



Health system readiness for radioligand therapy in the UK

SITUATION ANALYSIS REPORT

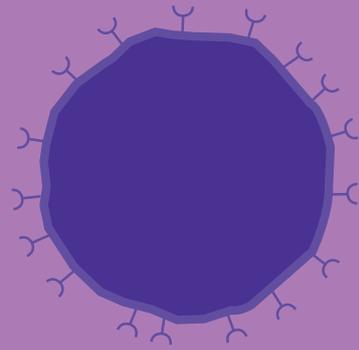


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The
**Health Policy
Partnership**

[research, people, action]



ABOUT THE RADIOLIGAND THERAPY READINESS ASSESSMENT PROJECT

This report was developed by The Health Policy Partnership in collaboration with a UK Expert Advisory Group. It is part of a broader piece of work aiming to define what is needed to establish system-level readiness for radioligand therapy in the UK. It is supported by other documents, including a policy action blueprint on health system readiness for radioligand therapy in the UK and an associated national framework. For more details, please visit www.radioligandtherapy.com

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ABOUT THE HEALTH POLICY PARTNERSHIP

The Health Policy Partnership (HPP) is an independent research organisation, working with partners across the health spectrum to drive the policy and system changes that will improve people's health.

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THIS REPORT IS ENDORSED BY:



Foreword

Radioligand therapy is a highly targeted and precise approach to cancer care. It has been shown to significantly improve survival and quality of life for people with certain neuroendocrine cancers, among other cancers. It is a rapidly developing therapeutic approach, with new applications on the horizon in prostate cancer, lymphoma and other cancers.

As the number of people who would benefit from radioligand therapy is likely to increase exponentially over the next decade, existing services urgently need to be evaluated and scaled up appropriately. Current integration of radioligand therapy into cancer care in the UK is far from optimal. Access is dependent on where a person lives in the UK, and some people with neuroendocrine neoplasms are having to travel over 200 miles to get treatment. There must be equity of access to both established types of radioligand therapy and new types likely to be available soon. Without appropriate planning and policy change, existing gaps in reimbursement, workforce and infrastructure will become even bigger barriers in years to come. The UK is not yet ready for the future of radioligand therapy as a core component of cancer care.

To ensure that radioligand therapy is available to all people who might benefit from it, we need a multi-sectoral systems approach to its integration, alongside proactive planning and investment. This report aims to clarify the overarching challenges and opportunities for greater integration of radioligand therapy into practice, both now and in the future. It provides valuable insight into where policy change is needed, with the way forward presented in the policy action blueprint, *Creating a ready health system for radioligand therapy in the UK*. We hope that these materials act as a catalyst in health policy discussions and planning for radioligand therapy, and ultimately contribute to a shared vision of health system readiness as we look to the future of cancer care.

We cannot ignore that the NHS has been put under tremendous pressure as a result of the COVID-19 pandemic and Brexit, exacerbating the existing gaps and challenges in cancer care and healthcare more generally. But we must use this as an opportunity to ‘build back better’, learning from the past and keeping patient needs at the heart of decisions that shape the future of the NHS. As radioligand therapy is a truly multidisciplinary approach, no one group alone can realise its full potential. We must all work together to ensure that we are ready to sustainably deliver high-quality, innovative cancer therapies, such as radioligand therapy, now and in the future.

Dr John Buscombe,
Barts Health NHS Trust

Nikie Jervis,
Neuroendocrine Cancer UK

Executive summary

Radioligand therapy is a highly targeted cancer therapy.

A radioligand is made of two parts: a ligand, which is able to find cancer cells that present a particular receptor, and a radioisotope, which is able to treat the cancer.^{1,2} Radioligands find and deliver radiation directly to cancer cells, regardless of where these cells are located in the body.

Radioligand therapy has been shown to significantly improve survival and quality of life for people with certain types of neuroendocrine neoplasms (NENs), lymphoma and prostate cancer.³⁻⁸ Unlike conventional cancer therapies, radioligand therapy's targeted interaction with cancer cells leaves healthy cells largely unaffected, reducing treatment side effects.^{9,10}

In the UK, radioligand therapy is licensed for use in NENs and lymphoma. The therapy is also under investigation for use in other types of cancer and will require system changes for its delivery in larger patient populations in the future.

The UK needs to be ready for the wider use of radioligand therapy. Planning for expansion of the approach requires multidisciplinary and multi-sectoral collaboration. Everyone involved in cancer care must work together to actively integrate radioligand therapy into all areas of the health system to ensure that it is available to all people who could benefit from it.

THE UK WILL NEED TO COMMIT TO:

- **greater recognition and leadership for radioligand therapy** to drive proactive planning and investment
- **enhanced and expanded data collection systems** to inform and support appropriate funding, reimbursement and resource planning for radioligand therapy
- **embedding of radioligand therapy into current professional training and licensing practices** to enable sufficient workforce capacity to deliver the therapy as it expands to new applications and patient populations in the future
- **clear clinical guidelines and national care pathways** to facilitate referrals and optimal sequencing of radioligand therapy, and to ensure all people who could benefit are offered it as a therapeutic option
- **secured logistics and infrastructure for radioligand therapy** so that procurement and delivery are timely and effective
- **scaled up and equitable access to radioligand therapy** to guarantee its appropriate delivery to patient populations of all sizes and needs.

