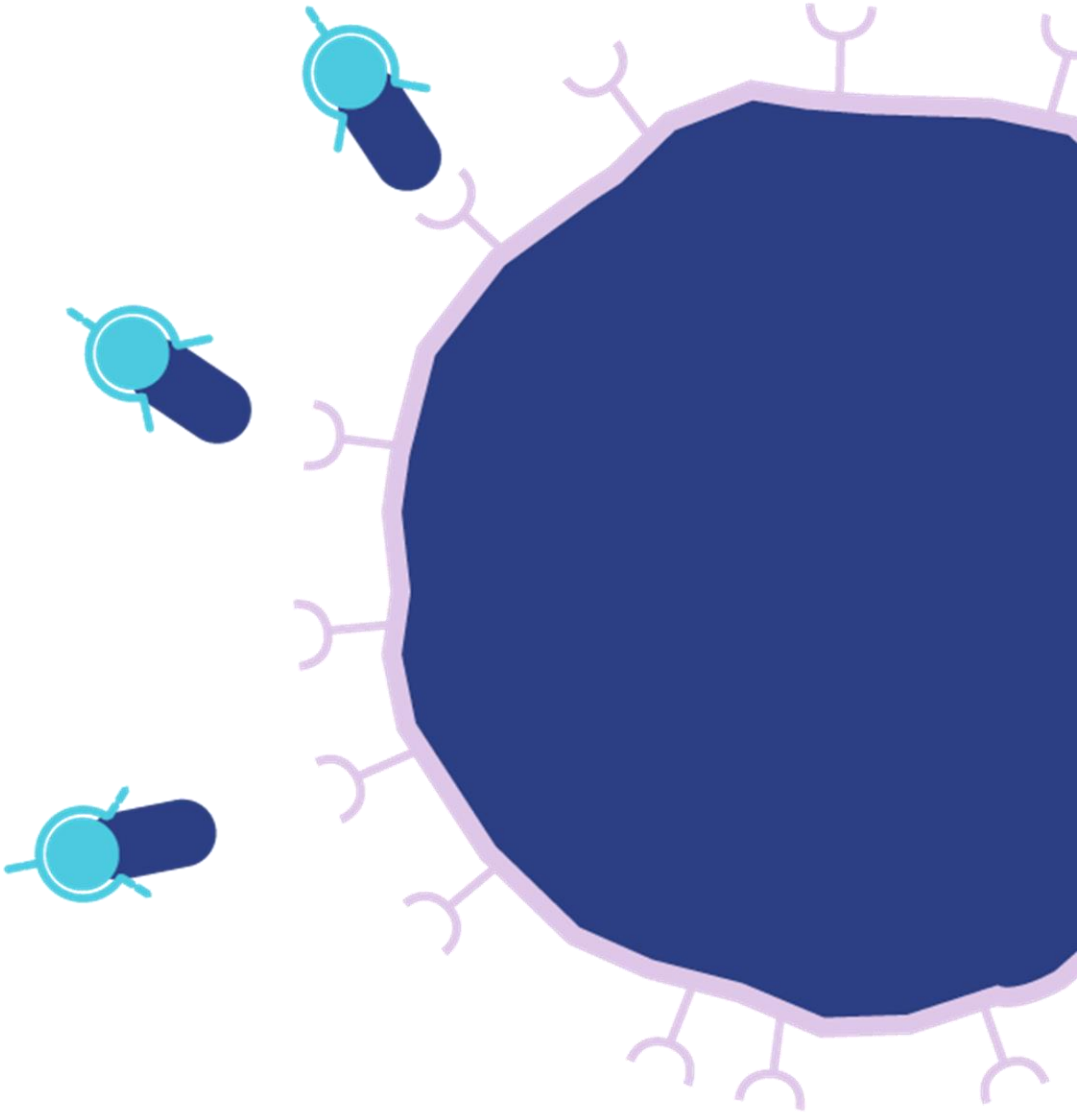

The Health Policy Partnership
[research, people, action]

Health system readiness for radioligand therapy in the US

Service provision

Working paper

November 2021

This working paper has been developed by The Health Policy Partnership and Avalere Health in collaboration with a US Expert Advisory Group. The group has had full editorial control over all national-level outputs. The project is supported through an unrestricted grant from Advanced Accelerator Applications, a Novartis Company, with additional support from Nordic Nanovector.

Contents

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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 US. It explores current integration and future readiness for the therapy 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. It captures the provision of radioligand therapy services in US, from referral and imaging practices to administration of the therapy and follow-up. Throughout the paper, we focus on the situation in neuroendocrine tumors, lymphoma, and prostate cancer.

