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# Health system readiness for radioligand therapy in the UK

## Service provision

Working paper

September 2021

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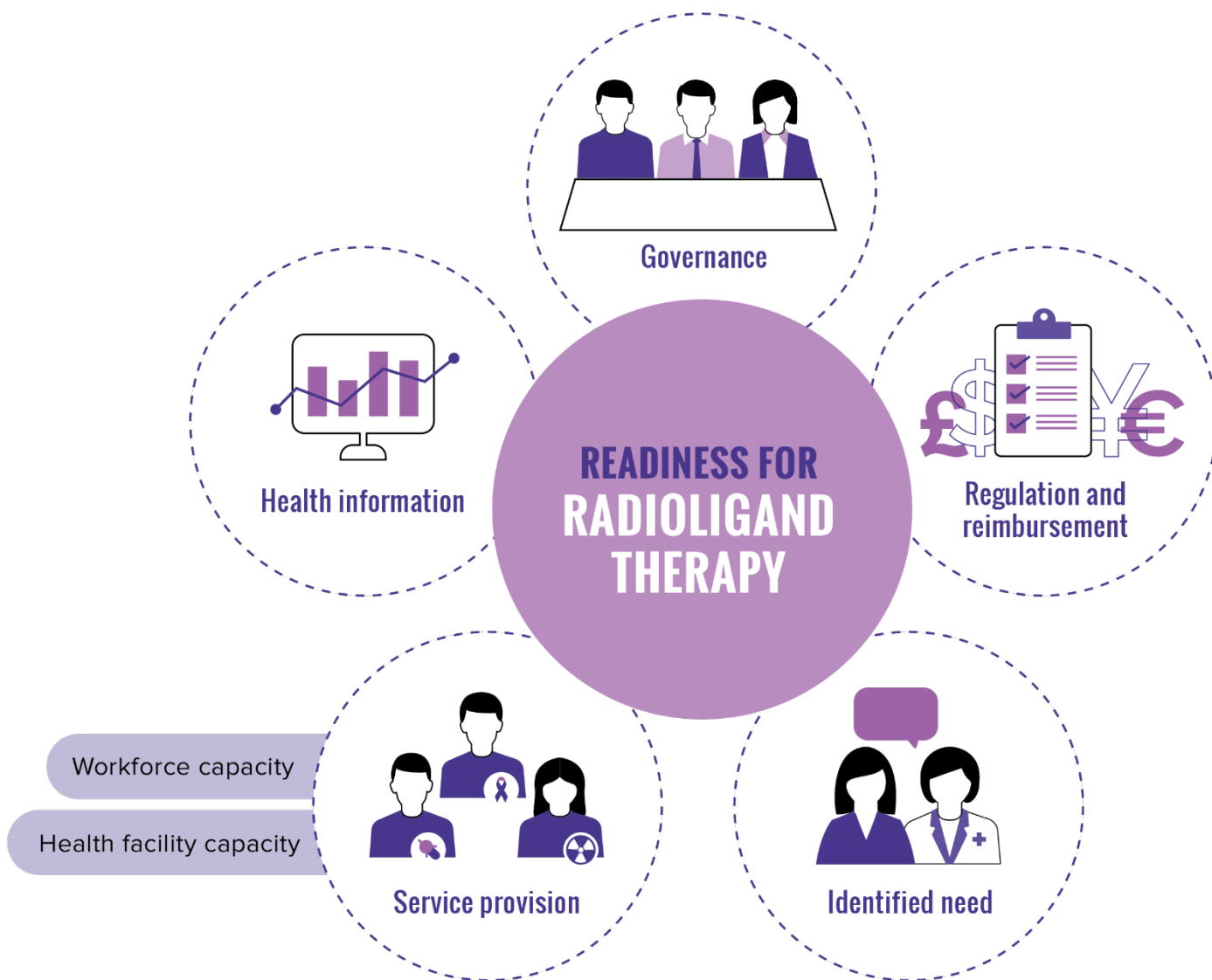
## About this working paper

**This working paper 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 explores current integration and future readiness for the approach as it relates to service provision, one of the five domains of the Radioligand Therapy Readiness Assessment Framework (*Figure 1*). The working paper provides answers to questions from the framework, with key findings from relevant subdomains outlined in a summary assessment at the start of each section. We focus on the situation in neuroendocrine neoplasms, lymphoma and prostate cancer in England, though we also include examples from across the devolved nations. Many of the findings in this paper may be applicable across the UK and in other areas of cancer care.

- This working paper is supported by other documents on health system readiness for radioligand therapy in the UK. For more details, please visit: [www.radioligandtherapy.com/framework/UK](http://www.radioligandtherapy.com/framework/UK)

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

Figure 1. Domains of the Radioligand Therapy Readiness Assessment Framework



## What is service provision?

**Provision of safe and effective cancer care services is fundamental to ensuring positive outcomes for people with cancer.** Service provision is defined as the inputs (such as the health workforce, infrastructure and equipment) and outputs (such as diagnostic, therapeutic and follow-up services) required for the direct delivery of care.<sup>1</sup>

## What does optimal provision of radioligand therapy look like?

**As for all service provision, several key characteristics should be met for the delivery of radioligand therapy:**<sup>2</sup>

- **Comprehensive coverage:** services should cover all stages of care, from initial screening and eligibility assessments through to follow-up care.
- **Accessibility:** people should not face barriers to using appropriate health services. For example, there should be no obstacles to use caused by cost, language, geography or complex referral pathways.
- **Continuity:** care should be consistent throughout an individual's treatment and across networks, clinical indications and types of intervention.
- **Quality:** safe, effective and appropriate care should be delivered in a timely fashion.
- **Coordination:** there should be a clear pathway for care that is communicated to the person receiving care, and good connections between different types of care, departments and hospitals.
- **Person-centredness:** care should be organised around and receptive to the people receiving it, rather than the clinical indication or finances.
- **Accountability and efficiency:** care should be well managed and adapted based on performance outcomes, with an emphasis on limiting resource waste.

**Integrating radioligand therapy into cancer care requires a full understanding of the approach's unique attributes.** Because the approach uses radioactive material, specific regulations for production, delivery and disposal of radiopharmaceuticals must be followed. Radioisotopes decay over time, which means that the logistics involved in transferring radioligand therapy from production to site of use must be seamless. Finally, radioligand

therapy is often used alongside paired imaging agents which aid with diagnosis and eligibility assessment, and service provision must be structured in a way that supports both imaging and therapeutic elements. In light of these unique characteristics, provision of radioligand therapy requires appropriate infrastructure and a highly trained and multidisciplinary workforce equipped with appropriate knowledge and skills – in terms of referrals, imaging, treatment and follow-up – to provide effective and safe care throughout the patient pathway.