This report aims to support policymakers, decision-makers and the wider cancer community in taking action to build readiness for radioligand therapy in the UK.

Introduction

What is radioligand therapy?

Radioligand therapy is a highly targeted cancer therapy. A radioligand is made of two parts: a ligand, which is able to find cancer cells that present a particular receptor, and a radioisotope, which is able to treat the cancer (*Figure 1*).^{1,2} Radioligands find and deliver radiation directly to cancer cells, regardless of where these cells are located in the body. The mechanism by which radioligand therapy works is not specific to any particular tumour type, therefore the therapy could be applied to cancers where a suitable receptor is identified.

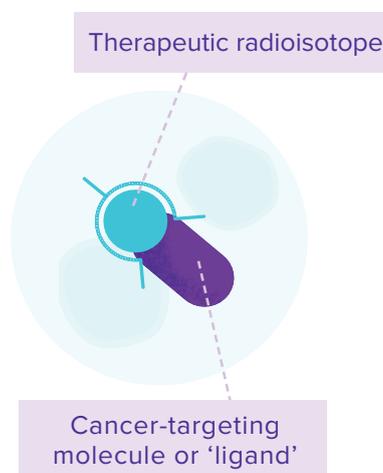


FIGURE 1. Radioligand

Radiopharmaceutical therapy, of which radioligand therapy is a subtype, is well established in cancer care.

It has been a core component of thyroid cancer care in the UK for over 70 years,^{9,11} and has an established role in the management of bone metastases.^{9,12} Radioligand therapy builds on this foundation, moving from organ-level to cellular-level precision.

Radioligand therapy has been shown to significantly improve survival and quality of life for people with certain types of cancers.

The approach has demonstrated markedly longer progression-free survival and improved health-related quality of life for people with certain types of neuroendocrine neoplasms (NENs), lymphoma and prostate cancer.^{3,4,6,7,10,13} It has also been shown to increase the proportion of people with lymphoma who achieve complete remission and improve overall survival for people with prostate cancer.^{8,13} Unlike traditional cancer therapies, radioligand therapy's targeted interaction with cancer cells leaves healthy cells largely unaffected, thereby reducing side effects of treatment.^{1,9,10}

This document uses the term radioligand therapy, but there are various terms used for the approach, including molecular radiotherapy, peptide-receptor radionuclide therapy (PRRT), systemic radiation therapy, targeted radionuclide therapy and targeted radiotherapy. If the ligand used is an antibody, the approach is known as radioimmunotherapy.

Use of radioligand therapy

Radioligand therapy is currently licensed by the Medicines and Healthcare products Regulatory Agency (MHRA) for use in certain types of NENs and lymphoma. The National Institute for Health and Care Excellence (NICE) has given positive guidance for use of radioligand therapy in the same types of NENs.¹⁴ NICE has not assessed its use in lymphoma,¹⁵ where it is seldom used in practice.¹⁶

The incidence of both NENs and lymphoma is rising in the UK.

Over 5,000 people are diagnosed with NENs each year, and incidence is increasing.¹⁷ Upwards of 16,000 people are diagnosed with a type of lymphoma every year.¹⁸⁻²⁰ The rising number of people with NENs and lymphoma may translate into a growing use of existing radioligand therapy approaches.

Radioligand therapy is under investigation for use in multiple other clinical indications and will require new models for its delivery in larger patient populations in the future.

The therapy is being investigated for use in indications including metastatic castration-resistant prostate cancer (mCRPC), metastatic breast cancer and cancers of the central nervous system (see *Appendix*).²¹⁻²⁵ These cancers are more common than NENs and affect much larger patient populations, necessitating consideration of future readiness and new models of delivery for the approach.

Radioligand therapy could significantly change care for men with prostate cancer. The therapy is precise and can be personalised, allowing us to select the people who can truly benefit from it.

PROFESSOR HEATHER PAYNE
University College London Hospitals

Preparing for the future: taking a systems approach

Planning for future uses of radioligand therapy

The UK needs to be ready for the wider use of radioligand therapy in the future. The expanding application of the approach to more cancers and larger patient populations raises questions around how it can be funded and delivered effectively and in a timely manner. Preparing the health system for radioligand therapy sets a precedent for integrating new, innovative cancer therapies into clinical practice. It also supports NHS England's ambition for every person diagnosed with cancer to have access to personalised care, and reinforces the UK's position at the forefront of innovation.²⁶

Healthcare in the UK is undergoing significant changes, with Brexit and NHS England reforms potentially having considerable impact on the way medicines are regulated, transported and delivered to patients. Following Brexit, the European Union's regulatory frameworks for cancer medicines no longer apply to the UK. As a result, the MHRA is now the only relevant medicines regulator for products being used in the UK,²⁷ which has important implications for the approval of future radioligand therapies, as well as their transportation. NICE's strategy for 2021–2026 prioritises faster evaluation of innovative technologies and may facilitate swift evaluation of new radioligand therapies.²⁸ Recently announced reforms to NHS England, which aim to reconfigure the organisation of care to improve integration between settings,^{29 30} may also positively impact radioligand therapy by enhancing multidisciplinary working among the many specialties involved in its delivery.

