal. This requires dedicated infrastructure and licencing. Logistics are time-critical, as these drugs decay and lose activity between manufacture and administration.

To date, the use of MRT in Wales is limited to a small number of long-established indications, in particular thyroid cancer, and selected cases of metastatic prostate cancer. These are locally commissioned by Local Health Boards (LHBs). Capability varies considerably between the three Welsh Cancer Centres, and patient access is uneven.

The specificity of MRT i.e., therapy delivered directly to cancer cells and having little effect on healthy cells, leads to an appealing view of benefits in terms of improvements in both symptoms and survival.

There is a growing pipeline of new MRT agents for a range of cancers. It is therefore reasonable to assume that new agents will come into general use over the next few years for common indications and as such, MRT will grow in terms of volume and range.

However, current infrastructure and specialist workforce in Wales is inadequate to accommodate a developing MRT service. Furthermore, Wales is currently unable to take part in MRT clinical trials and has limited opportunity to take an active part in the general UK MRT uplift. Commissioning of MRT is complex and will take time and local commissioning of these complex and specialised services would result in inequity and delays.

There is clear ambition and appetite to deliver enhanced and new MRT services across all three Welsh Cancer Centres, with positive dialogue and collaboration in place.

Although there is no immediate urgency, it is recommended a strategic national MRT commissioning workplan is put in place and that this is commenced promptly. It is recommended that this workplan is established as part of a forward-looking All Wales Molecular Radiotherapy (AWMOL) group, which should include considerations for infrastructure and workforce development.

Over the next 12-18 months, the priority is to bring the 3 Welsh Cancer Centres to the point where they can sustainably deliver existing oral and intravenous MRTs (principally

Radioiodine for thyroid cancer and Radium for prostate cancer) for their local populations. This is an eminently achievable prerequisite for future expansion of MRT.

Indeed, it is essential to prepare for future provision of a developing MRT repertoire in Wales, so that Welsh citizens can access an equitable, timely and sustainable MRT service.

Strategic Case

1. Introduction

This paper has been written in response to a request from the Director General Health and Social Services/NHS Wales Chief Executive Health and Social Services Group in April 2022. This request was based upon a case put forward for a need for a Welsh strategy for MRT. Funding was allocated by Welsh Government (WGov) on a fixed-term basis (18 months) for a Programme Manager to develop this piece of work, which has now concluded in this report.

The purpose of this report is to set out the context, challenges and opportunities for an All Wales Molecular Radiotherapy (MRT) service, that will have capacity and expert capability to meet the anticipated increased demand for MRT over the next ten years. It considers the requirements in terms of infrastructure, workforce, and research, development and innovation (RD&I).

2. Context

Molecular Radiotherapy (MRT) is the use of oral or injectable radioactive therapeutic pharmaceuticals. MRT agents are mainly used in the treatment of some specific cancers, but there are also non-oncological indications. Therapeutic radiopharmaceuticals should be regarded as distinct from diagnostic radiopharmaceuticals, commonly used in nuclear medicine and PET-CT, although there is an overlap in terms of specialist workforce, logistics and infrastructure requirements.

The field of MRT is expanding in parallel with advances in molecular imaging, and the requirement to deliver MRT is expected to increase significantly over the next decade[1]. For the Welsh population to fully benefit from molecular radiotherapy advances, in terms of improvements in both symptom control and survival, patients need to be able to access the agents easily, regardless of where they live. In turn, this requires the healthcare systems within Wales (and the UK) to effectively commission and provide the new agents, as well as invest in the workforce and physical environments to ensure safe delivery[1].

[1] Review of molecular radiotherapy services in the UK, 2021, Royal College of Radiologists

The use of radioactive materials is multidisciplinary, and requires highly skilled and specialist staff, specialist facilities and equipment. There are stringent legislative, regulatory and safety considerations, time constraints and manufacturing limitations.

Considering the likely patient benefits, alongside the complexity surrounding service delivery and the currently limited and uneven capacity and capability in Wales, it would be prudent to put mechanisms in place that can ensure timely and equitable service provision to Welsh citizens: something that is currently lacking.

In March 2022, AWMOL, in collaboration with WHSSC, produced a report "Development of Molecular Radiotherapy Services in Wales" . One of its key recommendations was that WHSSC should be commissioned to carry out a strategic review of the future of MRT in Wales to consider demand projections, estates, staffing requirements and research. As such, on 28 July 2022 the Director General, Health and Social Services/NHS Chief Executive, Welsh Government appointed Dr Sian Lewis (Managing Director, WHSSC) as the Senior Responsible Officer (SRO) for the All Wales Molecular Radiotherapy Programme with the mandate for WHSSC to develop a national strategy for MRT.

The All Wales MRT Programme was launched in May 2023 with a remit to report to Welsh Government (WGov) by summer 2024. The programme is supported by the AWMOL group and accountable to the Programme Sponsor, the Deputy Director of Health Science at Welsh Government.

A key driver for the programme was the urgent need to plan and prepare for Lu177 PSMA MRT for metastatic castration-resistant prostate cancer pending technology appraisal by NICE[2]. It was widely expected to be approved in 2023, with immediate pressure for provision by a service that was not remotely equipped for the task. However, after three NICE technology appraisals in 2023, Lu177 PSMA did not gain approval within its marketing authorisation[3]. Whilst the urgency of Lu177 PSMA has waned, it has nevertheless provided an opportunity to assess baseline and current MRT services in Wales, undertake an independent horizon scan of the future MRT pipeline and identify the opportunities, gaps and risks to preparedness for new, innovative MRT agents.

Existing agents radium-223 (Ra223) and iodine-131 (I131) have been used for many years and do not fall under the requirements for specialised commissioning. New MRT agents/treatments will be commissioned as specialist services by the NHS Wales Joint Commissioning Committee (NWJCC). It is important to capture the ambitions and intent of the three Welsh Cancer Centres (CCs) to ensure alignment with respective Integrated

[2] Lu177 PSMA (Lutetium PSMA) is a molecular radiotherapy treatment to treat patients with advanced metastatic castration resistant prostate cancer

[3] Recommendations | Lutetium-177 vipivotide tetraxetan for treating PSMA-positive hormone-relapsed metastatic prostate cancer after 2 or more treatments | Guidance | NICE – published 15 November 2023

Medium-Term Plans (IMTPs), the NWJCC Integrated Commissioning Plans (ICPs) and national/regional strategic plans.

The report has been developed with input from an All Wales group of stakeholders from the molecular radiotherapy community, which includes professionals, research, industry, health organisations and international experts.
This document sets out:

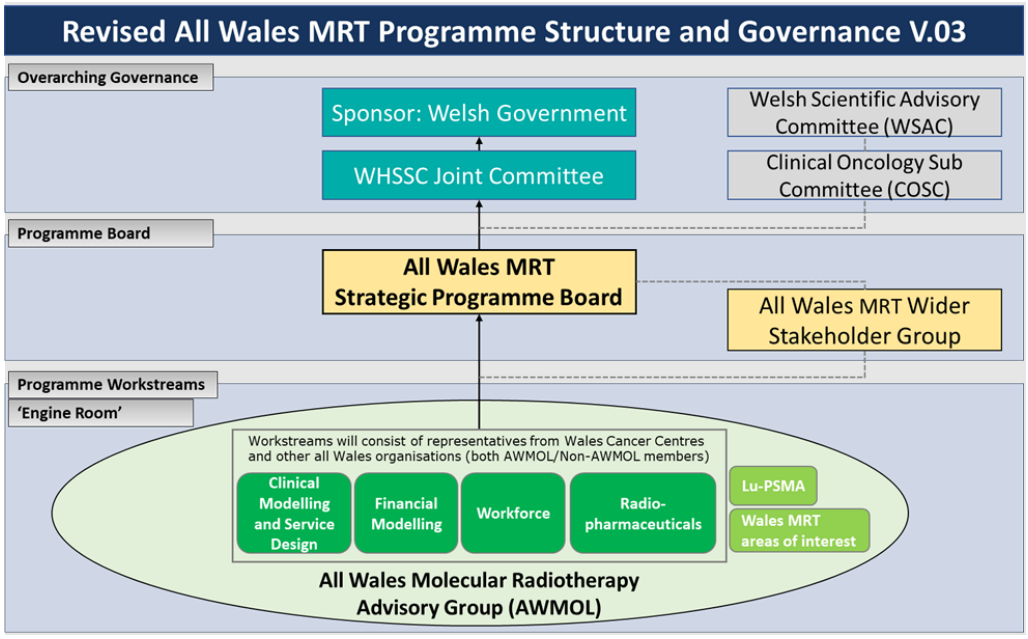
- An overview of current services and explains the current strategic placement of MRT services in Wales.
- The case for change in terms of the gap between existing arrangements and future service needs.
- Determines all-Wales objectives to answer the gaps.
- Recommendations to answer the potential all-Wales MRT service in terms of the operational capabilities and service changes required to satisfy the identified needs.