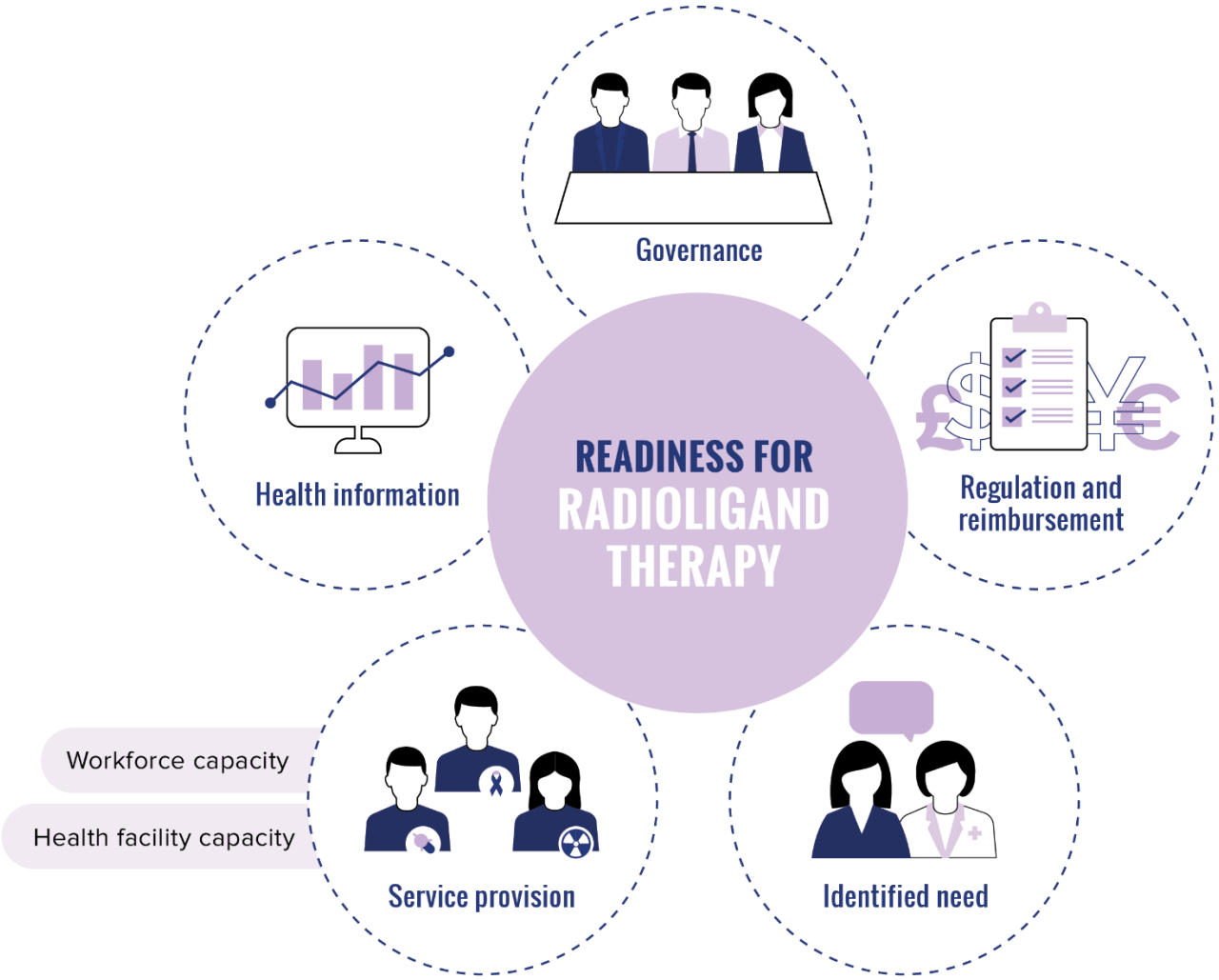
- This working paper is supported by other documents on health system readiness for radioligand therapy in the US. For more details, please visit: www.radioligandtherapy.com/framework/US

Terminology

This working paper uses the term radioligand therapy to refer to peptide-receptor radionuclide therapy (PRRT), prostate-specific membrane antigen (PSMA) therapy, and radioimmunotherapy. We appreciate that there are a variety of other terms that may be used for radioligand therapy.

Radioligand therapy is a specific subtype of radiopharmaceutical therapies. Where possible, this working paper includes data relating to radioligand therapy. However, where research about radioligand therapy is not specifically available, we may refer more broadly to radiopharmaceutical therapies.

Figure 1. Domains of the Radioligand Therapy Readiness Assessment Framework: US



What is service provision?

Provision of safe and effective cancer care is fundamental to ensuring positive outcomes for people with cancer. Health systems are only as effective as the services they provide.[1] 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 provision of care.[2] For any health intervention, several important characteristics should be met:[1]

- **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 socioeconomic status, race, language, geography, or complex referral pathways.
- **Continuity:** care should be consistent throughout a person'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-centeredness:** care should be organized 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.

What does optimal provision of radioligand therapy look like?

As a highly multidisciplinary and collaborative approach, radioligand therapy requires clear care pathways to promptly identify and refer people who are eligible. Broadly speaking, six steps are required for the seamless and high-quality delivery of radioligand therapy in the US:[3]

1. Patient eligibility should be assessed using factors including pathology, distribution of disease, conventional imaging, and functional imaging with positron emission tomography (PET) and/or gamma-imaging in some indications.[4] Service provision must be structured in a way that supports both imaging and therapeutic elements of radioligand therapy, as well as engagement between the referring physician and nuclear medicine or radiology experts. This can be done in the context of a multidisciplinary tumor board.

2. The eligible patient is referred to a facility or physician authorized to deliver radioligand therapy.

3. The physician (Authorized User, AU) will then review and confirm the person's eligibility. Separately, reimbursement or payment for the therapy will be confirmed. The AU will then work together with the referring physician and multidisciplinary team to develop a personalized treatment plan.