Ensuring system readiness for radioligand therapy

Planning for radioligand therapy requires a multidisciplinary and multi-sectoral approach. By nature, delivering radioligand therapy safely and effectively necessitates engagement from a number of different medical disciplines and sectors, forming a holistic approach. As the therapy is expanded to new applications, further disciplines will also need to be involved.

Establishing readiness for the integration of new radioligand therapies is an essential step in improving cancer care and, ultimately, patient outcomes. Readiness for radioligand therapy means the necessary people, policies, processes, infrastructure and resources are in place to facilitate its adoption into clinical practice in a timely manner (*Box 1*). These components must have sufficient flexibility to ensure that the approach can be integrated in the most effective way within an ever-evolving context.

BOX 1.



What do we mean by integration and readiness in the context of radioligand therapy?

Integration is the adoption and assimilation of radioligand therapy into every aspect of a health system (i.e. governance, regulation, reimbursement and service delivery frameworks) in order to ensure its availability to all people who may benefit from it.

Readiness is the ability of the health system to rapidly and sustainably adapt policies, infrastructure and processes to support integration of a new radioligand therapy.

Understanding these different components of readiness requires a systems approach. To this end, we have developed a readiness assessment framework for radioligand therapy.³¹ It allows us to investigate what is required to plan for integration of radioligand therapy into the UK health system, built around five domains of cancer care: governance, regulation and reimbursement, identified need, service provision and health information.

This document outlines the policy barriers and opportunities for the better integration of radioligand therapy within cancer care in the UK, today and in the future. It provides a comprehensive summary of the current integration of radioligand therapy, looking specifically at NENs, lymphoma and prostate cancer, and clarifies the necessary system-level components that need alignment to ensure readiness for the approach. We hope it will support policymakers, decision-makers and the wider cancer community in understanding which areas of the health system require policy action for better integration of radioligand therapy into cancer care in the UK.

Integration and readiness for radioligand therapy: potential barriers and opportunities

1



Recognition and leadership

2.



Data collection and analysis

3.



Professional training and licensing

4.



Clinical guidelines and care pathways

5.



Logistics and infrastructure

6.



Equitable access



Recognition and leadership

Awareness and understanding of radioligand therapy are insufficient among people with cancer who could benefit from it. Demand for novel therapies is frequently driven by people with cancer who are knowledgeable about and eligible for a particular therapy. In the UK, information on radioligand therapy for people with lymphoma is very limited. Patient-facing information about NENs is more commonly available, but rarely fully explains when the approach may be provided.³²⁻³⁶ In addition, there are many terms used for radioligand therapy, which makes it difficult to establish awareness and a common understanding. Clear and consistent patient information materials are needed to improve knowledge of radioligand therapy among people with cancer, so that they may ask about it in the context of their own care. These materials should be effectively disseminated by patient organisations and patient forums. The British Nuclear Medicine Society and the UK and Ireland Neuroendocrine Tumour Society (UKINETS) are currently working to develop a comprehensive patient information sheet for people with NENs.³⁷

Knowledge of radioligand therapy is generally limited outside of neuroendocrine tumour and nuclear medicine communities.

Widespread clinical recognition of radioligand therapy and its potential in cancer care is important as it means the approach can be considered as a therapeutic option for eligible patients. Currently, nuclear medicine physicians and other physicians with experience treating people with NENs have good awareness of radioligand therapy.³⁸

Greater recognition of the approach is needed among all members of the lymphoma and prostate cancer multidisciplinary teams, to ensure it can be appropriately considered in these indications. To improve understanding of the approach among healthcare professionals, the British Nuclear Medicine Society is contributing knowledge, advice and best practice on radioligand therapy to England's Learning Healthcare System for radiotherapy, which commits to creating a shared culture of learning and improvement among stakeholders involved in healthcare.³⁹ A 2021 white paper from the Department of Health and Social Care outlines NHS changes aiming to support greater collaboration

To establish longevity for radioligand therapy, there needs to be continuous and evolving dialogue between nuclear medicine and all specialists involved in cancer care where radioligand therapy has potential for patients.

DR JOHN BUSCOMBE
Barts Health NHS Trust

across specialties.³⁰ Closer collaboration between all specialties involved would be an opportunity to improve awareness and understanding of radioligand therapy.

Minimal political recognition of the value of radioligand therapy in cancer care contributes to its limited integration into clinical practice.

Political understanding of the approach, its system-wide infrastructure requirements and its value for patients contributes to appropriate planning for its integration. However, policymakers have yet to actively engage in discussions on radioligand therapy and may not be fully informed about its potential benefits for people with cancer and the wider health system. Raising the political profile of radioligand therapy requires patient involvement, clinical buy-in and local leadership. There needs to be a long-term collaborative effort between all people involved in cancer care, precision medicine and health system innovation more generally.

Inclusion of radioligand therapy in national plans for cancer will be key to driving commitment and creating strategic direction for its integration into cancer care.

National plans for cancer outline ambitions and commitments to improve cancer services and outcomes. There is no specific reference to radioligand therapy for cancers in *The NHS Long Term Plan*, but the plan does commit to providing more personalised care and investing in safer and more precise cancer treatments.²⁶ This demonstrates recognition of the value of targeted, precise and personalised therapies for people with cancer.