3. Programme approach

The programme was established adopting a proportionate approach to programme/project management, with a mix of programme board, workstreams, AWMOL and ad hoc group meetings/sessions reporting via WHSSC (**Figure 1**). This allowed positive reach into respective organisations and good communication and collaboration with Cancer Centres (CCs). The workstreams were incorporated into the AWMOL group meetings, thereby allowing the AWMOL to support and make best use of time of a niche group of stakeholders and experts.

The programme also engaged with the National Institute for Health and Care Research Innovation Observatory (NIHR IO) to undertake a horizon scan on behalf of NHS Wales - specifically, an analysis of pipeline MRT agents including late-stage clinical trials. This independent assessment is a key piece of work that has helped to further understand the MRT landscape and to shape the 'what next' in Wales.

Figure 1: Programme governance structure from project onset to March 2024



This report has been developed using a tailored mix of methodologies, recognising the complexities of organisational and financial responsibilities of WHSSC, hosted by CTMUHB, and Welsh Cancer Centres, hosted by respective Health Boards/Trusts.

4. Strategic context

This section of the report outlines the strategic context for the All Wales MRT Programme by providing an organisational overview and explaining how the proposals are strategically placed to support the delivery of organisational goals. It includes:

- An overview of the lead organisation and stakeholders.
- An analysis of population needs including demographic growth and disease prevalence.
- An outline of how the programme is essential to achieving the overall business strategies and aims of NHS Wales.
- A description of how the programme contributes to strategic goals within the context of the therapeutic services.
- An overview of interdependencies with other relevant programmes and strategies.

4.1 Organisation overview

In 2021, the All Wales Molecular Radiotherapy Group (AWMOL) was formed as a subgroup of the Clinical Oncology Sub Committee (COSC) of the Welsh Scientific Advisory Committee (WSAC). AWMOL was set up specifically to advise Welsh Government (WGov) and the Welsh Health Specialised Services Committee (WHSSC) on the provision of Molecular Radiotherapy (MRT) services for the people of Wales. Membership of the

AWMOL group is multidisciplinary and includes representatives from all Welsh Cancer Centres, WHSSC and Welsh Government.

The All-Wales MRT Programme has been led AWMOL, under the auspices of the Welsh Health Specialised Services Committee (WHSSC). WHSCC's responsibilities moved to the NHS Wales Joint Commissioning Committee (NWJCC) on 1st April 2024. Other key stakeholders for the programme are:

- All Health Boards in NHS Wales;
- Velindre University NHS Trust;
- MRT providers in NHS England commissioned by NWJCC;
- Welsh Government;
- Health Education and Improvement Wales (HEIW);
- NHS Executive
- Wales Cancer Network and other relevant specialist groups or organisations (e.g. Royal College of Radiologists);
- National Imaging Academy Wales (NIAW);
- Digital Health and Care Wales (DHCW).

This report has been written in collaboration with:

- Consultant Radiologists;
- Nuclear Medicine departments;
- Medical Physics departments;
- Cancer MDTs and non-cancer MDTs, and
- Consultant oncologists.

4.2 Population needs: Disease Prevalence

Although Welsh population growth over the next 10 years will be modest, Wales is projected to realise growth in the 65+ population of around 130,000 by 2031, which is a significant demographic shift. An aging population will mean increased overall demand for health and care services[4].

Population ageing will mean a greater prevalence of age-related conditions, such as dementia and chronic conditions affecting the heart, musculoskeletal and circulatory system. Data from Cancer Research UK correlates increased incidence of cancer with age at diagnosis[5].

4.3 NHS Wales strategy and aims

The proposals outlined within this report are aligned with the national strategic context, supporting a broad range of national strategies and policies. An analysis of these is

[4] Future of an Ageing Population, Government Office for Science, 2016
[5] Cancer Research UK, https://www.cancerresearchuk.org/health-professional/cancer-statistics/incidence/age#heading-Zero, Accessed May 2024

provided in **Table 1** below, showing how an all-Wales MRT service will support their delivery.

Table 1: Alignment with national strategies

Strategy/Policy	Summary	How the All Wales MRT service supports this
The quality statement for cancer (May 2022) [8]	The introduction of quality statements was signalled in *A Healthier Wales* and has been described in the National Clinical Framework as the next level of national planning for specific clinical services. It forms part of the enhanced focus on quality in healthcare delivery that was described in A Healthier Wales and the Quality and Safety Framework. Health boards and trusts are responsible for planning and delivery of cancer services in line with professional standards and the quality attributes set out below. Health Boards and trusts will be directed, supported and enabled to deliver improved cancer services by the NHS Executive function. This will be discharged through its Wales Cancer Network Board, which will be supported with national funding.	Patients across Wales will have access to equitable services, that are evidence-based radiotherapy and/or systemic anti-cancer therapies. It will assist in the Quality Statement's aim that all eligible patients are offered access to research trials and Wales provides excellent supporting infrastructure for cancer research. Furthermore, it contributes to clinicians working in cancer pathways work at the top of their license or are supported to improve their skill mix and are also enabled to take part in the quality assurance cycle and research activity. It also addresses precision medicine, which enables better targeting of treatments.
The Parliamentary Review of Health and Social Care in Wales. Final Report. (January 2018) [9]	The Parliamentary Review set out a vision for the future, to include health and social care moving forward together and developing primary care services out of hospitals. The Review's recommendations focus on key themes around seamless care, a great place to work and maximising the benefits of technology and innovation.	Providing seamless care. Improving facilities. Providing greater opportunities to attract a highly skilled workforce Maximising the benefits of technology and innovation.
A Healthier Wales: Our Plan for Health and Social Care (June 2018) [10]	*'A Healthier Wales'* is the Welsh Government's response to the Parliamentary Review. It sets out the vision of a 'whole system approach to health and social care' which is focused on health and wellbeing, and on preventing physical and mental illness. It focuses on 'providing more joined-up services, in community settings', and shifts the emphasis from treating illness to prevention and supporting people to stay well and lead healthier lifestyles.	Addressing the recommendations set out in the Parliamentary Review as described above. Focusing on improving access to services that will enable earlier interventions.
The Wellbeing of Future Generations (Wales) Act 2015 [11]	The Wellbeing of Future Generations Act is about improving the social, economic, environmental, and cultural wellbeing of Wales. It makes the public bodies listed in the Act think more about the long-term, work better with people and communities and each other, look to prevent problems and take a more joined-up approach.	Deliver a sustainable service that focuses on: Addressing health inequalities Improving outcomes for patients Attracting and developing a highly skilled workforce.

4.4 MRT Service strategic aims

Akin to the rest of the UK, MRT services in Wales face a number of significant challenges, for example:

- MRT is an expanding treatment modality.
- Inequitable distribution of resources in terms of equipment, facilities, accompanying diagnostics and workforce.
- Inequitable distribution of resources and funding in terms of research, development and innovation.

Such challenges provide compelling reasons to prepare for a transformation in the provision of MRT services in Wales. To respond effectively, it is essential that a coordinated implementation plan for MRT in NHS Wales is developed. These strategic challenges are summarised in **Figure 2** below. The All Wales MRT Programme has sought to identify the way forward to address population needs, while aligning with the strategic direction of Wales and addressing specific strategic issues within the cancer network.