**Clear care pathways are necessary to promptly identify and refer people who are eligible for radioligand therapy.** Broadly speaking, there are five steps required for the delivery of the approach:

1. Patient eligibility should be assessed. In some indications, positron emission tomography–computed tomography (PET-CT) or single-photon emission computed tomography–computed tomography (SPECT-CT) imaging is performed to determine patient eligibility.
2. The cancer multidisciplinary team should develop a personalised treatment plan for eligible patients.
3. The therapy can then be ordered or prepared.
4. A dedicated team of experts with radioligand therapy experience and appropriate licensing can administer the treatment. Radioligand therapy should be administered in a designated clinical facility supplied with high-quality imaging and therapeutic equipment, in line with radiation protection regulations. The facility should also have the necessary capacity and processes to effectively manage radioactive waste and remain within its disposal limits.
5. Patient follow-up must be completed, both between cycles and at the end of the therapy.

For more on the radioligand therapy delivery pathway, see the [Appendix](#).

# 1 Workforce capacity

## Summary assessment

Indicators	Assessment
<p>How are nuclear medicine specialists involved in multidisciplinary decision-making around treatment in the UK?</p>	<p>Nuclear medicine specialists play an essential role in planning and delivering radioligand therapy.</p> <p>For neuroendocrine neoplasms, nuclear medicine physicians are typically involved in the cancer multidisciplinary team (MDT), enabling prompt consideration of radioligand therapy as a therapeutic option. However, prostate cancer and lymphoma MDTs do not typically involve nuclear medicine physicians, thereby possibly restricting consideration of radioligand therapy for people with these cancers.</p>
<p>Which healthcare professionals are involved in managing and delivering radioligand therapy in the UK?</p>	<p>The professionals involved in prescribing, coordinating and delivering radioligand therapy generally include the following:</p> <ul style="list-style-type: none"> <li>• Medical oncologist or equivalent referring physician</li> <li>• Nuclear medicine physician</li> <li>• Clinical nurse specialist</li> <li>• Radiopharmacist</li> <li>• Medical physics expert</li> <li>• Clinical scientist</li> <li>• Radiation protection adviser</li> <li>• Radioactive waste adviser</li> <li>• Patient coordinator.</li> </ul> <p>The composition of the team will differ according to clinical indication and clinical facility's size.</p>
<p>Is there sufficient capacity in the UK to meet current demand for radioligand therapy?</p>	<p>There are currently limited numbers of nuclear medicine physicians, radiopharmacists and medical physics experts who are licensed to deliver radioligand therapy. Moreover, there is an insufficient number of clinical nurse specialists and patient coordinators who can provide support for the approach.</p>

## 1.1 The cancer multidisciplinary team

### 1.1.1 Treatment decision-making

**Discussions around any cancer treatment begin in the MDT.** England's 2015–20 cancer strategy describes MDTs as the 'gold standard' of cancer services,<sup>3</sup> bringing together a range of experts to discuss patient diagnosis, referral, treatment and follow-up in a weekly tumour board meeting.<sup>4</sup> MDTs are used across England for all cancer types. Although the composition varies based on cancer type and available therapies, MDTs generally include medical oncologists, clinical nurse specialists, surgeons, radiologists, pathologists, palliative medicine physicians and pharmacists.<sup>5</sup> For certain cancers, such as neuroendocrine neoplasms (NENs), nuclear medicine physicians are also part of the cancer MDT.

**Inclusion of nuclear medicine in the MDT enables the prompt consideration of radioligand therapy as a therapeutic option for eligible patients.** Nuclear medicine physicians play an important role in the delivery of radioligand therapy as they are involved in both imaging and therapeutic aspects of the approach. Their role in the MDT is to provide expertise on imaging and the therapy,<sup>6</sup> enabling timely consideration of radioligand therapy as an option. Prompt initiation of radioligand therapy is important as it allows for increased chances of treatment success and improved patient outcomes.<sup>7</sup> Nuclear medicine physicians are not usually included in prostate cancer and lymphoma MDTs,<sup>7 8</sup> although this may need to change if radioligand therapy becomes licensed for use in these indications. As demand for radioligand therapy grows and its use expands, it may become increasingly difficult for nuclear medicine physicians to participate in every relevant MDT. Technological innovations introduced during the COVID-19 pandemic, such as growing use of virtual MDTs,<sup>9</sup> may make it easier for nuclear medicine physicians to become involved in a greater number of discussions.

**The existing role of imaging and radiotherapy in cancer care can help support the multidisciplinary delivery of radioligand therapy.** Radiologists and radiation oncologists are frequently members of the MDT.<sup>10</sup> Their roles include advising on imaging and radiotherapy, which are commonly used in prostate cancer and lymphoma.<sup>10 11</sup> Other members of the MDT (oncologists, haemato-oncologists, urologists etc.) are thus familiar with these specialties.<sup>11</sup> Radiologists and radiation oncologists can also be involved in the delivery of radioligand therapy, so this existing multidisciplinary working could help facilitate

delivery of the approach in lymphoma and prostate cancer. As awareness of radioligand therapy grows outside of the nuclear medicine community through further multidisciplinary working and training, the approach is more likely to be considered in all appropriate circumstances, even if a nuclear medicine physician is not available for every MDT.

- For more information on training of referring clinicians for radioligand therapy, see the working paper on [identified need](#).

### 1.1.2 Care pathways

**Where care pathways exist, they do not always clearly outline who should be considered for radioligand therapy and at what point in their care.** There is no formal National Institute for Health and Care Excellence (NICE) care pathway for NENs,<sup>12</sup> however, the UK and Ireland Neuroendocrine Tumour Society (UKINETS) ‘bitesize’ pathways provide a good indication of when radioligand therapy should be considered for some types of NENs.<sup>13 14</sup> Additionally, centre-specific pathways and informal networks do provide guidance on a smaller scale. However, formal NICE endorsement of the UKINETS bitesize pathways may help improve national consistency in use and availability of the therapy. While there are national NICE pathways for lymphoma and prostate cancer,<sup>15 16</sup> it remains unclear where radioligand therapy may fit into such pathways in the future. These challenges make it difficult for clinicians to know what radioligand therapy services are available and where to direct patients who may be eligible. However, efforts are being made to provide clarity on certain care pathways, such as that for prostate cancer (*Real-world example 1*). This collaborative process for developing an innovation-focused pathway should be applied across other indications to ensure a clear process for referring patients to radioligand therapy is established soon after approval.