Inconsistent and insufficient funding for radioligand therapy is an ongoing issue, but the UK's Health Technology Assessment programme may be useful in guiding reimbursement decisions for the approach.

There is increasing consensus among payers that medicines should be priced according to the added therapeutic value they deliver.⁴⁰ However, implementing value-based pricing is complicated by lack of available data,⁴¹ as is the case in radioligand therapy. For example, the Scottish Medicines Consortium did not recommend reimbursement of radioligand therapy in lymphoma due to insufficient evidence of its cost-effectiveness.^{15 42} More data in this area are emerging, with a recent

We have learned the hard way that there is a scarcity of funds for radioligand therapy. Without funding, there is no trained workforce or infrastructure to deliver this mode of therapy to patients who need it.

PROFESSOR JAMSHED BOMANJI

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NHS Foundation Trust

study indicating that the therapy may be cost-effective for NENs in Scotland.⁴³ Data generated by the National Institute for Health Research's Health Technology Assessment programme may also guide reimbursement decisions for NENs, lymphoma and prostate cancer.⁴⁴ Prospective evidence from large clinical trials on radioligand therapy in these cancers could be put through this programme. In addition, the upcoming reforms of the NHS²⁹ and NICE's strategy for 2021–2026²⁸ will likely have implications for funding and the broader provision of radioligand therapy.

Developing a strategic vision for radioligand therapy would encourage future readiness for the approach.

A powerful analogue is the UK's *Vision for Radiotherapy*,⁴⁵ which quantifies how many radiotherapy services should be made available to patients across the country in the future. It emphasises the importance of strong leadership, better public awareness and harnessing the power of data, and has stimulated the development of national plans, policies and service specifications. A similar national vision for radioligand therapy would serve as a useful foundation for expanding its availability and supporting its delivery in clinical practice.



To find out more, please refer to the working paper on governance



Data collection and analysis

Incomplete and inconsistent data collection on cancer makes it very challenging to plan for current and future integration of radioligand therapy into clinical practice.

National cancer data sets are inconsistent in terms of collecting information on disease stage, treatment outcomes and patient experience.⁴⁶⁻⁴⁸ Omission of these data points from cancer registries and clinical audits restricts our understanding of what proportion of the cancer population could benefit from radioligand therapy, today and in the future. Lack of real-world data on radioligand therapy also impedes our ability to assess its cost-effectiveness, which complicates decision-making around funding and reimbursement, and appropriate resource planning.

Minimal data collection on rare cancers is an issue for the wider integration of radioligand therapy into NENs care.

Data collection on NENs is low compared with more common cancers,^{49 50} and data are not collected systematically due to a lack of adequate resources and funding.^{51 52} This makes it very difficult to plan effectively for the better integration of radioligand therapy into NENs care.

To address this, the British Nuclear Medicine Society recently launched a national radioligand therapy registry in NENs⁵³ which, according to an expert, will collect information on patient demographics, diagnosis, previous treatments, radioligand therapy treatment cycle, side effects and outcomes.¹⁶ One expert noted that UK collaborations with Europe are essential to obtaining sufficient samples, resources and funding for data collection and analysis on NENs across Europe.⁵⁴ Following Brexit, the UK will continue to be involved in some initiatives, such as the European Neuroendocrine Tumor Society Registry, but it may no longer be able to participate in others, for instance in the European Reference Network for Rare Cancers (EURACAN).^{37 54} Although members of EURACAN have stated that a close relationship with the UK will continue in the interest of people with rare cancers,⁵⁵ it is currently unclear how this will be realised in practice.

Insufficient data are also collected on the workforce delivering radioligand therapy, hindering estimation of optimal workforce size and needs. Owing to insufficient data on the workforce involved in providing radioligand therapy, it is unclear how many healthcare professionals in the UK are trained and licensed to deliver the approach. However, experts have reported concerns about insufficient workforce capacity, especially with regard to nuclear medicine physicians and physicists, radiopharmacists, clinical nurse specialists and patient coordinators trained in radioligand therapy.^{38 54 56-61} The NHS People Plan commits to strengthening and growing the cancer nurse specialist workforce, which could act as an opportunity to increase capacity of cancer nurses involved in radioligand therapy.⁶² Similar opportunities should be created for other relevant specialties and roles.

Radioligand therapy spans many different specialties. Data are needed on workforce and training programmes to appropriately plan and be ready for radioligand therapy.

DR GLENN FLUX

Royal Marsden Hospital NHS Foundation Trust

Data collection efforts require sustainable funding. There may be opportunities to expand existing data sets to include data on radioligand therapy in common cancers. One relevant candidate is the Systematic Anti-Cancer Therapy (SACT) Dataset,⁶³ which is part of the Cancer Outcomes and Services Dataset (COSD),⁴⁶ but the challenges noted earlier would need to be overcome, and funding and dedicated workforce secured.

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To find out more, please refer to the working paper on health information



Professional training and licensing

There is limited training specific to radioligand therapy, leading to major concerns around not having sufficient workforce capacity to deliver the approach in the future.