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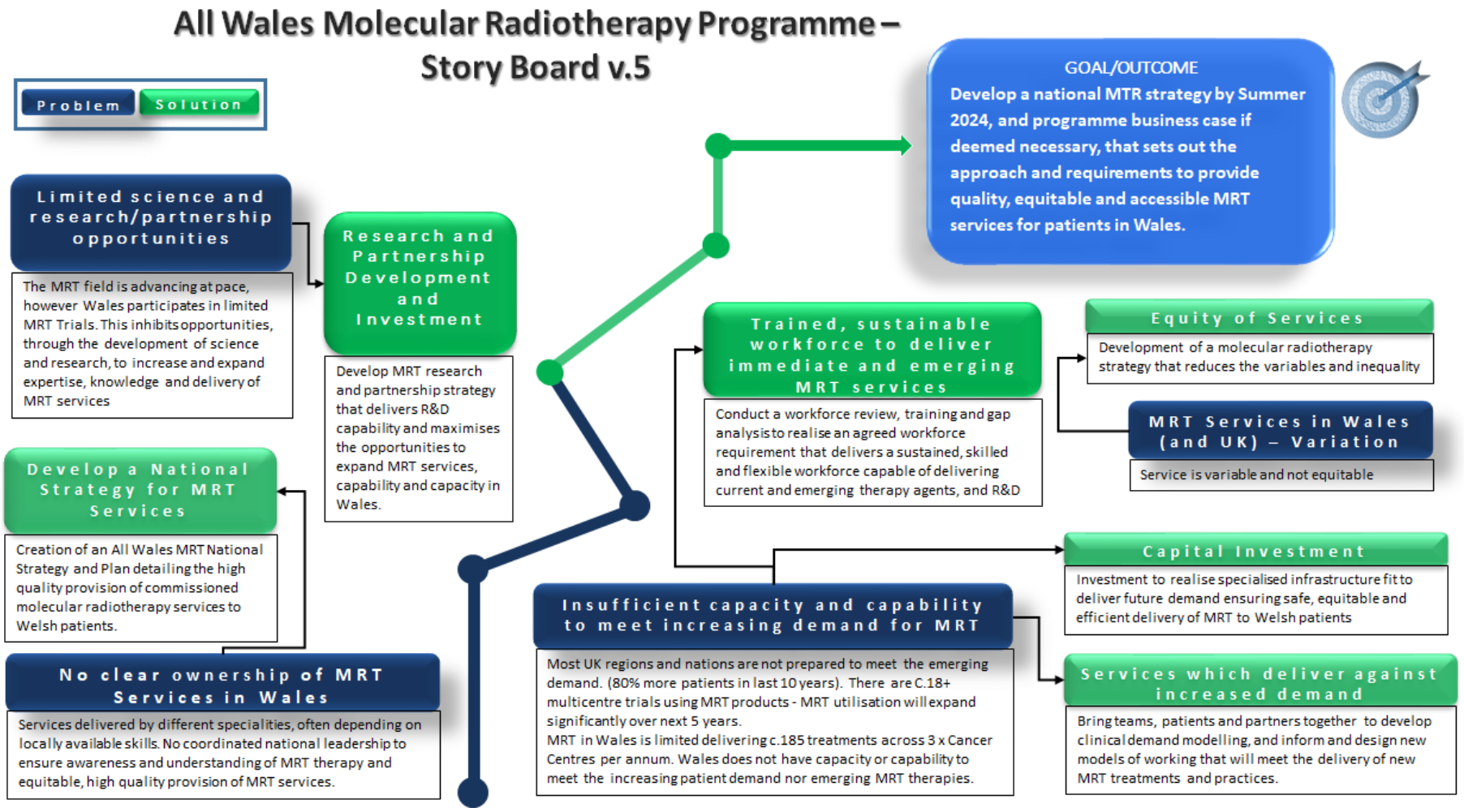
Figure 2: All Wales MRT Story Board



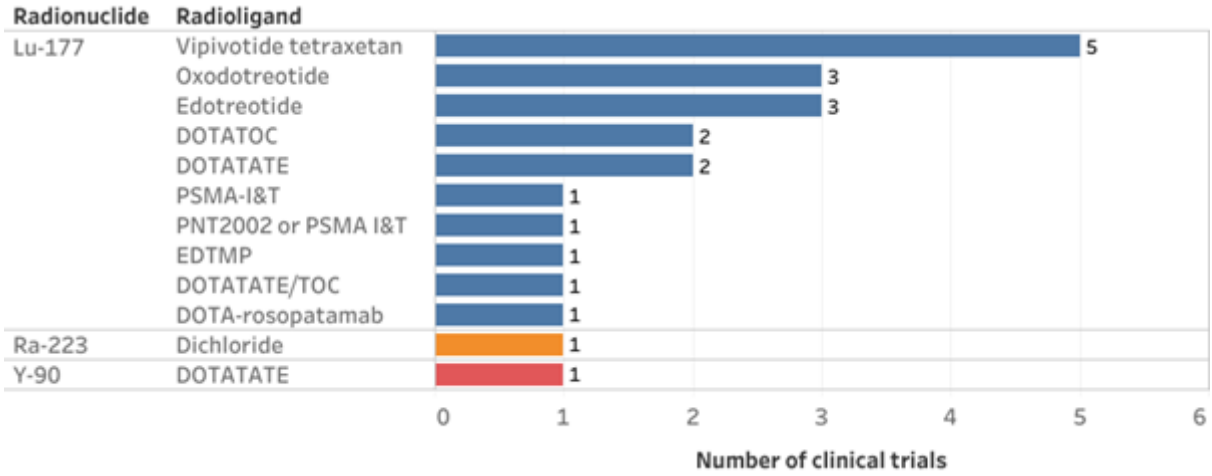
5. Future projections for MRT demand in Wales

The all-Wales MRT Programme radiopharmaceutical workstream collaborated with the NIHR IO, with a view to source evidence regarding new and upcoming MRT agents, and critically, grasp an approximation of timelines to inform planning.

NIHR IO report on horizon scan searches undertaken, which identified a total of 80 clinical trials that met the search criteria (https://www.io.nihr.ac.uk/wp-content/uploads/2024/05/IO-MRT-Scan-Report.pdf). After applying the agreed time limits (2020 – current) phase of development (phase 2/3, 3, and 4) and trial status (in progress) criteria, the final set of included trials amounted to 22.

Out of the 22 clinical trials identified, 20 were investigating radiopharmaceuticals containing Lu177 (**Figure 3**). Radiopharmaceuticals containing I131, Ra223, and Y90, were being investigated in one clinical trial each. One clinical trial was testing both Lu177 and Y90.

Figure 3: Volume of ongoing trial activity for therapeutic radioligands



5.1 Therapeutic Area Landscape analysis

All radioligand technologies were being investigated for cancer indications. Within these, Neuroendocrine tumours (NETs[6]) were being assessed the most, followed by prostate cancer. In terms of phase of clinical development, most of the clinical trials were in phase 3 (17, 77%) while a small proportion were in phase 4 (5, 23%). No clinical trials included in the final scan were in phase 2/3.

[6] Neuroendocrine tumours (NETs) are rare tumours that develop in cells of the neuroendocrine system. They are also called neuroendocrine neoplasms (NENs). There are a number of different types. The type you have depends on the particular cells that the tumour starts in.