### **Real-world example 1. Best Practice Pathway for prostate cancer**

Prostate Cancer UK worked with clinical experts from urology, radiology, and medical and clinical oncology to develop a Best Practice Pathway to better support healthcare professionals involved in prostate cancer diagnosis and care.<sup>17</sup>

The pathway lays out the optimal diagnostic, treatment and support pathway for prostate cancer patients. For example, the pathway shows clearly the treatments that should be considered at each stage of progression, which will help referring clinicians ensure they are considering all of the most appropriate therapies.<sup>18</sup>

Sections of this pathway have been endorsed by the National Institute for Health and Care Excellence (NICE) and it supports use of the most up-to-date, approved, cutting-edge research-led innovations. The pace of prostate cancer medical research currently requires it to be updated regularly, to ensure it includes emerging, approved therapies.

## **1.2 Workforce involved in prescribing and delivering radioligand therapy**

### **1.2.1 Roles and responsibilities**

**Experts from multiple departments are responsible for the safe planning, preparation and administration of radioligand therapy to people with cancer.** This includes some members of the cancer MDT, such as a medical or clinical oncologist, clinical nurse specialist and nuclear medicine physician (in the case of NENs), as well as experts on radiopharmacy and radiation protection (*Box 1*). Each expert has a unique role and well-defined responsibilities within the team.

### Box 1. Experts involved in the management and delivery of radioligand therapy

The composition of the team prescribing and delivering radioligand therapy will differ according to the clinical indication and size of the clinical facility, but experts involved generally include the following:

- |  |  |
|--|--|
| <p><b>Medical or clinical oncologist</b> (or, in some centres, a gastroenterologist or endocrinologist for NENs, a haemato-oncologist for lymphoma, or a uro-oncologist for prostate cancer)</p> | <ul style="list-style-type: none"> <li>• Pre-treatment: meets with the person with cancer, discusses the case with the MDT, and refers the person to the nuclear medicine physician for radioligand therapy eligibility assessment.</li> <li>• Treatment: prescribes and may administer the treatment if they hold an Administration of Radioactive Substances Advisory Committee (ARSAC) licence.</li> <li>• Post-treatment: involved in the MDT discussion regarding treatment response and performs follow-up after all cycles of treatment are completed.</li> </ul> |
| <p><b>Nuclear medicine physician</b></p>   | <ul style="list-style-type: none"> <li>• Pre-treatment: discusses patient eligibility for radioligand therapy with the MDT and performs imaging scans to assess eligibility (if appropriate).</li> <li>• Treatment: holds an ARSAC licence so may administer the treatment.</li> <li>• Post-treatment: involved in the MDT discussion regarding treatment response.</li> </ul>   |
| <p><b>Clinical nurse specialist</b></p>  | <ul style="list-style-type: none"> <li>• Pre-treatment: collates information on the person with cancer and discusses the case with the MDT. Also provides pre-treatment information and education to the patient – coordinating timing and social support, as required.</li> <li>• Treatment: provides information and support to the person undergoing treatment and their carers.</li> <li>• Post-treatment: performs initial follow-up between treatment cycles and coordinates blood tests and symptom/impact of treatment review.</li> </ul>                        |

**Radiopharmacist**

- Treatment: prepares the radiopharmaceuticals for administration.

**Medical physics expert**

- Treatment: prepares dosing of the treatment, if appropriate, and ensures its safe and accurate administration.

**Clinical scientist**

(in smaller centres, the medical physics expert may conduct this role)

- Pre-treatment: provides information to the person with cancer and their carers on radiation protection.

**Radiation protection**

**adviser** (this role may be filled by another member of the team, such as the medical physics expert)

- Responsible for ensuring appropriate radiation protection is in place throughout radioligand therapy preparation and delivery.

**Radioactive waste**

**adviser** (this role may be filled by another member of the team, such as the medical physics expert)

- Advises on the appropriate disposal of radioactive waste.

**Patient coordinator** (this role may be filled by another member of the team, such as the clinical nurse specialist)

- Schedules appointments and supports logistics around radioligand therapy throughout the treatment pathway.

For a detailed view of the radioligand therapy care pathway and how these roles interact, see [Appendix](#).

### 1.2.2 Capacity of experts involved in managing and delivering radioligand therapy

**There are limited numbers of nuclear medicine physicians licensed to prepare and deliver radioligand therapy, creating a barrier to use of the approach in clinical practice.** In 2018–19, there were an estimated 95 nuclear medicine physicians in the UK,<sup>19</sup> with most concentrated in the South East and North West of England.<sup>20</sup> Nuclear medicine physicians hold Administration of Radioactive Substances Advisory Committee (ARSAC) practitioner licences, which allow them to deliver radioligand therapy. Health Education England has recently invested in a training curriculum to support the conversion of radiologists into the field of nuclear medicine to reduce workforce capacity pressures.<sup>21</sup> This course will likely increase the number of nuclear medicine specialists in England.

**Cancer diagnoses and the development and delivery of radioligand therapy may also be impacted by the limited numbers of radiopharmacists and medical physicists.**

These specialists play an essential role in the development and provision of radioligand therapy, which can include dosimetry (*Box 2*). Even though licensed radioligand therapy in NENs is delivered ‘ready to use’ and its label does not require dosimetry as part of delivery,<sup>22</sup> limitations in the number of radiopharmacists and medical physicists may reduce the number of centres that are eligible to be involved in clinical trials or research. It is unclear how many radiopharmacists are trained in radioligand therapy or have ARSAC licences to conduct research with radioisotopes. A member of the UK Radiopharmacy Group has stated that the group is very concerned about the lack of trained radiopharmacy staff to manufacture and deliver radioligand therapeutic products.<sup>23</sup> Moreover, the Institute of Physics and Engineering in Medicine has highlighted that the lack of medical physics experts may delay patients’ diagnosis and, ultimately, treatment.<sup>24</sup>

- For more information on licensing requirements for clinical staff delivering radioligand therapy, see the working paper on [regulation and reimbursement](#).