4. The therapy is planned in line with relevant regulations and logistical requirements.

5. A dedicated team of experts with radioligand therapy experience and appropriate licensing administer the treatment in a designated clinical facility supplied with high-quality imaging and therapeutic equipment, in line with radiation protection regulations. The facility should have the necessary capacity and processes to effectively manage radioactive waste.

6. Patient follow-up and adverse events are addressed, both between cycles and at the end of the therapy, and should involve both AUs and referring physicians.

1 Workforce capacity

Summary assessment

Indicators	Assessment
How are Authorized Users (AUs) involved in multidisciplinary therapeutic decision-making in the US?	Nuclear medicine physicians, radiation oncologists, and nuclear radiologists may be involved in therapeutic decision-making through involvement in formal tumor boards or through informal multidisciplinary working. The extent of their involvement varies across and between institutions.
Which healthcare professionals are involved in managing and delivering radioligand therapy in the US?	The professionals involved in recommending, prescribing, coordinating, and delivering radioligand therapy generally include: • medical oncologist or equivalent referring physician (for example, a urologist, endocrinologist, gastroenterologist, or hematologist) • AU (nuclear medicine physician, radiation oncologist, or nuclear radiologist) • nuclear medicine technologist • radiopharmacist • radiation safety specialist • nurse. The individuals involved will differ according to the specific therapy and clinical facility's size.
Is there sufficient capacity in the US to meet current demand for radioligand therapy?	In 2019, there were 5,306 radiation oncologists, 28,025 radiologists, and over 18,000 nuclear medicine technologists. Between 1972 and 2020, 5,907 nuclear medicine physicians were certified. While not all of these healthcare professionals will be licensed to deliver radioligand therapy, experts believe that there will be an increase in the number of physicians seeking advanced training to become an AU. As such, there should be enough physicians to meet the increased demand for radioligand therapy anticipated in the future.

Optimal delivery of radioligand therapy requires highly multidisciplinary care, but this form of working is not consistently available across institutions. Multidisciplinary tumor boards are used throughout the US for all types of cancer care and may include representatives of specialist nursing, medical oncology, radiation oncology, surgery,

urology, endocrinology, gastroenterology, hematology, pathology, radiology, and nuclear medicine, alongside holistic roles such as specialists in palliative care and pain management, social care, and primary care.[5] Physicians and healthcare professionals from these varied departments are responsible for ensuring the concerted and safe planning, preparation, and administration of radioligand therapy to people with cancer.[3 6] Each healthcare professional involved in the team directly administering radioligand therapy has a unique role and well-defined responsibilities (*Box 1*). However, as each center decides on the composition of the cancer tumor board and approach to radioligand therapy delivery, the extent to which multidisciplinary care is accessed by patients can vary significantly.[7-11] Centers may facilitate multidisciplinary collaboration and communication through many different channels (*Real-world example 1*), but greater and more consistent efforts are required in order to ensure that every person undergoing radioligand therapy receives truly multidisciplinary care.

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 the following experts are generally involved:[6 12]

- **Medical oncologist:** communicates with the nuclear medicine team about potentially eligible patients, evaluates patients' progress on a periodic basis, and monitors for potential adverse events.
- **Authorized User:** may be a nuclear medicine physician, radiation oncologist, or nuclear radiologist. An AU is involved in tumor board meetings to determine the appropriateness of radioligand therapy and help identify and manage appropriate candidates; orders any necessary imaging or additional testing to confirm eligibility prior to treatment; reviews the risks, benefits, and alternatives to radioligand therapy with the patient; prepares and delivers the radioligand therapy; evaluates treatment response and manages toxicities alongside other physicians; and is ultimately responsible for ensuring safe delivery in accordance with all applicable regulations and policies. They may also provide education to the patient and their loved ones, collect informed consent, and discharge post-

treatment. AUs have different licensing statuses that influence the therapies which they can be responsible for.

- **Radiopharmacist:** orders, receives, stores, and maintains the inventory of radiopharmaceuticals and related supplies.
- **Hospital pharmacist:** orders correct dosage of therapy, provides antiemetics, amino acids and other pre- and post-treatment interventions.
- **Radiation safety officer:** responsible for ensuring all institutional and regulatory requirements are met, including training staff on procedures, preparation of treatment rooms, and management of contaminated materials.
- **Nuclear or oncology nurse:** provides patient education, pre- and post-treatment support, administration of antiemetics, and monitoring during therapy.
- **Nuclear medicine technologist:** directly assists the AU in administration of the radioligand therapy; orders, receives and inspects the therapy upon receipt from manufacturer; and performs other related tasks.

Additional team members may include a gastroenterologist, endocrinologist, or hematologist; they can help identify appropriate patients, assist with treatment, and address side effects. They may also provide follow-up care. These healthcare professionals may or may not be based in the same institution as the rest of the experts involved in managing and delivering radioligand therapy.[11] For example, they may practice in community settings, introducing additional challenges to multidisciplinary working.