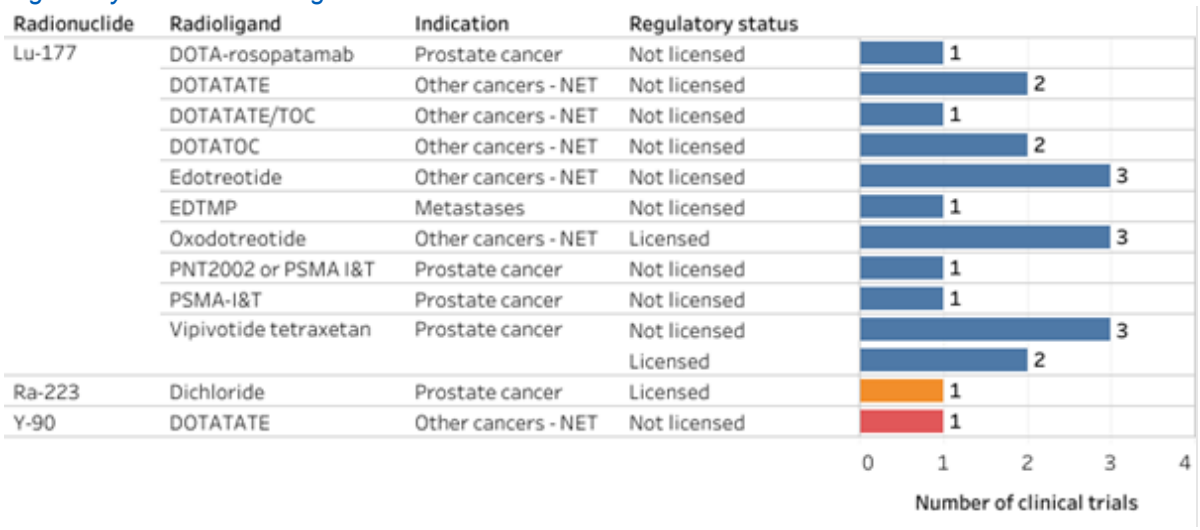
5.2 Trial location

More than half of the clinical trials for assessing therapeutic radioligand technologies were being conducted in Europe or global trial locations half of which included European trial locations. UK was included in the trial locations of 6 global clinical trials.

5.3 Regulatory information

The analysis revealed four radionuclides and twelve radioligands in the horizon scan. Among these, two ligands (oxodotreotide and vipvotide tetraxetan), radiolabelled with Lu177 are licensed by the MHRA (**Figure 4**) for NETs and prostate cancer, respectively. Dichloride radiolabelled with Ra223 is also licensed by the MHRA for prostate cancer.

Figure 4: Regulatory status of radioligands



5.4 NICE appraisals

NICE technology appraisals (TAs) follow strict methodology and result with recommendations on the use of new and existing medicines and treatments within the NHS. NICE base their recommendations on a review of clinical and economic evidence.

The NHS is legally obliged to fund and resource medicines and treatments recommended by NICE's technology appraisals. The NHS Constitution states that patients have the right to drugs and treatments that have been recommended by NICE for use in the NHS, if their doctor believes they are clinically appropriate.

When NICE recommends a treatment 'as an option', the NHS must make sure it is available within 3 months (unless otherwise specified) of its date of publication. This means that, if a patient has a disease or condition and the doctor responsible for their care thinks that the technology is the right treatment, it should be available for use, in line with NICE's recommendations[7].

[7] Technology appraisal guidance | NICE guidance | Our programmes | What we do | About | NICE

Importantly, only one MRT agent is currently selected by NICE for appraisal, however no date has been selected for the work to commence (ID6315; Lutetium oxodotreotide with octreotide for newly diagnosed unresectable or metastatic gastroenteropancreatic neuroendocrine tumours)[8].

5.5 Timelines

Topic selection for NICE ID6315 was done in June 2023, however no date for the technology appraisal has been noted. This is the only "live" topic relating to an MRT on the NICE workplan.

Regarding clinical trials in the UK - there are four phase 3 clinical trials investigating new therapeutic radioligand technologies where UK was among the trial locations. All these clinical trials have study completion dates in 2026 and beyond. One phase 3 clinical trial in Sweden for Lu177 DOTATOC is scheduled to complete in October 2025 (**Figure 5**).

Figure 5. Number of clinical trials in phase 3 stage of clinical development for therapeutic radioligand technologies

Radionuclide	Ligand	Condition	Location	UK Locations	Sponsor	Primary Completion Date
Lu-177	DOTA-rosopatamab	Prostate cancer	Not available	No	Telix International Pty Ltd	2025-06
	DOTATATE/TOC	Other cancers - NET	Global	No	RayzeBio, Inc.	2025-07
	DOTATOC	Other cancers - NET	Europe	No	Lund University Hospital	2025-10
					Region SkÃ¥ne	Not available
	Edotreotide	Other cancers - NET	Europe	No	Grupo Espanol de Tumores Neuroendocrinos	2028-03
			Global	Yes	ITM Solucin GmbH	Not available
						2024-09
	EDTMP	Metastases	Asia	No	AIIMS Jodhpur	Not available
	Oxodotreotide	Other cancers - NET	Asia	No	Jiangsu HengRui Medicine Co., Ltd.	2026-12
					Sinotau Pharmaceutical Group	2024-12
	PNT2002 or PSMA I&T	Prostate cancer	Global	Yes	POINT Biopharma	2023-12
	PSMA-I&T	Prostate cancer	Global	No	Curium US LLC	2024-01
	Vipivotide tetraxetan	Prostate cancer	Global	Yes	Novartis Pharmaceuticals	2025-07
						2022-10
			Not available	No	Novartis Pharmaceuticals	2028-01
Lu-177, Y-90	Dotatate	Other cancers - NET	Europe	No	POLATOM	Not available

There are no phase 4 Lu177 clinical trials taking place in the UK. The soonest completion date for a phase 4 Lu177 clinical trial will be in March 2025. A Bayer sponsored Ra223 trial is live in the UK, however as noted earlier on in this paper, Ra223 is considered a non-specialised radionuclide. Thus, while of interest, it will likely not bring about significant additional demands surrounding infrastructure and workforce.

[8] Project information | Lutetium oxodotreotide with octreotide for newly diagnosed unresectable or metastatic gastroenteropancreatic neuroendocrine tumours [ID6315] | Guidance | NICE

Figure 6. Number of clinical trials in phase 4 stage of clinical development for therapeutic radioligand technologies

Radionuclide	Ligand	Condition	Location	UK Locations	Sponsor	Primary Completion Date
Lu-177	Dotatate	Other cancers - NET	North America	No	Vanderbilt-Ingram Cancer Center	2025-03
	Oxodotreotide	Other cancers - NET	Europe	No	University Hospital, Antwerp	2029-04
	Vipivotide tetraxetan	Prostate cancer	North America	No	Mayo Clinic	2029-12
					Novartis Pharmaceuticals	2033-07
Ra-223	Dichloride	Prostate cancer	Global	Yes	Bayer	2025-05

5.6 Horizon scan summary

To date, the use of therapeutic radioligand technologies to treat cancer has mainly been limited to a small number of niche indications, such as thyroid cancer and NETs. According to Wadsley and Flux[9], in the last decade there has been a rapid increase in the number of publications relating to the use of therapeutic radioligand technologies across a range of cancers, including colorectal, hepatocellular, breast, and prostate. However, therapeutic radioligand technologies are still only delivered by a relatively small number of centres. This rapid growth presents challenges for service delivery and healthcare economics at a national scale.[1]

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. Engagement with pharmaceutical companies manufacturing these radioligand technologies is essential to ascertain, which of the above therapeutic radioligand technologies would be brought to the UK for clinical use in the NHS.

The knowledge of these new and upcoming clinical indications of interest and radioligands will shape future planning and allow NHS Wales to prepare for the adoption of new therapeutic radioligand technologies in clinical use.

[9] Wadsley J, Flux G. Molecular Radiotherapy Comes of Age. Clinical Oncology. 2021;33(2):65-7. Available from: https://doi.org/10.1016/j.clon.2020.12.004

6. The case for change

This section of the report establishes the case for change that is driving the All Wales MRT Strategic Programme, providing a clear understanding of:

- The objectives (what the service is seeking to achieve).
- Existing arrangements (what is currently happening).
- Business needs (what is required to close the gap between existing arrangements and where the service needs to be in the future).

6.1 All Wales MRT service objectives

These objectives describe what the service is seeking to achieve. Objectives were informed through engagement with service providers (**Table 2**).

Table 2: Proposed objectives for MRT in Wales

PROGRAMME OBJECTIVE	OBJECTIVE DESCRIPTION
OBJECTIVE 1	To improve the preparedness of NHS Wales for new and upcoming MRT service provision for Welsh patients.
OBJECTIVE 2	To improve NHS Wales capability for MRT service delivery, which includes establishing research, development and innovation infrastructure.
OBJECTIVE 3	To focus on reducing variance in MRT service provision.