## Box 2. What is dosimetry?

Dosimetry is a way of calculating how much radiation is absorbed by cells. High doses of radiation can kill cancerous cells, but too much radiation can be toxic.<sup>25</sup> The amount of radioactivity administered is different from the radiation absorbed in the body. For example, absorbed radiation dose varies between different tissue types, people and radioisotopes.<sup>26</sup> Calculating the amount of radiation absorbed can therefore improve our understanding of the safety and efficacy of a therapy.<sup>25 27</sup>

Dosimetry is a particularly important aspect of research and development. All therapies undergo toxicity studies as part of the development process, and therapies using radiation are no different. In the context of radioligand therapy, dosimetry can be used to determine the amount of radioactivity that will effectively treat a cancer. Other clinical trials and studies may use dosimetry to investigate new therapeutic radioisotopes or test more personalised treatments and potential adaptations to existing therapeutic protocols. A highly-skilled medical physicist typically performs dosimetry based on scans of the targeted region, in close collaboration with other professionals.<sup>27</sup>

While commonly used in research and development, dosimetry is not routinely completed in clinical practice for radioligand therapy. The Ionising Radiation (Medical Exposure) Regulations note that dose verification, which can be done through dosimetry, should be completed for each person receiving radiopharmaceuticals.<sup>28</sup> However, not all centres in the UK have the capacity or experience to perform dosimetry.<sup>29</sup> The label for licensed radioligand therapy in NENs, which is delivered 'ready to use', does not specify the need for dosimetry.<sup>22 30</sup> It is likely that this will be the same for applications of the approach which are currently under investigation in lymphoma and prostate cancer.

**Shortages of other key practitioners may also be a barrier.** There is an insufficient number of clinical nurse specialists and patient coordinators to facilitate delivery of radioligand therapy.<sup>31-34</sup> Because radioligand therapy is a highly personalised treatment which involves multidisciplinary working, the support offered by nurse specialists and patient coordinators is essential to the smooth delivery of the approach. Patient coordinators help facilitate care among the different departments involved in radioligand therapy, and ensure

that people with cancer have a single point of contact throughout their care (*Real-world example 2*).<sup>34</sup> Nurse specialists can advocate for people with cancer, reinforce information about radioligand therapy, and help with symptom management and treatment questions. The presence of a nurse specialist is associated with improved quality of care for people with lymphoma.<sup>35</sup> It is unclear how many nurse specialists are involved in radioligand therapy across the UK. However, shortages of nurse specialists are a serious concern for all cancer care: an additional 2,500 nurse specialists – an increase of 84% – are required to meet the basic needs of people with cancer.<sup>36</sup> The NHS People Plan provides a promising opportunity to strengthen and grow the cancer nurse specialist workforce as it offers training grants for 350 nurses to become cancer nurse specialists.<sup>37</sup> It will be important for this training to address radioligand therapy to ensure that nurses have an adequate understanding of the approach, to support increasing demand.

- For more information on training of nurse specialists for radioligand therapy, see the working paper on [identified need](#).

### **Real-world example 2. The patient coordinator's role in delivering radioligand therapy**

The patient coordinator is often the first point of contact for people undergoing radioligand therapy.<sup>34</sup> They are responsible for scheduling appointments for imaging, therapy administration, blood tests and follow-up. While the coordinator is not part of the MDT, they are a core part of the team which delivers radioligand therapy and are in close contact with all professionals involved in the therapy's pathway. The number of patient coordinators for radioligand therapy is extremely limited in England,<sup>34</sup> largely because the role is not currently funded by the NHS. In centres without a patient coordinator, radiologists, nurses or other healthcare professionals may fulfil these coordination responsibilities. Some centres consider the role essential for optimal delivery of radioligand therapy and fund it directly.<sup>38</sup> However, as yet, there is no formal radioligand therapy training curriculum for patient coordinators.

**There is concern that wider approval of radioligand therapy could substantially exacerbate these existing workforce challenges.** If use of radioligand therapy is expanded to prostate cancer, it is thought that the number of people eligible for the therapy may increase at least tenfold.<sup>39</sup> This raises questions around how such a volume of treatment can be delivered effectively and in a timely manner with the existing licensed workforce.

## 2 Health facility capacity

### Summary assessment

Indicators	Assessment
<p>Are diagnosis and eligibility assessments for radioligand therapy appropriate to meet current and future demand in the UK?</p>	<p>Limited imaging capacity for radioligand therapy in neuroendocrine neoplasms (NENs) and prostate cancer is currently a major barrier to assessing whether a person is eligible for the approach. This may continue in the future if more investment is not provided for imaging infrastructure and workforce training.</p> <p>In lymphoma, diagnostic or imaging radioisotopes are not required to assess eligibility for radioligand therapy.</p>
<p>Is the built environment in the UK appropriate to the delivery model of radioligand therapy?</p>	<p>Apart from challenges around imaging infrastructure, sites providing radioligand therapy are appropriately equipped to deliver the approach, generally as an outpatient procedure, with lead-lined rooms, dedicated bathrooms, equipment and storage space for radioactive waste.</p>
<p>How are radioligand therapy services organised in the UK health system?</p>	<p><b>Current provision of radioligand therapy in NENs:</b> Radioligand therapy for NENs is largely, though not exclusively, provided in the UK's 13 European Neuroendocrine Tumor Society (ENETS) Centers of Excellence. There are significant geographical inequalities in access, with services mostly provided in the South East and North West of England. However, there is good collaboration between centres to reduce impact of geographical inequalities.</p> <p><b>Future provision of radioligand therapy:</b> A total of 14 sites are currently involved in clinical trials for the delivery of radioligand therapy in lymphoma and/or prostate cancer. These sites, alongside those with experience of radioligand therapy in NENs, will likely provide emerging radioligand therapies if they are approved. The Radiotherapy Operational Delivery Networks also look promising for the greater integration of radioligand therapy into healthcare.</p>

## 2.1 Imaging capacity for radioligand therapy

**Molecular imaging is an essential component of delivering radioligand therapy to people with solid tumours, but numerous factors lead to its limited capacity in the UK.** For solid tumours such as NENs and prostate cancer, PET-CT or SPECT-CT can be used to estimate response to radioligand therapy, which allows clinicians to give the approach only to people who might benefit from it.<sup>40 41</sup> These imaging techniques can also be used to assess response to the therapy and refine future treatments. However, there are many challenges to ensuring access to this imaging technique, including cost, expertise and radioisotope production<sup>42-44</sup> – as seen in the case of imaging with gallium-68 DOTATATE/TOC in NENs (*Real-world example 3*). Despite these challenges, efforts are underway to scale-up imaging infrastructure and services for future needs (*Real-world example 4*).

- For more information on imaging in radioligand therapy, see the working paper on [regulation and reimbursement](#).