Real-world example 1. Examples of multidisciplinary collaboration methods

In many healthcare institutions, formal cancer care teams (tumor boards) are established to facilitate multidisciplinary therapeutic decision-making.[13] [14] There is no standard guidance for how tumor boards should be managed, so each facility develops its own protocols and ways of working. Generally, tumor boards gather on a regular basis (weekly to monthly) to discuss complex cases, people with less common types of cancer, or unsuccessful treatments.[13] As tumor boards may be conducted virtually, there is significant potential to expand access to multidisciplinary expertise and care to rural or underserved communities.[14] Specific patterns of multidisciplinary working that have proved effective for radiopharmaceutical therapies include the following:

- As part of the NETTER-1 trial, the research team at the Dana-Farber Cancer Institute implemented a single point of contact from the nuclear medicine department, who was responsible for seamless coordination of care among members of the multidisciplinary team.[12]
- The nuclear medicine department of the Mayo Clinic Florida used an email distribution list to maintain communication with members of the team providing radioligand therapy.[6] Joint appointments are organized between the patient, medical oncology, and radioligand therapy delivery teams, to reduce confusion and miscommunication that might occur between treatment cycles.[6]
- When licensed radioligand therapy was available for lymphoma at Northwestern Memorial Hospital, there was a clear (though informal) referral pathway between the Division of Hematology and Oncology and the Division of Nuclear Medicine. Nurse practitioners and colleagues in the nuclear medicine department played vital roles in coordinating care across these specialties.[15]
- Some community practices do not have enough patients eligible for radionuclide therapies to justify employing full-time radiation oncologists, nuclear medicine physicians, or associated technologists and radiopharmacists. One oncologist at a smaller center noted that employing certain specialists part-time ensured that there is adequate workforce capacity to deliver radiopharmaceutical therapies for people with prostate cancer, without it being prohibitively expensive.[11]

Further integration of nuclear medicine physicians and radiation oncologists into multidisciplinary teams will help increase awareness of radioligand therapy. Radioligand therapy may be delivered by licensed AUs in the radiation oncology or nuclear medicine departments. While radiation oncologists may traditionally work more closely with medical oncologists and other specialties, the role of nuclear medicine professionals has historically been more limited. As such, members of the nuclear medicine community may not be as fully ingrained into multidisciplinary care processes or tumor boards outside of neuroendocrine tumors (NETs).[16] As multidisciplinary working is one way in which lead professionals become aware of radioligand therapy, the limited involvement of nuclear medicine physicians in care may mean that many lead physicians do not consider the therapy when appropriate. Ultimately, this could mean that people who might benefit from the therapy are not referred for it. Together, radiation oncologists and nuclear medicine physicians may be able to become more engaged in multidisciplinary working, increasing awareness of the therapy and helping streamline referral processes.

- For more information about healthcare professional awareness of radioligand therapy, read the working paper on identified need.

1.1 Current and future workforce

It seems that the radioligand therapy workforce is sufficient to meet current demand. In 2019, there were 5,306 active radiation oncologists, 28,025 radiologists (including all sub-disciplines), and more than 18,000 nuclear medicine technologists in the US.[17 18] In addition, the American Board of Nuclear Medicine reported certification of 5,907 nuclear medicine physicians between 1972 and 2020.[19] It must be noted that only specific subdisciplines of radiologists are AUs. Moreover, radiation oncologists will not necessarily have training specifically for radioligand therapy – although it is typically part of their training, the specifics will depend on where each physician received their training. All nuclear medicine physicians are trained to deliver radioligand therapy as part of their residency and fellowship training.[4]

Workforce capacity does not seem to be a primary concern for the future. Historically, the number of medical students seeking training in nuclear medicine has been decreasing.[2021] However, with many new therapeutic approaches in the pipeline, experts believe this trend will reverse, and anticipate an increase in the number of medical professionals seeking advanced training in nuclear medicine.[16] In addition, educational programs and professional organizations are encouraging training to equip current and

future AUs with the knowledge to safely and effectively deliver radiopharmaceutical therapies.[22] Discussions are also ongoing around the potential expansion of AU licenses to new specialties,[23-25] which may ultimately help expand the radioligand therapy delivery workforce. As a result, experts have suggested that the number of professionals delivering radioligand therapy is likely to keep pace with any future demand.

- For more details on healthcare professional awareness and training for radioligand therapy, read the working paper on identified need.

2 Health facility capacity

Summary assessment

Indicators	Assessment
Are staging and eligibility assessments for radioligand therapy appropriate to meet current and future demand in the US?	PET and gamma scans are required to assess eligibility for radioligand therapy in neuroendocrine tumors (NETs) and prostate cancer. Access to this imaging is variable, and may be particularly limited in rural areas. Molecular imaging is not required to assess eligibility for radioligand therapy in lymphoma, so the availability of these scans is not considered a factor affecting use of the therapy.
How are radioligand therapy services organized in the US health system?	**Current provision of radioligand therapy:** Radioligand therapy services are provided to patients via different care models, including centers of excellence, general nuclear medicine, and radiation oncology departments. At present, approximately 200 sites across 44 states offer the therapy for NETs. Although at least 280 sites are listed as providing currently licensed radioligand therapy for lymphoma, experts suggest that the therapy is not readily available. **Future provision of radioligand therapy:** Radioligand therapies currently under investigation in prostate cancer and lymphoma are available in centers involved in clinical trials. These are typically academic centers of excellence and integrated delivery networks.
Is the built environment in the US appropriate for the delivery of radioligand therapy?	Sites providing radioligand therapy must be appropriately equipped to deliver the approach, typically as an outpatient procedure, with lead-lined rooms, dedicated bathrooms, equipment, and storage space for radioactive waste, as required.