6.2 Existing arrangements

There are currently three Cancer Centres delivering MRT in Wales, each differing in services that are delivered and population numbers:

- North Wales Cancer Treatment Centre (Betsi Cadwaldr UHB)
- Velindre Cancer Centre (Velindre NHS Trust)
- South West Wales Cancer Centre (Swansea Bay UHB)

Welsh Cancer Centres (CCs) are delivering a limited repertoire of well-established treatments such as Radioiodine (I131) for thyroid cancer and benign thyroid disease, and Radium (Ra223) palliative treatment for prostate cancer bony metastases. Collectively across the three Welsh CCs in 2022/23 there were circa 100 I131 treatments for benign thyroid disease; 72 treatments for I131 thyroid cancer; and 64 treatments for Ra223 prostate cancer. The later Ra223 figure does not include patients from Hywel Dda and SBUHB referred and treated in Bristol on behalf of SWWCC, which is unable to deliver this treatment in Swansea. In 2023-24, 13 patients from Swansea Bay and Hywel Dda received this treatment at Bristol, with an estimated additional 13 patients not receiving

treatment as too unwell or unwilling to travel. Overall, circa 236 I131 and Ra223 MRT treatments were administered in Wales 22/23.

There is clear ambition and appetite to deliver enhanced and new MRT services across all three CCs with positive dialogue and collaboration between CCs, the AWMOL group and MRT programme.

Although Wales remains relatively static and is not uniform in its delivery of MRT services (this is the case across most UK regions and nations)[1], it is, nevertheless, satisfactorily positioned to move forward with pragmatic plans and actions to increase respective CC's MRT capability and capacity. To match the ambition, conservative investment will be required in infrastructure, training and specialist staff to administer and manage increased services.

6.3 Baseline of infrastructure, regulatory and building requirements for MRT services

During Q3 2023/24, the MRT Radiopharmaceutical Workstream undertook an all-Wales baseline exercise to define and record the key infrastructure, regulatory and building requirements for a core MRT service.

Represented by all three CCs, the group also used the exercise to develop and agree MRT service levels in Wales. Critically, these are aligned to NHSE's draft service levels and service specification 2322[10].

Table 3 outlines the agreed core requirements for service Levels 1-3:

- Level 1 outlines I131 and Ra223 treatments delivered as an outpatient service and are of lower complexity.
- Level 2 outlines I131, Ra223 and future Lu177 dotatate treatments delivered as an outpatient or inpatient service with additional service support provision.
- Level 3 outlines Selective Internal Radiation Therapy (SIRT) which is commissioned by NHSW and delivered by NHSE providers.

Tables 4 & 5 provide an overview of the Welsh Cancer Centres' baseline assessment of current capability set against core service Level 1 and Level 2 requirements, respectively.

[10] NHS ENGLAND draft Service Specification 2322 'Radiotherapy services, Molecular Radiotherapy'. Expected date of publication April 2024

Table 3 – Core service levels 1-3 infrastructure, regulatory and buildings requirements for specified molecular radiotherapy treatments.

CORE SERVICE LEVELS 1 - 3	Core Service Infrastructure, Regulatory and Buildings Requirements for Specified MRT																			
	Emitter type (α, β, γ)	Diagnostic or pre-therapy imaging		IR(ME)R licenses		Environmental (NRW) Permit	Post-therapy imaging for verification & dosimetry services		Radiopharmaceutical Management				Full resuscitation equipment including oxygen and suction	Outpatient - Day case		Inpatient - Overnight case			Specialist staffing (specify) e.g. Specialist Nurses	Provision of MRT services
		PET scan	Gamma camera	Practitioner	Employer		Gamma camera	Dosimetry software	Radiopharmaceutical Ordering	Radiopharmaceutical Receipt	Radiopharmacy Manufacturing	On site draw up – isolators/LFC/safe		Shielded uptake rooms	Hot toilet access	Shielded room	Hot toilet access	In-patient suite availability		
Level 1																				
I-131 Radioiodine (Benign thyroid disease) (Outpatient)	**β, γ**			**x**	**x**	**x**			**x**	**x**		**x**				**p**	**p**	**p**		
I-131 Radioiodine (Thyroid Cancer) (Outpatient)	**β, γ**			**x**	**x**	**x**	**x**		**x**	**x**		**x**		**x**	**x**	**p**	**p**	**p**		
Level 2																				
I-131 Radioiodine (Thyroid Cancer) (Inpatient)	**β, γ**			**x**	**x**	**x**	**x**		**x**	**x**		**x**	**x**			**x**	**x**	**x**	**x**	
Ra-223 Radium Chloride (Prostate Cancer)	**α, β, γ**			**x**	**x**	**x**			**x**	**x**		**x**	**x**			**11**	**p**	**p**	**x**	
Lu-177 dotatate/dotatoc/dotanoc (Neuroendocrine malignancy)	**β, γ**	**Ga**[12]		**x**	**x**	**x**	**x**	**x**	**x**	**x**		**x**	**x**	**x**	**x**	**p**	**p**	**p**	**x**	
Level 3																				
Y-90 Selective Internal Radiation Therapy (SIRT)[13]	**β**		**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**		**x**	**x**					**x**	**x**	

X *Indicates core service infrastructure, regulatory and building requirements;* ***p*** *(Plan) will require day patient facilities but plan to ensure access to in-patient facilities).*

[11] Not required for Ra-233 treatment.

[12] Each patient requires an octreotide gamma camera or gallium-68 PET scan. Currently, Ga PET scans are not available in Wales.

[13] SIRT is not delivered as a service in Wales.

Table 4 – Wales Cancer Centres' Existing Core Service Infrastructure, Regulatory and Buildings Baseline for Specified Molecular Radiopharmacy Treatments

WALES CANCER CENTRES' Service Baseline Level 1	Wales Cancer Centres' Core Service Infrastructure, Regulatory and Buildings Baseline for Specified MRT																		
	Emitter type (α, β, γ)	Diagnostic or pre-therapy imaging		IR(ME)R licenses		Environmental (NRW) Permit	Post-therapy imaging for verification & dosimetry services		Radiopharmaceutical Management				Full resuscitation equipment including oxygen and suction	Outpatient - Day case		Inpatient - Overnight case			Specialist staffing (specify) e.g. Specialist Nurses	Provision of MRT services
		PET scan	Gamma camera	Practitioner	Employer		Gamma camera	Dosimetry software	Radiopharmaceutical Ordering	Radiopharmaceutical Receipt	Radiopharmacy Manufacturing	On site draw up – isolators/LFC/safe cabinet/carbon filter extraction		Shielded uptake rooms	Hot toilet access	Shielded room	Hot toilet access	In-patient suite availability		
Level 1																				
I-131 Radioiodine (Benign thyroid disease) (Outpatient)	**β, γ**			**x**	**x**	**x**			**x**	**x**		**x**				**p**	**p**	**p**		
VCC				x	x	x			x	x		x	x		x	p	p	p		**X**
SWWCC				x	x	x			x	x		x				p	p	p		**X**
NWCTC				x	x	x			x	x		x				p	p	p		**X**
I-131 Radioiodine (Thyroid Cancer) (Outpatient)	**β, γ**			**x**	**x**	**x**	**x**		**x**	**x**		**x**		**x**	**x**	**p**	**p**	**p**		
VCC				x	x	x	x		x	x		x	x		x	p	p	p		**X**
SWWCC				x	x									x	x	p	p	p		
NWCTC	**β, γ**			x	x	x	x		x	x		x				p	p	P		

Green squares indicate active capability; Amber squares highlight no onsite core service capability and/or limited onsite capability – risks attached and requires action/monitoring.