### **Real-world example 3. PET-CT imaging with gallium-68**

PET-CT imaging with gallium-68 DOTATATE/TOC is used to accurately stage and select people with NENs for radioligand therapy, and is considered superior to other imaging modalities.<sup>45 46</sup> However, establishing gallium-68 DOTATATE/TOC PET-CT services is challenging due to the high cost of the technology and imaging agent and the limited number of professionals licensed to carry out and interpret the scans.<sup>43</sup> In addition, gallium-68 has a half-life of 68 minutes and therefore must be produced by on-site generators, which are associated with high set-up capital costs<sup>44</sup> and only produce enough gallium-68 for two or three scans per day.<sup>47</sup> As a result of these challenges, adoption into routine clinical practice in the UK has been slow.<sup>43</sup> Only ten centres in the UK offer gallium-68 DOTATATE/TOC PET-CT services for NENs – nine of which are located in and around London.<sup>48</sup> As a consequence, many people with NENs must travel long distances to access imaging to be assessed for radioligand therapy eligibility.<sup>49 50</sup>

**Different imaging options are being investigated to increase imaging capacity for radioligand therapy.** The challenges confronted for gallium-68 DOTATATE/TOC PET-CT imaging will be relevant to any PET-CT techniques using gallium-68, including the emerging gallium-68 prostate-specific membrane antigen (PSMA) for prostate cancer, if approved.<sup>43</sup> However, a proposal for gallium-68 PSMA PET-CT has previously been rejected by the Specialised Services Commissioning Committee based on the need for stronger evidence of clinical effectiveness focused on patient outcomes, which is difficult to assess for diagnostic radiotracers.<sup>42</sup> To overcome some of these challenges and prepare for the expansion of imaging to large patient populations, other imaging techniques such as SPECT-CT are also being used. In addition, new imaging agents for prostate cancer are currently under investigation, such as fluorine-18, which can be produced at a larger scale, is more cost-effective and has a longer half-life.<sup>44</sup> The disadvantage of using fluorine-18 is that uptake by the body can be seen in both benign and malignant tumours, which may lead to possible higher rates of false-negative and false-positive results.<sup>44</sup>

#### **Real-world example 4. Scotland's readiness for new prostate cancer services**

NHS Scotland is preparing for the future of prostate cancer care by increasing the infrastructure for gallium-68 PET-CT imaging services.<sup>51</sup> By improving the detection of advanced prostate cancer through use of these tests, it is hoped that Scotland will be better prepared for the fast introduction of new PSMA-targeted techniques in the future. These imaging services will be funded by NHS Scotland and were expected to be provided in September and November 2020 at four centres, in NHS Greater Glasgow and Clyde, NHS Tayside, NHS Lothian and NHS Grampian. However, the introduction of these services has been delayed.<sup>52</sup>

NHS England is working with Prostate Cancer UK and nuclear medicine physicians on its plans for PET-CT imaging services, while NHS Wales has made considerable progress in increasing the availability of PET-CT.<sup>53</sup>

**Eligibility assessments for radioligand therapy in lymphoma do not depend on nuclear imaging.**<sup>11</sup> As such, issues around access to PET-CT and SPECT-CT are not an important consideration for integration or readiness in this indication.

## 2.2 Clinical infrastructure for radioligand therapy

**Apart from challenges around imaging infrastructure, sites providing radioligand therapy are appropriately equipped to deliver the approach.** Radioligand therapy is generally performed as an outpatient procedure, with some exceptions for people requiring additional inpatient support.<sup>54 55</sup> Although limited in number, sites providing radioligand therapy in the UK are equipped with lead-lined rooms, dedicated bathrooms, necessary equipment and appropriate storage space for radioactive waste. However, owing to the number of departments involved in the delivery of radioligand therapy, these services may be located in different departments.<sup>39</sup> The lack of consistency within and between hospitals may complicate delivery processes but does not seem to impact the quality of the service delivered.

- For more information on infrastructural requirements for the delivery of radioligand therapy, see the working paper on [regulation and reimbursement](#).

## 2.3 Organisation of and access to radioligand therapy services

### 2.3.1 Current provision of radioligand therapy

**Radioligand therapy is well established for the management of NENs in centres of excellence, but there are significant geographical inequalities in access.** In the UK, NENs care is provided in approximately 30 sites, 13 of which are certified European Neuroendocrine Tumor Society (ENETS) Centers of Excellence.<sup>14</sup> Radioligand therapy is provided through these centres or other specialist clinics. There are many benefits to centralisation of NENs care, including improved access to expertise, enhanced MDT meetings and improved patient follow-up and care coordination.<sup>56</sup> In fact, an expert has noted that the failure of a previous radioligand therapy in lymphoma was in part because the approach was immediately offered to as many centres as possible (*Real-world example 5*).<sup>8</sup> Despite the benefits of centralisation, it does unfortunately result in a certain level of geographical disparities in access. South-east and north-west England are the best-served

localities for radioligand therapy services and relevant clinical trials,<sup>54</sup> and also have the highest density of nuclear medicine physicians.

#### **Real-world example 5. Limited historical uptake of radioligand therapy in lymphoma**

In 2004, ibritumomab tiuxetan (Zevalin) was licensed for use in certain types of lymphoma in the UK.<sup>57</sup> At the time, the therapy's developers attempted to get the approach supplied by as many centres as possible.<sup>8</sup> This may have actually limited uptake of the approach at the time, as some sites may not have been sufficiently familiar with radioligand therapy or had the expertise or confidence to administer it.<sup>8</sup>

Other factors which contributed to limited use of the approach included a lack of NHS funding,<sup>58 59</sup> declining interest from the therapy's developers,<sup>11</sup> complex delivery processes which included dosimetry,<sup>59</sup> and limited multidisciplinary working.<sup>11 59</sup> Now this therapy is rarely, if ever, administered for the management of lymphoma.<sup>59</sup> Novel applications of radioligand therapy currently under investigation for lymphoma would need to overcome historical perceptions of the approach and consider a different strategy for its roll out.

- For more information on licensing approvals of radioligand therapy, see the working paper on [regulation and reimbursement](#).