2.1 Imaging capacity for radioligand therapy

Molecular imaging is essential for delivering radioligand therapy in some types of cancer, but availability is geographically variable**.** PET or gamma scans are used to detect and localize tumors as a core aspect of eligibility assessments for radioligand therapy for NETs and prostate cancer.[26-29] However, establishing and maintaining a PET service can be cost-prohibitive for smaller practices, and there is variable coverage for PET procedures,[30] especially in rural areas.[4 11] As a result, access to and availability of imaging can be very uneven, which may delay or challenge diagnostic and therapeutic

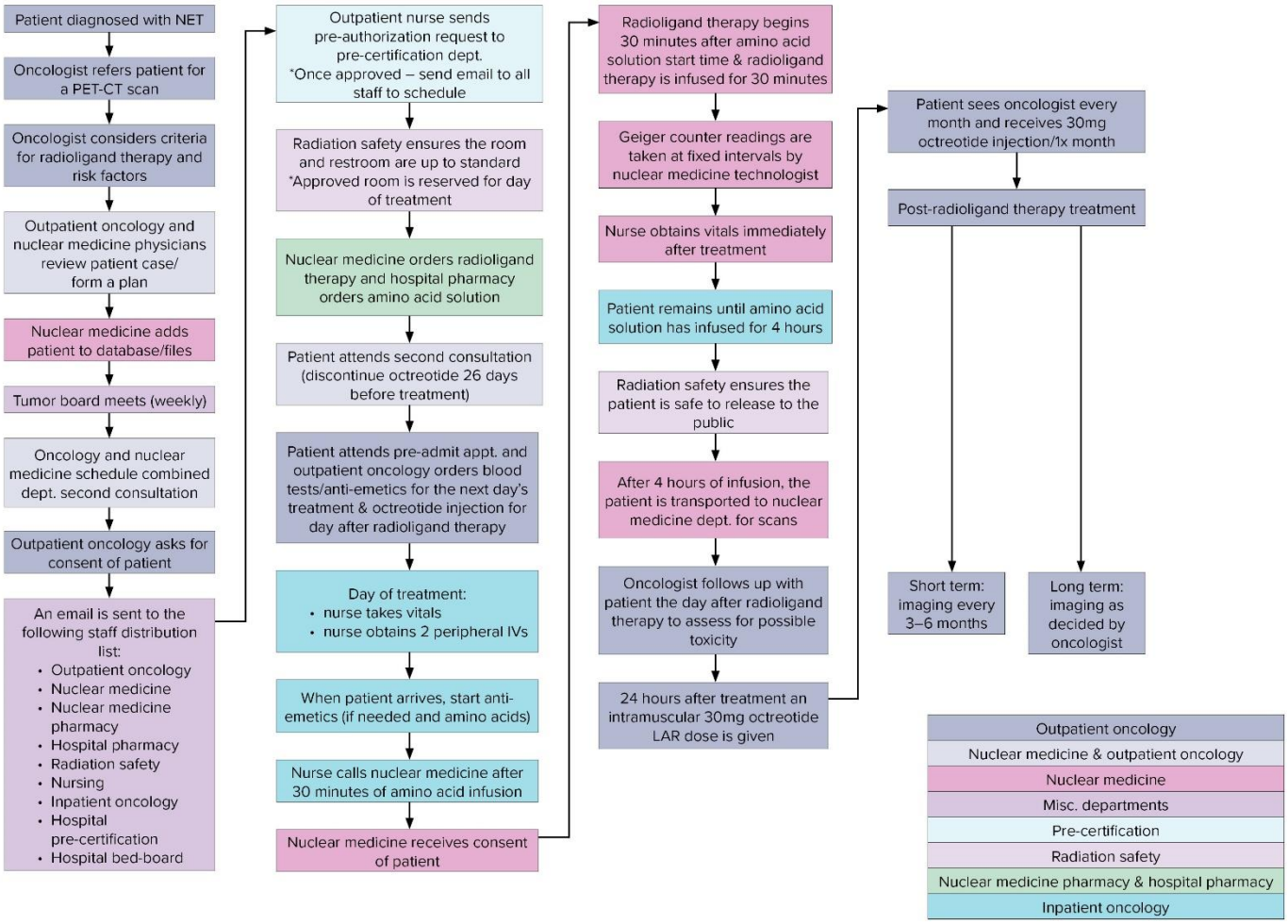
decision-making. If this remains unresolved, imaging could become a barrier to the wider use of radioligand therapy for NETs and prostate cancer. Molecular imaging is less critical to assess eligibility in lymphoma (although the standard-of-care fluorodeoxyglucose PET scan can be used to evaluate the distribution of disease and assess response to radioligand therapy).[4] Therefore, increasing imaging capacity would bring most value for the treatment of NETs and prostate cancer.