Radioligand therapy is included in the nuclear medicine training curriculum,⁶⁴ but is absent from training curricula for referring physicians, clinical nurse specialists and patient coordinators.^{57 65-70} Healthcare professionals involved in care for NENs may become familiar with radioligand therapy through European guidelines and multidisciplinary working.⁷¹ However, other healthcare professionals may not have the appropriate knowledge to consider radioligand therapy as a possible therapeutic option for their patients, or to support patients and relevant staff throughout the process. Lack of funding for radioligand therapy training magnifies this gap, creating downstream effects on referrals, eligibility assessments and delivery of therapy. Medical training bodies and professional societies will need to update their training curricula in line with radioligand therapy approvals, and upfront funding should ideally be allocated to training programmes.

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To find out more, please refer to working paper on identified need

Formal radioligand therapy training is needed for all healthcare professionals, especially clinical nurse specialists, to support people with cancer as much as possible in making decisions about treatment.

NIKIE JERVIS

Neuroendocrine Cancer UK

Limited training may also lead to insufficient numbers of trained healthcare professionals having licences to administer radioligand therapy in the future.

The therapy's use of radioactive substances requires health practitioners to obtain licences issued by the Administration of Radioactive Substances Advisory Committee (ARSAC) to safely deliver the approach.⁷² However, extensive ARSAC training requirements may deter healthcare professionals from obtaining a licence. As of 2018, there were an estimated 1,100 clinicians who held ARSAC licences in the UK.⁷³ It is uncertain how many are involved in radioligand therapy but, according to experts, this proportion is very small and will be insufficient to meet future demand.^{38 74} COVID-19 restrictions on movement have meant that health practitioners have not been able to attend site visits, which are a required component for ARSAC licensing applications. ARSAC has not provided guidance on fulfilling in-person licensing requirements under these circumstances. It is important that ARSAC licensing procedures be adapted to facilitate and encourage uptake of licences, even during unprecedented events.

Allowing for greater flexibility for other professionals to play a role in nuclear medicine could be an important way forward.

Nuclear medicine physicians are typically responsible for administering radioligand therapy, as they hold an ARSAC licence. Medical oncologists may also hold ARSAC licences, although this is less common. Health Education England has recently invested in a training curriculum to support the annual conversion of five radiologists into the field of nuclear medicine,^{16 75} which means more people will have the necessary training for obtaining ARSAC licences. Similar courses should be developed to support the training of other healthcare professionals who may become involved in the administration of radioligand therapy.

The number of ARSAC licence holders needs to increase, and for that to happen, people need adequate training.

PROFESSOR NEIL HARTMAN

Swansea Bay University Health Board



Clinical guidelines and care pathways

Radioligand therapy is included in European guidelines for NENs and its use is well established in the UK; however, its inclusion in professional guidelines for lymphoma does not reflect its current use. ENETs guidelines,⁷¹ updated in 2017 and endorsed by UKINETS,⁷⁶ are the most frequently used guidelines in the UK. They provide comprehensive and up-to-date detail on the management of NENs and recommend the use of radioligand therapy in this indication.^{77,78} The British Society for Haematology recommended radioligand therapy in guidelines on the management of follicular lymphoma published in 2020,⁷⁹ but the approach is very rarely used in practice.¹⁶ NICE's 2016 guidelines for non-Hodgkin's lymphoma do not reference radioligand therapy,⁸⁰ as it had not been assessed for that indication.¹⁵ It is important that the most frequently used clinical guidelines are promptly updated as new therapies are licensed, to reflect the most recent and valid evidence, help standardise clinical practice and improve patient outcomes.

There is a lack of clarity in national care pathways regarding who should be referred for radioligand therapy and at what point in their care. There is no NICE pathway for NENs; however, the UKINETS 'bitesize' pathways provide good indication of when radioligand therapy should be considered for some types of NENs.^{81,82} Formal NICE endorsement of these pathways may help improve national consistency in use and availability of the therapy. While there are national NICE pathways for lymphoma and prostate cancer,^{83,84} it is unclear where radioligand therapy would sit within the care pathway, and when and for whom it may be used in the future. To help clarify the place of new treatments in the national prostate cancer pathway, Prostate Cancer UK developed a best practice pathway.⁸⁵ It supports use of the most up-to-date, approved, cutting-edge, research-led innovations; sections of the pathway have been endorsed by NICE. The pace of medical research in prostate cancer currently requires the pathway to be updated regularly, to ensure it includes newly approved therapies.

Similar adaptable pathways should be developed for NENs and lymphoma.⁸⁶ Radioligand therapy should also be considered for inclusion in national care pathways for other cancers if and when appropriate. Equally importantly, there is a need for initiatives that enhance cross-specialty collaboration between referring physicians and those delivering radioligand therapy. This can help streamline care pathways and improve patient access to the approach.

Without the development of a care pathway, we cannot truly know where radioligand therapy fits in the prostate cancer pathway and could deliver most benefit.

KAREN STALBOW

Prostate Cancer UK



Logistics and infrastructure

Radioligand therapy uses radioisotopes which decay in a matter of days or hours, and it therefore requires seamless logistics. Effective delivery of radioligand therapy requires carefully orchestrated manufacturing, transport and preparation of radiopharmaceuticals. It also necessitates dedicated infrastructure and mechanisms for waste disposal, in line with ionising radiation regulations.⁸⁷ The existing model for manufacturing, transporting and preparing radioligand therapy is suitable for administering the therapy to a limited number of people per week,³⁸ hence the need to develop different models for larger patient populations. These models of delivery will need to account for differences in radiopharmaceuticals, eligibility assessment techniques and number of treatment cycles.