### 2.3.2 Future provision of radioligand therapy

**If radioligand therapy is used in new indications, it will likely be provided at sites with established infrastructure, workforce and referral pathways.** There are currently 14 centres participating in clinical trials for radioligand therapy in the UK (12 in England and two in Scotland). Nine centres are involved in the VISION trial investigating radioligand therapy in metastatic castration-resistant prostate cancer, and nine centres are administering the approach as part of the LYMRIT-37-01 trial in follicular lymphoma.<sup>60 61</sup> According to experts, these sites will likely be selected to provide radioligand therapy should it be approved for clinical care, as they already have the necessary people, materials and pathways in place.<sup>6 58</sup> In geographical areas with no trial centres, radioligand therapy will likely be provided at centres with experience in delivering radioligand therapy in NENs or

other targeted radioisotope therapies such as radium-223 dichloride.<sup>6 62</sup> This will allow for healthcare professionals to become familiar with delivery pathways before the approach is used more widely.<sup>8</sup>

**Over time, provision of radioligand therapy may be expanded to other centres.** If the delivery of radioligand therapy in clinical practice is associated with positive outcomes at sites with established infrastructure and expertise, these sites can serve as models for the provision of radioligand therapy more widely. At that point, the recently established Radiotherapy Operational Delivery Networks may offer a promising opportunity for the greater integration of radioligand therapy into healthcare (*Real-world example 6*).<sup>39</sup> Each Network is aligned to one or more NHS Cancer Alliance, which are fundamental to the delivery of cancer care across England. Use of the Radiotherapy Operational Delivery Networks could help ensure equitable access to radioligand therapy across England and sustainable and consistent integration of the approach.

#### **Real-world example 6. Radiotherapy Operational Delivery Networks**

In 2019, NHS England commissioned the establishment of 11 networks to support the delivery of radiotherapy, brachytherapy and radioligand therapy in England.<sup>63</sup> A key aim of these Operational Delivery Networks is to ensure patients in all regions have equitable access to specialist services. Accordingly, each network includes at least one large tertiary centre of sufficient size to provide the full range of radiotherapy treatments in all sub-specialist areas, including rare cancers.<sup>63</sup> However, in rare cases where a network is unable to deliver a particular service, people may be sent to other networks where that treatment is available.<sup>64</sup>

As radioligand therapy uses radiation, its delivery is included in the networks' remit. However, at present the networks focus on improving access to other innovative therapies, such as external beam radiotherapy, and radioligand therapy delivery is extremely limited.<sup>64</sup> In the future, making use of existing operations and structures within these networks may be the most efficient and sustainable way of achieving widespread access to radioligand therapy.<sup>65</sup>

## Conclusion

**Radioligand therapy services need to be better supported by the Government, the NHS and Cancer Alliances to achieve optimal integration into cancer care.** Radioligand therapy for NENs is generally well integrated and effectively provided. However, for more widespread adoption in new types of cancer in the future, many elements need to be addressed: lack of integration into clear NICE care pathways; limited numbers of trained professionals; insufficient imaging capacity for eligibility assessments; and geographical inequalities in access to services. Planning for the greater integration of the approach into cancer care in the UK will require significantly more support for the workforce – in terms of recruitment and increased capacity to deliver each step of radioligand therapy promptly and safely. In addition, it will require much greater investment in imaging infrastructure and an expansion of services across the country to ensure eligible people with cancer can readily access the treatment they need.

## Appendix. Radioligand therapy delivery pathway

Pathway step	Activities	Indication-specific information
<b>Referral and assessment</b>	<ul style="list-style-type: none"> <li>The MDT meets to discuss the eligibility of a person with cancer for radioligand therapy.</li> </ul>	<ul style="list-style-type: none"> <li><b>NENs and prostate cancer:</b> the referring clinician refers the person with cancer to the nuclear medicine physician for assessment via PET-CT or SPECT-CT imaging.</li> <li><b>Lymphoma:</b> the MDT may consider B-cell subtyping information when determining whether the person with cancer is eligible for radioligand therapy. This procedure may not be necessary for novel applications of the approach in this indication.</li> </ul>
<b>Treatment planning</b>	<ul style="list-style-type: none"> <li>The MDT makes the decision to use radioligand therapy. It plans imaging and therapeutic appointments with support from the patient coordinator.</li> <li>The clinical nurse specialist and clinical scientist provide information to the person with cancer and their carers about the therapy and radioprotection more generally.</li> </ul>	<ul style="list-style-type: none"> <li><b>NENs and prostate cancer:</b> eligibility is determined by positive PET-CT or SPECT-CT scans and other inclusion criteria.</li> <li><b>Lymphoma:</b> people with refractory/relapsed CD20-positive B-cell follicular lymphoma and people in remission from CD20-positive B-cell follicular lymphoma are eligible for treatment.</li> </ul>
<b>Preparation</b>	<ul style="list-style-type: none"> <li>The radiopharmacist measures the therapeutic product to ensure accurate uptake.</li> </ul>	
<b>Administration</b>	<ul style="list-style-type: none"> <li>Radioligand therapy is administered by a licensed nuclear medicine physician or licensed medical oncologist. The medical physics expert is responsible for ensuring the safe and accurate administration and the clinical scientist is responsible for managing radioactive waste during and after treatment.</li> <li>This professional also conducts PET-CT or SPECT-CT scans to assess for tumour progression.</li> </ul>	<ul style="list-style-type: none"> <li><b>NENs:</b> radioligand therapy is administered in four cycles, scheduled by the patient coordinator. Blood tests are conducted following each cycle and health checks are monitored throughout by the clinical nurse specialist and/or nuclear medicine nursing staff.</li> <li><b>Prostate cancer and lymphoma:</b> radioligand therapy only requires one administration cycle.</li> </ul>
<b>Follow-up</b>	<ul style="list-style-type: none"> <li>The MDT discusses the patient's response to the therapy and develops future management plans. The medical oncologist (or patient's lead physician) continues to monitor and follow-up with the person post-treatment.</li> </ul>	
<p>MDT, multidisciplinary team; NENs, neuroendocrine neoplasms; PET-CT, positron emission tomography–computed tomography; SPECT-CT, single-photon emission computed tomography–computed tomography</p>		