2.2 Provision of radioligand therapy

2.2.1 Provision of currently approved radioligand therapy

Use of radioligand therapy is well established in some large centers, but there are significant variations in its provision. Radioligand therapy can be delivered to people with NETs in approximately 200 sites across 44 states,[31] primarily as a hospital-based outpatient treatment in large academic or integrated centers.[6 12 27 28] Radioligand therapy for lymphoma is listed as being provided in at least 280 sites.[32] Care in both situations tends to require inpatient admission only in clinically or socially complex cases.[7 27 28] To account for the wide variety of center-level infrastructure and expertise, guidelines for the delivery of radioligand therapy have been designed to be adaptable.[28] As a result, the specific care model and pathway will depend on the patient's health insurance, geographic location, and healthcare institution. As each institution adapts guidelines to fit its own needs and capabilities, and employs different care processes, the quality of care may vary depending on where a person receives treatment. *Figure 2* provides an example of a care model employed in NETs at one large institution, developed to improve availability of the therapy.

Figure 2. Example workflow model for delivering radioligand therapy for NETs at the Mayo Clinic Florida[6]



Note: This workflow has been adapted to remove specific therapy names. The workflow helps indicate the level of detail and specificity that may help sites plan for the delivery of radioligand therapy; however, the exact steps and allocation of responsibility may vary between sites. For example, at other institutions the radiation oncologist may undertake the tasks allocated to the nuclear medicine physician.

Provision of radioligand therapy is further complicated by the lack of clear, consistent referral pathways. Large academic medical centers may have established processes for prescribing, referring people for, and delivering radioligand therapy within their institution,[9,15] but smaller centers may not. As there are no official or generalized referral pathways for radioligand therapy, this process can be challenging and costly. Interestingly, even in centers where referral pathways for radioligand therapy exist, an expert has suggested that physicians may be reluctant to use the pathways if they are too complex.[33] Perverse financial incentives may also limit the extent to which physicians are willing to make referrals.[15] A clear and simple referral pathway for each type of radioligand therapy would therefore be

hugely beneficial to guide physicians regarding when and how to refer eligible patients for the therapy, and to ensure that it is available as an option to all people who might benefit.

- For more details on reimbursement of radioligand therapy, read the working paper on regulation and reimbursement.

Limited availability of currently licensed radioligand therapy for lymphoma means that some service delivery systems are not regularly used. Radioligand therapy was initially licensed for use in lymphoma in the US in 2002.[34] However, despite demonstrated increases in progression-free survival and complete response,[35 36] experts have stated that the therapy is underutilized.[33 37] Factors driving limited uptake of the therapy included the fact that it was labor-intensive and referral pathways were complex, which made oncologists less willing to prescribe it.[33] Inadequate reimbursement procedures also played a role.[15] Limited usage created a downward cycle of decreasing sales and production. As production has become increasingly unreliable, an expert has noted that clinicians are less likely to consider the therapy as an option for their patients.[15] Moreover, declining use of radioligand therapy has resulted in fewer clinicians being familiar with or aware of the therapy,[37] further driving this downward cycle. These experiences can provide valuable lessons when working to ensure that other novel therapies can be made available to people who might benefit from them.

2.2.2 Clinical infrastructure

Sites currently providing radioligand therapy are appropriately equipped to deliver it. As radioligand therapy is generally provided as an outpatient procedure, current infrastructure largely seems appropriate to deliver care in this way.[15] Sites providing radioligand therapy are equipped with lead-lined rooms, dedicated bathrooms, necessary equipment, and appropriate storage space for radioactive waste. Challenges may arise should the number of people being referred for radioligand therapy increase dramatically.[38] Bulky waste items, such as paper and other disposables following treatment, may overwhelm storage facilities if space is limited or patient numbers increase. However, these center-specific capacity challenges may be easily overcome with experience, planning and targeted (but minimal) investment.

2.2.3 Future provision of radioligand therapy

New models of care and care pathways will be required for novel applications of radioligand therapy. The current model of care for NETs seems largely appropriate, but challenges will emerge if the therapy is expanded to larger populations of people with prostate cancer and lymphoma, who are more frequently seen in community settings. As such, new models of care may be required to facilitate use of any new radioligand therapies, both within large academic centers and community settings. Recognizing the lack of adequate care pathways, the American Society for Radiation Oncology (ASTRO) convened a multidisciplinary group of experts in 2020 to create a framework for developing these pathways. The framework can be broadly applied to all radiopharmaceutical therapies, now and in the future.[3] This is a timely step to ensure readiness for the growing spectrum of radiopharmaceuticals (*Real-world example 2*).

- For more on guidelines which include radioligand therapy, read the working paper on governance.

Real-world example 2. Radioligand therapy delivery pathways fit for the future

In 2020, based on anticipated growing use of radiopharmaceuticals such as radioligand therapy, ASTRO convened a multidisciplinary taskforce to develop a collaborative, patient-centered care pathway. It created a framework for developing a pathway of care for radioligand therapy, while acknowledging challenges that a potential increase of treatment options and a larger population of complex cancer patients can bring.[3] The framework outlines key steps across the pathway:

- Identification
- Referral
- Consultation
- Pre-therapy treatment planning
- Clinical coordination
- Prescription
- Administration
- Follow-up.