Table 5 – Wales Cancer Centres' Core Existing Service Infrastructure, Regulatory and Buildings Baseline for Specified Molecular Radiopharmacy Treatments

WALES CANCER CENTRES' Service Baseline Level 2	Wales Cancer Centres' Core Service Infrastructure, Regulatory and Buildings Baseline for Specified MRT																			
	Emitter type (α, β, γ)	Diagnostic or pre-therapy imaging		IR(ME)R licenses		Environmental (NRW) Permit	Post-therapy imaging for verification & dosimetry services		Radiopharmaceutical Management				Full resuscitation equipment including oxygen and suction	Outpatient - Day case		Inpatient - Overnight case			Specialist staffing (specify) e.g. Specialist Nurses	Provision of MRT services
		PET scan	Gamma camera	Practitioner	Employer		Gamma camera	Dosimetry software	Radiopharmaceutical Ordering	Radiopharmaceutical Receipt	Radiopharmacy Manufacturing	On site draw up – isolators/LFC/safe cabinet/carbon filter extraction		Shielded uptake rooms	Hot toilet access	Shielded room	Hot toilet access	In-patient suite availability		
Level 2																				
I-131 Radioiodine (Thyroid Cancer) (Inpatient)	**β, γ**			**x**	**x**	**x**	**x**		**x**	**x**		**x**	**x**			**x**	**x**	**x**	**x**	
VCC				x	x	x	x		x	x		x	x	x	x	x	x	x	x	**X**
SWWCC				x	x	x	x		x	x		x	x			x	x	x	x	**X**
NWCTC				x	x	x	x		x	x		x	x			x	x	x	x	**X**
Ra-223 Radium Chloride (Prostate Cancer)	**α, β, γ**			**x**	**x**	**x**			**x**	**x**		**x**	**x**				**p**	**p**	**x**	
VCC				x	x	x			x	x		x	x				p	p	x	**X**
SWWCC				x	x	x			x	x		x	x				p	p	x	
NWCTC				x	x	x			x	x		x	x				p	p	x	**X**
Lu-177 dotatate/dotatoc/dotanoc (Neuroendocrine malignancy)	**β, γ**	**Ga**[14]		**x**	**x**	**x**	**x**	**x**	**x**	**x**		**x**	**x**	**x**	**x**	**p**	**p**	**p**	**x**	
VCC				x	x	x	x		x	x		x	x	x	x	p	p	p	x	

[14] Each patient requires an octreotide gamma camera or gallium-68 PET scan. Currently, Ga PET scans are not available in Wales.

Green squares indicate active capability; Amber squares highlight no onsite core service capability and/or limited onsite capability – risks attached and requires action/monitoring. Red squares denote nil capability – service risks attached and requires corrective action.

SWWCC						x	x	x	x	x		x	x	x	x	p	p	p	x	
NWCTC			x			x	x		x	x		x	x			p	p	p	x	

6.4 Overview of Existing MRT Services at the North Wales Cancer Treatment Centre

The North Wales Cancer Treatment Centre (NWCTC) currently provides well established I131 Radioiodine and Ra223 Radium services for BCUHB patients, represented in **Tables 4 and 5**. Low and high dose I131 treatments for thyroid cancer are provided as inpatient services with a dedicated inpatient suite with ante-room, patient room and ensuite located on the main cancer ward. Ra223 treatments are batched monthly as an outpatient treatment session. Administration levels are manageable, however current infrastructure, mobile PET and staffing levels are a limiting factor to developing services beyond current levels.

6.5 Overview of Existing MRT Services at the Southwest Wales Cancer Treatment Centre

The Southwest Wales Cancer Centre (SWWCC) currently provides I131 Radioiodine services for both benign thyroid disease and thyroid cancer, represented in **Tables 3, 4 and 5**. The service is delivered via a dedicated outpatient room in NM2 building with an ensuite room (room 7, ward 11) also available to I131 patients. Administration levels are manageable, however current infrastructure, mobile PET and staffing levels are a limiting factor to developing services beyond current levels.

SWWCC are in the process of repatriating Ra223 service from Bristol[15]. Both areas of work are being progressed by respective CCs with support and advice from the AWMOL, MRT programme, NWJCC and respective boards/trusts, as required

6.6 Overview of Existing MRT Services at the Velindre Cancer Treatment Centre

VCC provides I131 Radioiodine (thyroid cancer (high dose)) and Ra223 Radium Chloride services with the agreement to repatriate 177Lu dotatate services from London Royal Free to VCC for treatment of neuroendocrine tumours (NETS)[15] and the ambition to participate in future STAMPEDE 2 trials for 177Lu PSMA.

I131 Radioiodine service is delivered via two dedicated private ensuite treatment rooms explicitly used for I131 Radioiodine (thyroid cancer) patients. Ra223 Radium Chloride (prostate cancer) is currently delivered in a dedicated injection room within the main Nuclear Medicine (NM) department with access to a NM toilet, which is also used by diagnostic patients. There is an ensuite ward based room suitable for delivery of Lu177 dotate which would allow day case or inpatient treatment. There is no radiopharmacy to produce radiopharmaceuticals onsite at VCC, however there are facilities for dispensing which includes a 'Hot lab' room.

[15] Both areas of work are being progressed by respective CCs with support and advice from the AWMOL, MRT programme, WHSSC and respective boards/trusts, as required.

Future MRT services to be clinical oncology medical led within the NM department at VCC. Radiologists with expertise in NM for diagnostic imaging for treatment verification are in post, and the delivery of treatments undertaken by NM with CNS support.

The new VCC estate (expected in 2028) will provide more space and capacity. The estate is not deemed to be a limiting factor. It will include five multipurpose shielded day case therapy rooms with ensuite toilet facilities. When not operational, these rooms can be decontaminated and returned for use by non-NM patients. Furthermore, admissions would be possible, if required.

6.7 Existing funding arrangements

I131 and Ra223 treatments are long standing and not considered "specialised", therefore they have been funded through local commissioning arrangements at Health Board/Trust Level. Lu177 dotatate is commissioned by the NHS Wales Joint Commissioning Committee (NWJCC).

6.8 Existing leadership and decision making

Current leadership and decision making regarding MRTs is done on a local level, at each Cancer Centre.

6.9 Manufacture and supply of radiopharmaceuticals

It is a basic property of a radionuclide that it decays over time, at a set rate, described by its half-life. For a radiopharmaceutical compound this correlates precisely with therapeutic activity and therefore clinical utility. The workstreams considered the complexity of manufacturing and handling requirements of therapeutic radiopharmaceuticals. Each new agent will vary in half-life and have its own unique time-sensitive supply chain.

6.10 Existing workforce

Staff involved in the administration of MRT products are nurses, physicists, clinical technologists, oncologists and nuclear medicine physicians. The Medical Physics Expert (MPE) role is a legal requirement, especially for preparedness of 'new' MRTs. These positions need to be on-site during service delivery.

To be able to administer radioactive substances to patients, there needs to be:

- an IR(ME)R Employer Licence, that includes the relevant procedure, specifically for the site at which the administrations will take place, and
- at least one clinician with an IR(ME)R Practitioner Licence that includes the relevant procedure.

These are commonly referred to as ARSAC licences. Both licences are obtained by application to the Administration of Radioactive Substances Advisory Committee (ARSAC). To be successful, applications will need to demonstrate adequate facilities, procedures

and support staff (Employer Licence) and knowledge, training and experience (Practitioner Licence). The formal process of training, registration and supervision can take many months and different MRTs require a differing number of cases to be observed. It is more difficult if the supervision takes place in a distant centre.

Workforce considerations extend beyond the focus on the Clinical Practitioner license holder. There are likely to be opportunities for extended roles within a functioning MRT service. The roles involved in the MDTs and delivery of MRT include:

- Referring clinicians,
- Clinicians with Practitioner ARSAC license,
- Clinical scientists,
- Nurses,
- Clinical technologists
- Medical Physics Experts (MPEs) specialising in Nuclear Medicine

A list of workforce competencies required to deliver MRT can be found in **Figure 7**. Furthermore, an approximation of whole-time equivalents (WTEs) and roles for MRT service delivery on a site is described in **Table 6**. Please note this is an outline of workforce requirements and there will be variation at each site.