Imaging infrastructure is insufficient for current and future radioligand therapy needs. Molecular imaging using positron emission tomography–computerised tomography (PET-CT) and single-photon emission computed tomography–computerised tomography (SPECT-CT) is used to assess eligibility for, and response to, radioligand therapy in NENs and prostate cancer. However, there is insufficient infrastructure, funding and trained workforce to enable equitable access to these techniques across the UK.⁸⁸⁻⁹⁰ Moreover, even though a given radioligand therapy typically has a diagnostic ‘pair’, the licensing processes are not linked, which may limit patients’ access to the approach.

NHS England's 2019 Health Infrastructure Plan delivers a £2.8 billion investment to upgrade and build infrastructure, making it fit for the future.⁹¹ The plan is a promising opportunity to overcome clinical infrastructure barriers that could limit the use of radioligand therapy, although this is not explicitly referenced. There remains the need for a focused drive to secure funding for the therapy.

The UK government will also need to consider the impact of Brexit. Radioisotopes used in radioligand therapy for NENs (and potentially other cancers) are manufactured outside of the UK.⁹² Production schedules must be planned months in advance to ensure they do not degrade during transport. Brexit has already caused disruptions and delays in transport of some radioisotopes, sometimes rendering them unusable.⁹³ Brexit has also imposed additional costs for transport and customs.⁹³ The UK government has not yet provided an approach to coping with these issues. More clarity is needed from the Department of Health and Social Care on how this will be dealt with in the short and long term. Providers must work with all actors involved in radiopharmaceutical supply chains, both in the UK and in the rest of Europe, to ensure current and future procurement challenges are foreseen and resolved.



To find out more, please refer to working paper on regulation and reimbursement



Equitable access

The existing model of care for radioligand therapy is not fit for common cancers affecting larger populations. For radioligand therapy to reach its full potential, models of care must be suitable for all patient populations who could benefit from the approach. The current model of care for radioligand therapy was developed for NENs, a rare cancer affecting a small number of people. The therapy is mainly, though not exclusively, provided in European Neuroendocrine Tumour Society (ENETS) Centers of Excellence. There are currently 13 ENETS Centers of Excellence in the UK, 11 of which are in England, and the remaining two in Northern Ireland and Scotland.⁹⁴ While the clustering of specialist services may be appropriate for a rare cancer, it is not suitable for more common cancers. It also means there is some geographical variation in availability of radioligand therapy,^{49 95} and as a result some people with NENs may need to travel greater distances to access it.^{89 95}

As the use of radioligand therapy expands to more common cancers affecting larger populations, such as lymphoma and prostate cancer, models of care will need to be adapted to accommodate each cancer and patient population. Consideration must also be given to the location of services to ensure equitable access across the UK.

The establishment of Radiotherapy Operational Delivery Networks in 2019 is a promising opportunity for equitable access to radioligand therapy across England.

These 11 networks aim to improve access to radiotherapy and other radiation-based therapies, including radioligand therapy.⁹⁶ According to national service specifications, they will standardise tumour-specific treatment protocols and work to improve patient pathways and workforce sustainability. They will offer data-sharing and performance review mechanisms. They will also consider future service planning requirements and establish a process to ensure the roll-out of advanced therapies in line with national guidance. To ensure fair access to radioligand therapy across the UK, similar networks should be built by the devolved nations.

To guarantee equitable access to innovative treatments, we need the right services in the right places.

ROPINDER GILL
Lymphoma Action

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To find out more, please refer to the working paper on service provision

Conclusion

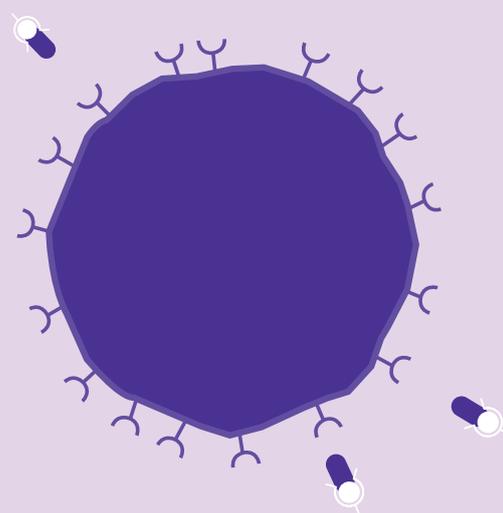
Use of licensed radioligand therapies varies between clinical indications, and there is low awareness and understanding of the approach among many people with cancer, healthcare professionals and policymakers. Radioligand therapy is commonly and effectively used in NENs, and as such many healthcare professionals involved in the management of NENs are aware of the therapy. However, it is very rarely used for the management of lymphoma, and limited awareness and understanding of the approach contributes to its lack of integration into plans for cancer care, funding frameworks and clinical practice. This is unsurprising in lymphoma care, as although the approach is licensed for use in the UK, it has not been assessed or recommended for this indication by NICE.