## References

1. Maser B, Force LM, Friedrich P, *et al.* 2020. Paediatric Oncology System Integration Tool (POSIT) for the joint analysis of the performance of childhood cancer programs and health systems. *J Cancer Policy*: 10.1016/j.jcpo.2019.100208
2. World Health Organization. Health service delivery. Available from: [https://www.who.int/healthinfo/systems/WHO\\_MBHSS\\_2010\\_section1\\_web.pdf](https://www.who.int/healthinfo/systems/WHO_MBHSS_2010_section1_web.pdf) [Accessed 16/11/20]
3. Independent Cancer Taskforce. Achieving world-class cancer outcomes: a strategy for England 2015-2020. Available from: [https://www.cancerresearchuk.org/sites/default/files/achieving\\_world-class\\_cancer\\_outcomes\\_-\\_a\\_strategy\\_for\\_england\\_2015-2020.pdf](https://www.cancerresearchuk.org/sites/default/files/achieving_world-class_cancer_outcomes_-_a_strategy_for_england_2015-2020.pdf) [Accessed 11/11/20]
4. Gray R, Gordon B, Meredith M. 2017. *Meeting Patients' Needs: Improving the effectiveness of multidisciplinary team meetings in cancer services*. London: Cancer Research UK
5. Specchia ML, Frisicale EM, Carini E, *et al.* 2020. The impact of tumor board on cancer care: evidence from an umbrella review. *BMC Health Serv Res*: 10.1186/s12913-020-4930-3
6. Buscombe J. 2020. Interview with Christine Merkel at The Health Policy Partnership [Telephone]. 21/09/20
7. Payne H. 2020. Interview with Emmanuelle Plucker at The Health Policy Partnership [Telephone]. 02/10/20
8. Orchard K. 2021. Interview with Christine Merkel at The Health Policy Partnership [Telephone]. 08/02/21
9. Sidpra J, Chhabda S, Gaier C, *et al.* 2020. Virtual multidisciplinary team meetings in the age of COVID-19: an effective and pragmatic alternative. *Quant Imaging Med Surg* 10(6): 1204-07
10. Tinsley J. 2021. Interview with Lucy Morgan at The Health Policy Partnership [Telephone]. 23/04/21
11. Buscombe J. 2021. Interview with Lucy Morgan at The Health Policy Partnership [Telephone]. 22/03/21
12. Neuroendocrine Cancer UK. 2021. *Barriers to Diagnosis*. United Kingdom: Neuroendocrine Cancer UK
13. UK and Ireland Neuroendocrine Tumour Society. UKINETS bitesize guidance: Pulmonary Neuroendocrine Neoplasms Treatment. Available from: <https://www.ukinets.org/wp-content/uploads/UKINETS-bitesize-guidance-Pulmonary-Neuroendocrine-Neoplasms-Treatment-290120.pdf> [Accessed 21/05/21]
14. UK and Ireland Neuroendocrine Tumour Society. Clinical Practice. Available from: <https://www.ukinets.org/net-clinics-clinical-practice/> [Accessed 17/12/20]

15. National Institute for Health and Care Excellence. Prostate cancer overview. Available from: <https://pathways.nice.org.uk/pathways/prostate-cancer> [Accessed 31/03/21]
16. National Institute for Health and Care Excellence. Non-Hodgkin's lymphoma overview. Available from: <https://pathways.nice.org.uk/pathways/non-hodgkins-lymphoma> [Accessed 31/03/21]
17. Prostate Cancer UK. Best Practice Pathway. Available from: <https://prostatecanceruk.org/about-us/projects-and-policies/best-practice-pathway> [Accessed 30/03/21]
18. Prostate Cancer UK. Prostate Cancer UK's best practice pathway: treatment. Available from: <https://prostatecanceruk.org/media/2498694/treatmentpathwaypathwaycommentaryupdate-nov2018-2-1.pdf> [Accessed 08/10/20]
19. Royal College of Physicians. Nuclear medicine: Workforce and job planning. Available from: <https://www.rcpmedicalcare.org.uk/developing-physicians/specialties/nuclear-medicine/workforce> [Accessed 19/08/20]
20. Buscombe J. 2016. Therapeutic Nuclear Medicine in the UK. In: McCready R, Gnanasegaran G, Bomanji JB, eds. *A History of Radionuclide Studies in the UK: 50th Anniversary of the British Nuclear Medicine Society*. Cham: Springer: 121-28
21. Health Education England. Nuclear Medicine. Available from: <https://kss.hee.nhs.uk/clinrad/nuclear-medicine/> [Accessed 30/03/21]
22. Stabin MG, Madsen MT, Zaidi H. 2019. Personalised dosimetry is a much for appropriate molecular radiotherapy. *Med Phys* 46(11): 4713-16
23. Hartman N. 2021. Personal communication by email: 08/01/21
24. Institute of Physics and Engineering in Medicine. Patients at risk of waiting longer for scans due to staff shortages. [Updated 15/11/18]. Available from: <https://www.ipem.ac.uk/NewsExternalAffairs/LatestNews/TabId/366/ArtMID/1595/ArticleID/317/Patients-at-risk-of-waiting-longer-for-scans-due-to-staff-shortages.aspx> [Accessed 18/05/21]
25. Society of Nuclear Medicine and Molecular Imaging. Fact Sheet: What is Radiation Dosimetry? Available from: <https://www.snmni.org/AboutSNMMI/Content.aspx?ItemNumber=31086> [Accessed 04/05/21]
26. Bodei L, Kidd M, Baum RP, *et al.* 2014. PRRT: Defining the paradigm shift to achieve standardization and individualization. *J Nucl Med* 55(11): 1753-6
27. European Association of Nuclear Medicine. 2017. *Internal Dosimetry Task Force Report on: Treatment Planning For Molecular Radiotherapy: Potential And Prospects*. Vienna, Austria: European Association of Nuclear Medicine
28. Legislation.gov.uk. The Ionising Radiation (Medical Exposure) Regulations 2017. Available from: [https://www.legislation.gov.uk/ukxi/2017/1322/pdfs/ukxi\\_20171322\\_en.pdf](https://www.legislation.gov.uk/ukxi/2017/1322/pdfs/ukxi_20171322_en.pdf) [Accessed 01/12/20]