Figure 7. List of workforce competencies required to deliver MRT[16]

Dashboard of competencies to deliver molecular radiotherapy within a networked hub centre

Person matched to role	Nuclear Medicine Specialist	Clinical oncologist	Radiologist*	Interventional radiologist**	Medical Physics expert	Specialist nurse
Patient selection	C	C	E	E	N/A	N/A
Theragnostic Imaging	C	N/A	E	E	Anc	Anc
Dosing	C	E	N/A	E	C	N/A
Safe administration	C	C/E	N/A	C	C	C
Dosimetry	Anc	Anc	Anc	Anc	C	N/A
Post treatment care	E	C	N/A	C/E***	C	C

Legend. C=Core competencies in higher specialist training, E= extended role competencies, C/E a mixture of both core and extended competencies. Anc= Useful ancillary role. N/A not applicable
*This would be a non nuclear medicine trained radiologist. ** Required for safe local administration of molecular radiotherapy, *** May be limited to interventional procedure aspects only

[16] J. Buscombe Clinical Oncology 33 (2021) 137e143

Table 6 – Potential staffing requirements identified for future MRT service delivery per delivery site

Role	Band	Service baseline requirements on site (WTE)	All Wales baseline requirements on site (WTE)
Administrator	Band 3	0.5	1.5
Clinical Technologist	Band 7	1.5	4.5
Specialist Nurse	Band 7	1.0	3
Clinicians with Practitioner license	Consultant Oncologist	0.5	1.5
	Consultant Nuclear Medicine Physician	0.5	1.5
Medical Physics Expert (specialising in Nuclear Medicine)	Band 8c	1.0	3
Other Clinical Scientist	Band 7	1	3
	RPA Band 8a	0.3	
Radiopharmacist	(unknown)	0.05	0.15
Diagnostic nuclear medicine staff	Band 5	0.5	1.5

6.11 Personalised dosimetry

To optimise MRT, it is advantageous to know what absorbed doses will be, or have been, delivered by the treatment. This is important as it ensures that the maximum doses are delivered to the diseased cells, e.g., tumour sites, and that doses to organs at risk are minimised. In theory this allows treatment planning, in the same way as for external beam radiotherapy and, indeed, IR(ME)R requires that all radiotherapeutic exposures are "individually planned and their delivery appropriately verified"

However, there are challenges with this. Unlike external beam radiotherapy, it is not possible to selectively control the radiation doses since the dose delivered to a particular volume depends on the uptake and residence time of the radiopharmaceutical, which is administered systemically. All that can be done to control doses overall is to alter the administered activity. Also, pre-treatment planning is difficult as the uptake and residence time can only be known after the radiopharmaceutical has been administered – unless there is a diagnostic 'version' of the MRT agent, i.e. the same molecule but labelled with a radionuclide that emits radiation that can be imaged prior to therapy with a gamma camera or PET scanner ('theranostics').

Some MRT agents do allow for gamma camera imaging after therapy and this allows the possibility of post-therapy verification and, potentially, dosimetry. Although such

dosimetry is strictly speaking only providing information on the absorbed doses to tissues from that treatment, in the case of treatments involving sequential administrations, the information gained could be used to adjust future 'fractions' to either maximise doses to disease sites or to restrict doses to normal tissues at risk from radiation.

Currently, however, the majority of MRT treatments are not planned according to the radiation doses delivered and the absorbed doses delivered at therapy are seldom calculated. This prevents personalisation and optimisation of treatment dosimetry.

Where possible, individualised MRT treatment planning should be routine practice[17]. However, this will require investment in terms of appropriately trained personnel, dosimetry software and nuclear medicine imaging capacity. Furthermore, the degree of investment will depend on the dosimetry protocol used, i.e., the number and nature of sequential scans, which determines the accuracy of the dosimetric results.

6.12 Service needs

There are several challenges within existing arrangements that mean over the long term it will prove increasingly difficult to be prepared for delivery of future MRT agents, so that patients in Wales can benefit from these novel and effective treatments.

A key driver for the MRT Programme was the need to plan and prepare for Lu177 PSMA[8]. However, after three NICE technology appraisals in 2022-23, it was not approved, within its marketing authorisation, for treating metastatic prostate cancer in adults.

Whilst the urgency of preparing for Lu177 for mCRP has waned, it has, nevertheless, provided critical learning for AWMOL and raised awareness, for the need to be prepared for future MRT agents coming online.

The NIHR IO horizon scan outlines that there is just one MRT due to be appraised by NICE soon. The likely timeline for phase 3 and phase 4 clinical trials to conclude is 2026 and beyond.

Indeed, when considering these timelines, the immediate lack of urgency around MRT service delivery and development risks complacency. There is significant complexity in preparing for an MRT service and the impact of standing still in this field will prove detrimental – becoming more static, driving forward inequity, increasing variance and reliance on NHSE providers for treatments that should be delivered in Wales.

Therefore, it is proposed that momentum is maintained in getting prepared for the future MRT agents. This will be enhanced by active engagement in the research environment, which will serve both preparedness and enhance staff and patient experience.

[17] Davis et al., 2023 https://doi.org/10.1016/j.ejmp.2023.103154

The main challenges include:

- Lack of preparedness and infrastructure to deliver future new MRTs, including:
    - Diagnostics
    - Facilities
    - Dosimetry
- To scale-up and to deliver future therapies would require additional staff. Workforce is a constraint, in particular long term technical and medical support.
- There is a limited provision of active RD & I surrounding MRTs in Wales.
- Current facilities and infrastructure limit the ability to broaden RD&I opportunities.
- There is a need for clear leadership and structured collaborative working, where up-to-date information regarding new agents and local site preparedness can accommodate effective service planning and commissioning.
- There is a limited mix of legacy funding streams and commissioning arrangements, thus there is a need to align, where possible, and to agree a commissioning statement for MRT in Wales.
- There is a need to ensure equity and standardisation of services.

These service needs are explored in greater detail in relation to each of the three objectives.

Objective 1: To improve the preparedness of NHS Wales for new and upcoming MRT service provision for Welsh patients.

As with all new specialised services it takes time to develop and grow capability and capacity, particularly when developing a national approach to commissioning niche services. The last eighteen months have been invaluable - giving the all Wales group of MRT experts the space to enhance their understanding and knowledge of extant and new MRT therapies; strengthen connections with Health Boards, Trusts and other organisations; create the AWMOL group and MRT programme; establish strategic lines of communication with the Clinical Oncology Sub Committee (COSC) and Welsh Scientific Advisory Committee (WSAC); and advocate the case to NWJCC and WGov for increased MRT ambition and services in Wales.

There are several areas of work that can be progressed to accelerate and enable future roll-out of novel MRTs. In essence, up front and early planning and investment will enable NHS Wales to realise the longer term benefits of experience, resilience and economies of scale when scaling up to deliver additional, new commissioned agents (see below **Table 7**).

Table 7 – Recommendations aligned with need and areas of develop to enable future MRT services in Wales

Area	Need	Recommendation
Leadership and decision making	To date, there has been an inordinate amount of positive dialogue and debate which needs to be harnessed and captured under agreed lines of responsibility so that, post programme, there is an all Wales MRT decision making process in place that supports and accelerates, as required, the development and implementation of future MRT commissioned services in Wales.	It is recommended that organisational responsibility and an accompanying process for assessing, commissioning and provisioning MRT in Wales (AWMOL, NWJCC, Cancer Network) is developed and formalised. It is recommended that AWMOL remains as an advisory group and the recommendations put forward in this document are taken on as the workplan.
Evidence base and informed	There is a need to put in place mechanisms to ensure that live horizon scanning is maintained, so that commissioners and local sites are informed and prepared for upcoming agents and NICE appraisals.	It is recommended that horizon scanning is built into the process mentioned above and is maintained on the agenda for all future AWMOL meetings.