While radioligand therapy is established in NENs care, its widespread integration into the health system is variable.

There is good provision of radioligand therapy in NENs, and it is included in professional pathways as well as relevant European clinical guidelines. However, data collection on radioligand therapy and NENs is insufficient to enable adequate allocation of resources and inform clinical practice. While ENETS Centers of Excellence have the necessary therapeutic infrastructure to provide radioligand therapy to people with NENs, there is ongoing difficulty in access to imaging infrastructure. Moreover, current models of care are not suitable for future use of the therapy and will need to be adapted to provide effective radioligand therapy and imaging services in more common cancers affecting larger patient populations.

The UK needs to be ready for the wider use of radioligand therapy in the future.

Planning for radioligand therapy requires a comprehensive systems approach. All people involved in cancer care need to work together to actively integrate radioligand therapy into areas of the health system that influence service delivery. Greater awareness and understanding of radioligand therapy are needed among people with cancer who are eligible for the approach, and among healthcare professionals whose patients may benefit from it. Recognition of the value of the therapy is also needed among policy- and decision-makers to drive optimal planning and investment. In addition, radioligand therapy must be better embedded into training curricula for all healthcare professionals who have a role in its delivery, and promptly updated clinical guidelines as well as clear national care pathways are needed to guide referrals and optimal sequencing of treatments. National data collection practices must be enhanced and expanded to systematically include radioligand therapy, and dedicated infrastructure needs to be built and upgraded to ensure it is fit for purpose and ready for the future of cancer care. Sustainable funding and adequate workforce capacity are crucial to achieving these plans and establishing system-wide readiness for the future introduction of new, life-enhancing radioligand therapies.



Glossary

This glossary provides definitions of terms as they are used in this report. They are derived from existing sources⁹⁷⁻¹⁰¹ and adapted for the purposes of this project.

Cancer community includes people with cancer or those who have survived cancer, cancer advocates, and all healthcare professionals working in cancer care.

Care pathway is the clinical process that patients go through, from eligibility for treatment to follow-up after treatment has been completed.

Clinical indication is a health condition that could benefit from a specific test, therapy or procedure. If a therapy has been established and approved by regulatory bodies, the therapy is said to be approved for a specified indication.

Computed tomography (CT) scans use X-rays to create images of the body at different angles. A computer uses these images to develop a 3D image. X-rays identify changes in bones and tissue caused by cancer or other disease.

Eligibility assessment is used to evaluate whether radioligand therapy is a suitable treatment option for a particular individual based on the outcome of specific, often imaging, tests.

Governance refers to a range of policies, standards and ways of working that directly impact the availability, accessibility and standards of delivery for any therapy, ultimately influencing health outcomes.

Health information refers to data that are collected, analysed and synthesised to support health-related decision-making.

Identified need is the potential need and demand for a specific healthcare intervention.

Integration is the adoption and assimilation of an intervention into every aspect of a health system (e.g. governance, regulation, reimbursement and service delivery) in order to ensure its availability to all people who may benefit from it.

Investigational therapy relates to a drug or medical procedure being assessed in clinical trials to evaluate safety and efficacy but which is not licensed for clinical use.

Ligand is a small molecule that selectively binds to a specific different molecule. Examples are a hormone binding to a receptor on a cell, or an antibody binding to an antigen.

Lymphoma is a type of blood cancer that affects the lymphatic system. Lymphoma develops when white blood cells grow uncontrollably. There are over 60 types of lymphoma, each requiring different treatment.

Metastatic cancer occurs when a cancer has spread to different parts of the body from where it originated.

Metastatic castration-resistant prostate cancer is an advanced type of prostate cancer that has spread to the bone and has become resistant to hormonal cancer therapy.

Multidisciplinary team is a group of healthcare professionals that work closely together to deliver comprehensive patient care. The team is responsible for each patient's diagnosis, management plan and assessment of treatment. It may include medical and radiation oncologists, surgeons, pathologists, nurses and other healthcare professionals.

Neuroendocrine neoplasms (NENs), also known as neuroendocrine cancers, are a group of cancers which occur in neuroendocrine cells. NENs arise from cells of the hormonal and nervous system that can develop in many different organs of the body. NENs include neuroendocrine tumours (NETs) and neuroendocrine carcinomas (NECs).

Nuclear medicine is a medical discipline that involves the application of radioactive substances to assess bodily functions and to diagnose and treat disease.

Positron-emission tomography (PET) scans use radioactive tracers to produce 3D images of the inside of the body. The scan shows how organs and tissues function, and can also provide evidence of the presence or absence of cancer.

Radiation is the emission of energy as electromagnetic waves or subatomic particles. This energy can be emitted by radioisotopes and used to diagnose or treat disease.

Radioactive waste includes radioactive materials, equipment and bodily fluids that have received exposure to radiation during a procedure using radiation.

Radioimmunotherapy is a treatment that uses a cancer-targeting antibody to deliver a radioisotope directly to cancer cells to kill them. It is used to treat certain types of lymphoma.

Radioisotope is an unstable form of a chemical element that emits radiation as it breaks down to a stable form. Radioisotopes may occur naturally or be made in a laboratory. Different radioisotopes have different properties and applications – for example, different radioisotopes would be used for diagnosing or treating a cancer.