Institutions may adapt the pathway to account for differing infrastructure and composition of the multidisciplinary team, and to ensure seamless logistics and care delivery.[6 12 28]

Creating care pathways with clear referral processes may be particularly beneficial if radioligand therapy is approved for use in indications predominantly treated in the community setting. Most prostate cancer and lymphoma care takes place in community-based settings, which often lack the infrastructure that larger academic centers may have for delivering radiopharmaceutical therapies. As such, physicians working in community centers need to be aware not only of the option of radioligand therapy for their eligible patients, but also of appropriate nuclear medicine centers outside of their institution and the appropriate referral pathway for the therapy.[10 33] In these cases, the lack of a center-specific referral process itself poses another significant barrier. Where awareness of radioligand therapy among clinicians is limited, they will simply not refer or prescribe it for eligible patients.[15] It is worth noting that there are increasing collaboration and connections between community and academic centers,[39] which may help facilitate referrals between different institutions.

Access to clinical trials for radioligand therapy is not equitable and, without careful planning, may inadvertently translate into inequalities in the future. Current clinical trials for radioligand therapy in prostate cancer and lymphoma typically have trial sites located in specialist centers in major metropolitan areas, including Atlanta, Baltimore, Houston, Los Angeles, New Orleans, New York, Portland, Tucson, Madison, and more.[40 41] As there are a limited number of clinical trial centers, travel time may make it difficult for people with cancer to participate in trials for radioligand therapy. Moreover, there is widespread acknowledgement of significant disparities in access to and uptake of clinical trials across the US. As many of these clinical trial centers may become licensed centers that provide radioligand therapy in the future, careful planning is required to ensure geographic inequalities in access are addressed and to extend future availability of the therapy to all who might benefit.

Conclusion

Increased multidisciplinary collaboration will be essential to enable provision of radioligand therapy in the complex, and often fragmented, US health system. Notable challenges to the current and future provision of radioligand therapy services include: unequal access to imaging for eligibility assessments; limited multidisciplinary working and care coordination; variable care provision and lack of clear care pathways; and unclear or non-existent referral protocols for the therapy. In the future, radioligand therapy will be provided across an increasing array of healthcare settings, necessitating a multidisciplinary and consensus-driven vision of how care should be optimally provided in all situations. As part of this, care providers must work together to overcome the unique challenge of referral pathways, with a focus on building pathways from community settings or centers that do not have pre-existing radioligand therapy programs. This will ensure that all referring physicians understand how and when to refer people eligible for the therapy, and importantly, how they will engage with patients during and after delivery of radioligand therapy. Finally, planning equitable access to radioligand therapy will be essential to avoid reinforcing or exacerbating any pre-existing inequalities in access to therapies or clinical trials.

References

1. World Health Organization. Health service delivery. Available from: https://www.who.int/healthinfo/systems/WHO_MBHSS_2010_section1_web.pdf [Accessed 16/11/20]

2. 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

3. Buatti JM, Pryma DA, Kiess AP*, et al.* 2020. A framework for patient-centered pathways of care for radiopharmaceutical therapy (RPT): An ASTRO consensus document. *Int J Radiat Oncol Biol Phys*: 10.1016/j.ijrobp.2020.11.048

4. Mittra E. 2021. Personal communication by email: 08/12/21

5. Living with NETs. Your multidisciplinary care team. Available from: https://www.livingwithnets.com/en-us/your-care-team/ [Accessed 22/12/20]

6. Kasi P, Maige C, Shahjehan F*, et al.* 2019. A care process model to deliver (177)Lu-dotatate peptide receptor radionuclide therapy for patients with neuroendocrine tumors. *Front Oncol*: 10.3389/fonc.2018.00663:

7. ACR–ACNM–ASTRO–SNMMI. 2020. *ACR–ACNM–ASTRO–SNMMI practice parameter for Lutetium-177 (Lu-177) dotatate therapy.* Reston, VA: American College of Radiology

8. Morris M. 2020. Interview with Michelle Bruno at Avalere Health [Telephone]. 10/14/20

9. Ennis R. 2020. Interview with Michelle Bruno at Avalere Health [Telephone]. 10/16/20

10. Mittra E. 2020. Interview with Michelle Bruno at Avalere Health [Telephone]. 10/14/20

11. Seiber P. 2020. Interview with Michelle Bruno at Avalere Health [Telephone]. 12/22/20

12. Abbott A, Sakellis C, Andersen E*, et al.* 2018. Guidance on (177)Lu-dotatate peptide receptor radionuclide therapy from the experience of a single nuclear medicine division. *J Nucl Med Technol* 46(3): 237-44

13. 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* 20(1): 1-14

14. U. C. Davis Comprehensive Cancer Care Network. Virtual Tumor Boards. Available from: https://health.ucdavis.edu/cancercarenetwork/virtualtumorboard/index.html [Accessed 06/08/21]

15. Gordon L. 2021. Interview with Lucy Morgan at The Health Policy Partnership [Telephone]. 07/20/21

16. Lee D. 2020. Interview with Michelle Bruno at Avalere Health [Telephone]. 10/07/20

17. Association of American Medical Colleges. 2020. Active Physicians in the Largest Specialties, 2019. Available from: https://www.aamc.org/data-reports/workforce/interactive-data/active-physicians-largest-specialties-2019 [Accessed 07/12/21]