Funding arrangements	There is a need for future new MRT agents funding proposals, including the live proposed VCC business case to repatriate Lu177 dotatate, to be undertaken via the NWJCC process.	It is recommended that long-standing I131 and Ra223 treatments remain at Health Board commissioning level. It is recommended that future commissioning processes consider that that these novel interventions will likely require additional infrastructure costs relating to new service start-up.
Workforce	The number of staff within the nuclear medicine community appropriately trained in MRT needs to be increased and research time needs to be protected. This includes clinicians, clinical scientists, technologists, nurses, and radiopharmacists. The ordering, receipt and administration processes are to be managed by suitably skilled personnel. Indeed, lack of an appropriately qualified and trained ARSAC license holder for any agent offers a single point of failure for MRT service provision at a site.	It is recommended that funding for training is identified and allocated so that ARSAC licence holders and other staff members in the MRT delivery team are appropriately trained. It is recommended that this funding is held nationally and allocated equitably across Wales. It is recommended that information from live horizon scanning feeds into planning for training and that this is done in advance of NICE appraisal publication dates, so that readiness is suitable. This is with a view that obtaining the appropriate ARSAC license ahead of NICE approval provides flex and permits incremental scale-up of delivery.
MRT agent supply*	Early engagement with manufacturers, procurement and learning from other providers' experiences to fully understand the end-to-end supply chain will be key to assuring service provision and business continuity.	It is recommended that the future AWMOL group sets out a mechanism through which they can engage with the manufacturers of novel MRT agents, so that their networks and facilitative offerings can be utilised effectively in Wales.
Facilities	Given the radioactive nature of MRTs, there are special requirements to permit safe handling, storage and administration. These are listed in detail within the NWJCC draft MRT service specification. There is a need for these requirements to be assessed by each site within Wales, when considering if they can/will deliver a novel MRT therapy. There is a need for up front review of existing facilities, so that pre-planned activities can be identified and routes to funding sought.	It is recommended that each Cancer Centre plans for their facility needs through local routes for funding, summarised in **Tables 4** & **5**. This should be supported and sighted at AWMOL, so that any joint working or learning opportunities can be sought.
Use of diagnostic imaging	Any novel MRT agent that is commissioned will impact on surrounding diagnostic and follow-up scanning.	Future consideration – essential for future commissioning and planning for service delivery.

	There is a need for this allocation to be considered at planning phase and for the services impacted by increased demand to be involved in discussions surrounding patient pathway planning.	
Dosimetry	There is a need for novel MRT agents to be considerate of any accompanying recommendations surrounding personalised dosimetry within the NICE Guidance.	Future consideration – essential for future commissioning and planning for service delivery.
Information Technology	There is a need for each Cancer Centre to identify any additional software or hardware that may be required to deliver novel MRT agents, such as personalised dosimetry software.	Future consideration – essential for future commissioning and planning for service delivery.
Standardisation and data collection	There is a need to plan up front so that PROMS and PREMS can be appropriately considered to inform future service delivery.	Future consideration – essential for future commissioning and planning for service delivery.
Local planning	Inclusion of MRT provision within respective ICP, IMTPs	Raise awareness at local site level of the potential requirements for IMTPs.

* *In the main, therapeutic radiopharmaceuticals will be purchased and manufactured in the EU and transported to the UK, as per regulations and agreed delivery schedules. The group adopted a balanced view in that it assumed new agents will be transported and delivered in ready-to-use vials which negates the requirements for local radiopharmacies. The ordering, receipt and administration processes are to be managed by suitably skilled personnel. The half-life for I131 8.02 days and Lu177 6.65 days have been used as a comparison of new agents, as identified in the horizon scan. Each agent will have its unique transport and handling requirements; however, the half-life data will help commissioners and providers to prepare and plan future supply solutions for new agents.*

Objective 2: To improve NHS Wales capability for MRT service delivery, which includes establishing research, development and innovation infrastructure

The value of research in transforming health and care is significant; additionally, staff satisfaction, recruitment and retention is higher among staff who are involved in research[18] . In support, a clear research thread runs through WGov strategies and plans.

Research is essential for advancing healthcare and contributes significantly to policy, practice, and the well-being of individuals and communities in Wales. Health and Care Research Wales (HCRW) has outlined its plan for improving health and care research in Wales from 2022 to 2025[19]. This plan aims to build on the legacy of research during the COVID-19 pandemic and drive improvements in health and social care research. The plan emphasises the importance of research that is of the highest international scientific quality, relevant to the needs and challenges in Wales, and capable of making a difference to policy and practice. It sets out actions to achieve better outcomes for patients, people, and communities across Wales.

Ensuring the infrastructure and process to support R&I activities are in place will enable clinical trials to open in Wales. This will support Patient's early access to care and potentially allow commercial income from MRT research, while also supporting cost recovery targets.

Indeed, setting out an MRT trials portfolio in Wales and contributing to development of consensus guidelines would bring multiple benefits to the Welsh Cancer Centres, Welsh patients, staff, reputation, and the Welsh economy. Additionally, the infrastructure involved in the set-up of clinical trial participation would be directly linked and contributory to the preparedness for MRT in Wales (Objective 1).

[18] https://www.england.nhs.uk/long-read/maximising-the-benefits-of-research/
[19] Research matters: our plan for improving health and care research in Wales 2022 - 2025

In 2016, National Cancer Research Institute (NCRI) published a paper on the opportunities present for research in MRT in the UK[20]. It set out several recommendations, such as:

- Multicentre phase III clinical and early phase studies in MRT are needed to gather clinical evidence and to optimise treatment protocols. These will ideally be academically led.
- A national database and consistent coding should be established to record MRT treatment, dosimetry and outcome data and so assess therapeutic efficacy of existing and new treatments.
- A national quality assurance group to deliver full quality assurance (QA) in MRT trials should be established. The steps and resources necessary for incorporating QA in MRT trials should be evaluated.

Within Wales there are currently no MRT trials underway due to lack of infrastructure and staff capacity and enabling this will ensure Welsh patients are represented in research.

Table 8 – Recommendations aligned with need to establish research, development and innovation infrastructure

Area	Need	Recommendation
Research into how MRT treatment can be optimised[21]	The majority of MRT treatments are not planned according to the radiation doses delivered and the absorbed doses delivered at therapy are seldom calculated. This prevents personalisation and optimisation of treatment and is potentially in contravention to the forthcoming EU Directive on basic safety standards for protection against the dangers arising from exposure to ionising radiation. UK centres need to be equipped for the change, and this provides a research opportunity[22].	It is recommended that protected time for research is granted to develop dosimetry-based treatment planning. Investment is necessary to support projects focused on optimisation and standardisation of dosimetry protocols. For example: It is recommended that research students are taken on, where available, to progress the research in the use of commercial dosimetry software. This should be done across organisational barriers wherever possible. Consider offering short research projects to MSc. Students from the Medical Radiation Physics course in Swansea University and BSc. students from the undergraduate Physics with Medical Physics course at Cardiff University.
Engage with commercial and academic partners/ sponsors	There is a need to put in place mechanisms to ensure that opportunities to be involved in clinical trials for MRT agents are taken in Wales.	It is recommended that AWMOL and its members continue to engage with commercial and academic partners and Sponsors, with a view to bring forward opportunities to AWMOL.

[20] https://www.ncri.org.uk/wp-content/uploads/CTRad-promoting-research-in-MRT-UK-June-2016.pdf
[21] Recommendations for Multicentre Clinical Trials Involving Dosimetry for Molecular Radiotherapy (clinicaloncologyonline.net)
[22] https://www.clinicalkey.com/#!/content/playContent/1-s2.0-S0936655520304465?scrollTo=%23bib9

Engage with devolved and other nations	There is a need to put in place mechanisms to ensure that opportunities to be involved in wider planning and engagement are taken.	It is recommended that AWMOL and its members continue to engage with partners and cross-border organisations, with a view to bring forward opportunities and updates to AWMOL. For instance, the UK MRT Consortium.

Objective 3: To focus on reducing variance in MRT service provision

Area	Need	Recommendation
Ensuring an equitable service	There is clear ambition and appetite to deliver enhanced and new MRT services across all three CCs. There is a need to address variation to existing and future MRT services.	It is recommended that equity and reducing variance is adopted as a working principle for all future workplans of AWMOL.

Conclusion

Although there is no immediate urgency, applying learning from the recent NICE review of Lu177 PSMA leads to the conclusion that we cannot stand still. We have a unique opportunity to "get ahead" of this scenario, where there is a clear pipeline of future MRT agents that will come into routine practice and an unmet need in terms of workforce planning and infrastructure.

The key recommendation from this collaborative report is that an all-Wales approach is maintained and that is work is continued in this area, so that Wales stands prepared and informed for the future. The primary avenue to succeed at this aim is to maintain the AWMOL group, with a refreshed scope for work to continue in a structured manner - taking on the recommendations within this paper as an active workplan.

With a requirement to focus on developing and training the Welsh workforce, in addition to attention on research, development and innovation, there may be future requirements for funding to support these aims.