Radioligand is a cancer-targeting molecule, or ligand, attached to a radioisotope. By choosing different radioisotopes to attach to the same type of ligand, the process can be tailored to either diagnose or treat a cancer.

Readiness is the ability of the health system to rapidly and sustainably adapt policies, infrastructure and processes to support integration of a new intervention.

Receptors are molecules on the surface of a cell that can receive certain substances in the blood.

Regulation defines why and when a healthcare intervention should be provided and how it can be delivered safely to patients, including the appropriate rules and safeguards that need to be in place.

Service provision encompasses the inputs (such as the health workforce, infrastructure and equipment) and outputs (such as diagnostic, therapeutic and follow-up services) required for the provision of healthcare.

Targeted therapy is a category of cancer treatment that exploits differences between healthy and cancerous cells. It can be used to target a treatment to cancerous cells with minimal effect on healthy cells.

Appendix

TABLE A1. Radioligand therapies licensed in the UK

Indication	Description of indication	Therapy licensed by MHRA/EMA for use in clinical practice in the UK	Therapy recommended by NICE
Gastroenteropancreatic neuroendocrine neoplasms	A rare type of neuroendocrine neoplasm that can form in the pancreas or in other parts of the gastrointestinal tract, including the stomach, small intestine, colon, rectum and appendix	Lutetium-177 oxodotreotide	Lutetium-177 oxodotreotide
Follicular lymphoma	The most common type of slow growing non-Hodgkin's lymphoma that develops from B cells. the abnormal B cells typically form in clumps inside lymph nodes	Yttrium-90 ibritumomab tiuxetan ^a	

EMA, European Medicines Agency; MHRA, Medicines and Healthcare products Regulatory Agency; NICE, National Institute for Health and Care Excellence

^a.Therapy not yet reviewed by NICE

TABLE A2. Clinical indications for radioligand therapy in international phase II and III clinical trials

Indication in phase II clinical trials ¹	Indication in phase III clinical trials ¹	Description
Carcinoid heart disease ¹⁰²	—	Carcinoid heart disease is a rare condition that is related to raised levels of peptides and hormones produced by neuroendocrine cancer cells. It usually affects the right-sided heart valves and leads to right heart failure
Central nervous system cancer ²³⁻²⁵		Central nervous system cancer begins in the brain or the spinal cord. It encompasses over 100 distinct tumour types
Lymphoma sub-types including relapsed indolent non-Hodgkin's lymphoma and relapsed/refractory follicular lymphoma ¹⁰³	—	Lymphoma is a type of cancer that develops in the lymphatic system
Neuroendocrine neoplasm sub-types including paraganglioma, pheochromocytoma and neuroendocrine breast tumours, among many others ¹⁰⁴⁻¹⁰⁷	Gastroenteropancreatic neuroendocrine neoplasms ¹⁰⁸	Neuroendocrine neoplasms arise from cells of the hormonal and nervous systems that can develop in many different organs of the body
Meningioma ^{23 24 109}	—	A meningioma is a tumour that grows from the tissues that line the brain
Metastatic breast cancer ²²		Metastatic breast cancer is breast cancer that has spread to other parts of the body
Metastatic castration-resistant prostate cancer ¹¹⁰	Metastatic castration-resistant prostate cancer ²¹	Metastatic castration-resistant prostate cancer is a cancer that has spread beyond the prostate gland and where hormone therapy is no longer effective in stopping or slowing the disease
Peritoneal solid tumours ¹¹¹	—	Peritoneal solid tumours are a rare type of cancer that are found in the lining tissue of the abdomen

^b. At the time of publication (2021)

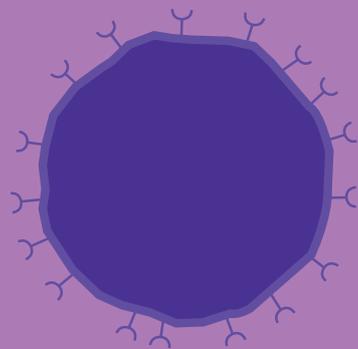
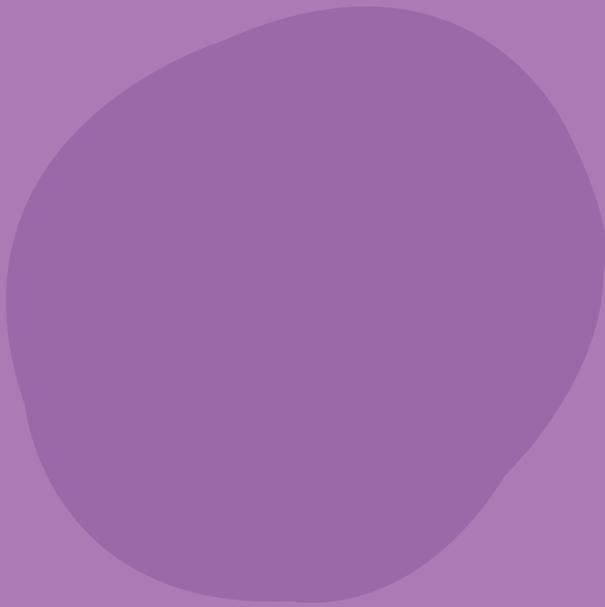
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