18. Occupational Outlook Handbook. Registered nurses [Online]. Available from: https://www.bls.gov/ooh/healthcare/registered-nurses.htm [Accessed 10/29/20]

19. Wenzel-Lamb N. 2021. Personal Communication by Email: 06/07/21

20. Ruddell JH, Eltorai AEM, Tang OY*, et al.* 2020. The Current State of Nuclear Medicine and Nuclear Radiology: Workforce Trends, Training Pathways, and Training Program Websites. *Acad Radiol* 27(12): 1751-59

21. Czernin J, Sonni I, Razmaria A*, et al.* 2019. The Future of Nuclear Medicine as an Independent Specialty. *J Nucl Med* 60(Supplement 2): 3S-12S

22. ASTRO. 2019. Required Training and Experience for Authorized Users for Radionuclide Therapy. Available from: https://www.astro.org/ASTRO/media/ASTRO/Blog/Multi-SocietalLettertoNRCreTraining.pdf [Accessed 20/05/21]

23. American College of Radiology. NRC staff recommends revised authorized user T&E rules for unsealed materials. [Updated 01/23/20]. Available from: https://www.acr.org/Advocacy-and-Economics/Advocacy-News/Advocacy-News-Issues/In-the-January-25-2020-Issue/NRC-Staff-Recommends-Revised-Authorized-User-TE-Rules [Accessed 09/14/20]

24. Razmaria A, Calais J, Czernin J. 2019. Delivering radionuclide therapies requires extensive training and competence: send a firm message to the NRC and your representatives. *J Nucl Med* 60: 1-2

25. Segall G. 2019. ABNM statement on ACMUI changes in authorized user training and education. *J Nucl Med* 60: 17N

26. Society of Nuclear Medicine and Molecular Imaging. 2018. *PRRT factsheet.* Reston, VA: SNMMI

27. Kendi AT, Halfdanarson T, Packard A*, et al.* 2019. Therapy with (177)Lu-dotatate: clinical implementation and impact on care of patients with neuroendocrine tumors. *AJR Am J Roentgenol* 213(2): 309-17

28. Hope TA, Abbott A, Colucci K*, et al.* 2019. NANETS/SNMMI Procedure Standard for Somatostatin Receptor-Based Peptide Receptor Radionuclide Therapy with (177)Lu-DOTATATE. *J Nucl Med* 60(7): 937-43

29. Lenzo NP, Meyrick D, Turner JH. 2018. Review of gallium-68 PSMA PET/CT imaging in the management of prostate cancer. *Diagnostics* 8(16): 1-17

30. Fischer BM, Siegel BA, Weber WA*, et al.* 2016. PET/CT is a cost-effective tool against cancer: synergy supersedes singularity. *Eur J Nucl Med Mol Imaging* 43(10): 1749-52

31. Lutathera. 2021. Find a treatment site. Available from: https://www.lutathera.com/find-a-treatment-site/ [Accessed 10/01/21]

32. Acrotech Biopharma. Find a Zevalin administrative facility. Available from: http://zevalin.com/hcp/zevalin-dosing-and-administration/find-a-zevalin-administration-facility/ [Accessed 09/24/21]

33. Gopal A. 2021. Case study: clinical readiness in the US. Launch of the Radioligand Therapy Readiness Assessment Framework; 06/09/21; Online event

34. Grillo-López AJ. 2002. Zevalin: the first radioimmunotherapy approved for the treatment of lymphoma. *Expert Rev Anticancer Ther* 2(5): 485-93

35. Witzig TE, Gordon LI, Cabanillas F*, et al.* 2002. Randomized controlled trial of yttrium-90-labeled ibritumomab tiuxetan radioimmunotherapy versus rituximab immunotherapy for patients with relapsed or refractory low-grade, follicular, or transformed B-cell non-Hodgkin's lymphoma. *J Clin Oncol* 20(10): 2453-63

36. Green DJ, Press OW. 2017. Whither radioimmunotherapy: to be or not to be? *Cancer Res* 77(9): 2191–96

37. Mittra E. 2021. Interview with Lucy Morgan and Christine Merkel at the Health Policy Partnership and Michelle Bruno at Avalere [Telephone]. 04/14/21

38. Lapi S. 2020. Interview with Michelle Bruno at Avalere Health [Telephone]. 06/10/20

39. Melas M, Subbiah S, Saadat S*, et al.* 2020. The community oncology and academic medical center alliance in the age of precision medicine: cancer genetics and genomics considerations. *Journal of Clinical Medicine* 9(7): 2125

40. Clinicaltrials.gov. Study of 177Lu-PSMA-617 In Metastatic Castrate-Resistant Prostate Cancer (VISION). [Updated 07/27/21]. Available from: https://www.clinicaltrials.gov/ct2/show/NCT03511664 [Accessed 08/03/21]

41. ClinicalTrials.gov. Study of Betalutin for Treatment of Relapsed or Refractory Non-Hodgkin Lymphoma (LYMRIT-37-05). [Updated 01/12/21]. Available from: https://www.clinicaltrials.gov/ct2/show/NCT02658968 [Accessed 07/02/21]