29. The Royal Marsden NHSFT. 2021. Services offered: Healthcare Providers. Available from: <https://www.royalmarsden.nhs.uk/royal-marsden-dosimetry-centre/services-offered-healthcare-providers> [Accessed 12/08/21]
30. European Medicines Agency. Lutathera EPAR Product Information. [Updated 27/01/21]. Available from: [https://www.ema.europa.eu/en/documents/product-information/lutathera-epar-product-information\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/lutathera-epar-product-information_en.pdf) [Accessed 10/06/21]
31. Jervis N. 2020. Personal communication by email: 16/12/20
32. Prostate Cancer UK. Clinical Nurse Specialist (CNS) workforce. Available from: <https://prostatecanceruk.org/about-us/projects-and-policies/clinical-nurse-specialist-cns-workforce> [Accessed 14/02/21]
33. British Society for Haematology. 2020. *British Society for Haematology workforce report 2019*. London: BSH
34. Bentley D. 2021. Interview with Emmanuelle Plucker at The Health Policy Partnership [Telephone]. 08/02/21
35. Scowcroft S, Gill R. 2021. Interview with Lucy Morgan at The Health Policy Partnership [Telephone]. 19/04/21
36. Macmillan Cancer Support. Addressing the Gap: Highlighting the need for growing the specialist cancer nursing workforce. Available from: [https://www.macmillan.org.uk/images/addressing-the-gap-report\\_tcm9-358808.pdf](https://www.macmillan.org.uk/images/addressing-the-gap-report_tcm9-358808.pdf) [Accessed 05/02/21]
37. NHS England. 2020. *WE ARE THE NHS: People Plan for 2020/2021 - action for us all*. Leeds: NHS England
38. Lamarca A. 2020. Interview with Christine Merkel at The Health Policy Partnership [Telephone]. 30/09/20
39. Buscombe J. 2020. The Future of Molecular Radiotherapy Services in the UK. *Clin Oncol*: 10.1016/j.clon.2020.11.012
40. Kulkarni HR, Singh A, Baum RP. 2016. Advances in the Diagnosis of Neuroendocrine Neoplasms. *Semin Nucl Med* 46(5): 395-404
41. Lenzo NP, Meyrick D, Turner JH. 2018. Review of Gallium-68 PSMA PET/CT Imaging in the Management of Prostate Cancer. *Diagnostics (Basel)*: 10.3390/diagnostics8010016
42. Young JD, Jauregui-Osoro M, Wong WL, *et al.* 2021. An overview of nuclear medicine research in the UK and the landscape for clinical adoption. *Nucl Med Commun*: 10.1097/mnm.0000000000001461
43. Scarsbrook AF, Barrington SF. 2016. PET-CT in the UK: current status and future directions. *Clin Radiol* 71(7): 673-90
44. Foley RW, Redman SL, Graham RN, *et al.* 2020. Fluorine-18 labelled prostate-specific membrane antigen (PSMA)-1007 positron-emission tomography - computed tomography: normal patterns, pearls, and pitfalls. *Clin Radiol* 75(12): 903-13

45. Janssen I, Chen CC, Millo CM, *et al.* 2016. PET/CT comparing 68 Ga-DOTATATE and other radiopharmaceuticals and in comparison with CT/MRI for the localization of sporadic metastatic pheochromocytoma and paraganglioma. *Eur J Nucl Med Mol Imaging* 43(10): 1784-91
46. Van Binnebeek S, Vanbilloen B, Baete K, *et al.* 2016. Comparison of diagnostic accuracy of 111 In-pentetreotide SPECT and 68 Ga-DOTATOC PET/CT: a lesion-by-lesion analysis in patients with metastatic neuroendocrine tumours. *Eur Radiol* 26(3): 900-09
47. Physics World. Cyclotron-based gallium-68 generator breaks production records. Available from: <https://physicsworld.com/a/cyclotron-based-gallium-68-generator-breaks-production-records/> [Accessed 16/12/20]
48. The Carcinoid Cancer Foundation. Find a facility. Available from: <https://www.prrtgalliumcenters.org/find-your-facility/> [Accessed 09/12/20]
49. Bomanji J. 2020. Interview with Emmanuelle Plucker at The Health Policy Partnership [Telephone]. 23/09/20
50. Jervis N. 2020. Interview with Emmanuelle Plucker and Christine Merkel at The Health Policy Partnership [Telephone]. 21/09/20
51. The Scottish Government. Better treatment for prostate cancer. Available from: <https://www.gov.scot/news/better-treatment-for-prostate-cancer/> [Accessed 26/10/20]
52. Scottish Clinical Imaging Network. SCIN Subgroup: PET-CT Working Group — Meeting Record. Available from: <https://www.scin.scot.nhs.uk/wp-content/uploads/2020/10/2020-10-05-SCIN-PET-CT-Minutes-v1.pdf> [Accessed 26/05/21]
53. Stalbow K. 2020. Interview with Emmanuelle Plucker at The Health Policy Partnership [Telephone]. 28/09/20
54. National Cancer Research Institute. 2016. *CTRad: identifying opportunities to promote progress in molecular radiotherapy research in the UK*. London: NCRI
55. University College London Hospitals NHS Foundation Trust. Molecular radiotherapy. Available from: <https://www.uclh.nhs.uk/our-services/find-service/cancer-services/radiotherapy/radiotherapy-treatment-options-and-equipment/molecular-radiotherapy> [Accessed 20/05/21]
56. European Neuroendocrine Tumor Society. About Centers of Excellence (CoE). Available from: [https://www.enets.org/about\\_enets\\_coe.html](https://www.enets.org/about_enets_coe.html) [Accessed 30/11/20]
57. European Medicines Agency. Zevalin ibritumomab tiuxetan. Available from: <https://www.ema.europa.eu/en/medicines/human/EPAR/zevalin> [Accessed 07/07/20]
58. Cooper M. 2021. Interview with Lucy Morgan at The Health Policy Partnership. 19/04/21
59. Illidge T. 2021. Interview with Lucy Morgan at The Health Policy Partnership [Telephone]. 01/06/21

60. Clinicaltrials.gov. Study of 177Lu-PSMA-617 In Metastatic Castrate-Resistant Prostate Cancer (VISION). [Updated 25/03/21]. Available from: <https://www.clinicaltrials.gov/ct2/show/NCT03511664> [Accessed 22/04/21]
61. Clinicaltrials.gov. A Phase I/II Study of Betalutin for Treatment of Relapsed Non-Hodgkin Lymphoma (LYMRIT-37-01). [Updated 01/04/21]. Available from: <https://clinicaltrials.gov/ct2/show/NCT01796171?term=177Lu&draw=2&rank=93> [Accessed 01/05/21]
62. Payne H. 2021. Interview with Christine Merkel at The Health Policy Partnership [Telephone]. 05/03/21
63. NHS England. Service Specifications: Operational Delivery Networks for Adult External Beam Radiotherapy Services. Available from: <https://www.england.nhs.uk/wp-content/uploads/2019/01/Operational-Delivery-Networks-for-External-Beam-Radiotherapy-Services-adults.pdf> [Accessed 09/12/20]
64. Wadsley J. 2021. Interview with Chris Melson at The Health Policy Partnership [Teleconference]. 24/05/21
65. Buscombe J. 2021. Interview with Chris Melson at The Health Policy Partnership [Telephone]. 29/04/21