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Unsealed Source: Scope of Practice for Radiopharmaceuticals Among United States Radiation Oncologists

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Abstract

Purpose: Our purpose was to determine the utilization of and barriers to implementation of radiopharmaceutical therapy (RPT) among U.S. radiation oncologists.

Methods and Materials: An anonymous, voluntary 21-item survey directed toward attending radiation oncologists was distributed via social media platforms (Twitter, LinkedIn, Facebook, Student Doctor Network). Questions assessed practice characteristics, specific RPT prescribing patterns, RPT prescribing interest, and perceived barriers to RPT implementation. Nonparametric χ^2 test was used for correlation statistics.

Results: Of the 142 respondents, 131 (92.3%) practiced in the United States and were included for this analysis. Respondents were well balanced in terms of practicing region, population size served, practice setting, and years in practice. Forty-eight percent (n = 63) reported prescribing at least 1 RPT. An additional 7% (n = 8) participate in RPT administration without billing themselves. Among those that actively prescribed RPT, the mean cumulative cases per month was 4.2 (range, 1-5). The most commonly prescribed radionuclides were radium-223 (40%; mean 2.8 cases/mo), iodine-131 (18%; mean 2.3 cases/mo), yttrium-90 (13%; mean 3.4 cases/mo), "other" (8%), samarium-153 (6%; mean 1.0 cases/mo), and strontrium-89 and phosphorous-32 (2% each; mean 1.8 and 0.4 cases/mo, respectively). Of those who answered "other," lutetium-177 dotatate was most commonly prescribed (8%). No significant ($P < .05$) association was noted between practice type, practice location, years of practice, or practice volume with utilization of any RPTs. Most radiation oncologists (56%, n = 74) responded they would like to actively prescribe more RPT, although 27% (n = 35) were indifferent, and 17% (n = 22) said they would not like to prescribe more RPT. Perceived barriers to implementation were varied but broadly categorized into treatment infrastructure (44%, n = 57), interspecialty relations (41%, n = 53), lack of training (23%, n = 30), and financial considerations (16%, n = 21).

Conclusions: Among surveyed U.S. radiation oncologists, a significant number reported prescribing at least 1 RPT. The majority expressed interest in prescribing additional RPT. Wide-ranging barriers to implementation exist, most commonly interspecialty

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relations, treatment infrastructure, lack of training, and financial considerations.

Introduction

Radiopharmaceutical therapy (RPT) is a growing branch of cancer treatment with several agents in clinical use,[1] new agents in phase 3 clinical trials,[2] and many other agents under development. Radiation oncologists (ROs) are specifically trained and certified to administer therapeutic radiation in the form of external beam radiation therapy (EBRT), brachytherapy, and RPTs; however, over the past 2 decades the field has dramatically shifted toward delivering EBRT.[3]

Becoming too dependent on a single modality has potential implications on the overall health of the specialty,[4] particularly as nationwide trends show a decrease in EBRT utilization rates.[5] A recent American Society of Radiation Oncology (ASTRO) study showed an increasing desire among ROs to expand their scope of practice, particularly with RPTs.[6]

Currently, there are limited data on RPT usage among domestic ROs. Therefore, we designed this survey to assess overall and specific RPT prescribing patterns, interest in expanding RPT usage, and barriers to RPT implementation among domestic ROs.

Methods and Materials

Survey design

An anonymous, Internet-based (REDCap) survey was developed to assess RPT usage among practicing ROs. The survey contained a total of 21 items and was divided into 4 domains: (1) demographics, (2) specific RPT prescribing patterns, (3) interest levels in expanding scope of practice with RPTs, and (4) perceived barriers to such expansion (Supplemental File 1). Questions focused on commonly used RPTs as well as those that are included as part of Accreditation Counsel for Graduate Medical Education RO residency case requirements: iodine-131, radium-223, yttrium-90, samarium-153, strontrium-89, phosphorous-32, and "others."

Participants and survey distribution

Practicing attending ROs were eligible for this survey. For this analysis, we focused only on domestic respondents. The survey was distributed via social media platforms: Twitter, LinkedIn, Facebook, and Student Doctor Network. Three authors (U.S., I.C., M.C.) created original promotional posts with a trackable link to the survey.[7] These posts were then "shared" by the remaining study authors to reach a wider audience. Responses were collected from February 2, 2021, to August 29, 2021. The survey was voluntary, participants remained anonymous, and responses were confidential.

Statistical analysis

Descriptive statistics were generated for categorical and numeric variables. Nonparametric χ^2 testing and logistic regression were used for correlation statistics. An alpha < 0.5 was considered significant for 2-sided P values. Statistical analysis was performed with Stata 16 software (StataCorp, 2019; Stata Statistical Software: Release 16; StataCorp LLC, College Station, TX).

Results

We received a total of 142 survey responses, of which 131 were from domestic attending ROs. Respondent demographics are available in Table 1. Years in practice was evenly distributed with 32% (n = 42) of attendings in practice >10 years, 22% (n = 29) 6 to 10 years, 22% (n = 29) 3 to 5 years, and 24% (n = 31) 0 to 2 years. Practice type included academic-main site among 41% (n = 54), academic-satellite in 17% (n = 22), and private practice/other in 42% (n = 55) of attendings. Forty-six percent (n = 60) of attendings served populations of >500,000, 22% (n = 29) between 200 to 500,000, 21% (n = 28) between 100 to 200,000, and 11% (n = 14) <100,000.

Forty-eight percent (n = 63) reported prescribing at least 1 RPT. An additional 16% (n = 21) participate in RPT administration without billing. Among those that actively prescribed RPT, the mean cumulative cases per month was 4.2 (range, 1-34). Figure 1 shows specific RPT prescribing patterns: radium-223 (40%; mean 2.3 cases/mo), iodine-131 (18%; mean 2.3 cases/mo), yttrium-90 (13%; mean 3.4 cases/mo), "other" (8%), samarium-153 (6%; mean 1.1 cases/mo), and strontium-89 and phosphorous-32 (2% each; mean 1.8 and 0.4 cases/mo, respectively). Of those who answered "other," all 11 respondents prescribed lutetium-177 dotatate. No significant ($P < .05$) association was noted between practice type, practice location, years of practice, or practice volume with utilization of any RPT.

The majority (56%, n = 74) of respondents stated they would like to actively prescribe more RPTs, and 27%

Table 1 Survey respondent demographics

Characteristics	All respondents (n = 131)
Years in practice	-
0-2	24% (n = 31)
3-5	22% (n = 29)
6-10	22% (n = 29)
>10	32% (n = 42)
Practice type	
Academic medical center-main site	41% (n = 54)
Academic medical center-satellite site	17% (n = 22)
Private practice	34% (n = 44)
Other	8% (n = 11)
Practice region	-
Northeast	34% (n = 44)
Midwest	21% (n = 28)
South	30% (n = 39)
West	15% (n = 20)
Population served	
<100,000	11% (n = 14)
>100,000-200,000	21% (n = 28)
>200,000-500,000	22% (n = 29)
>500,000	46% (n = 60)

(n = 35) were indifferent and 17% (n = 22) were not interested (Fig 2). Perceived barriers to implementation were varied (Fig 3), but broadly categorized into treatment infrastructure (44%, n = 57), interspecialty relations (41%, n = 53), lack of training (23%, n = 30), and financial considerations (16%, n = 21).

Discussion

In this study, almost half (48%) of survey respondents reported prescribing at least 1 RPT, most commonly radium-223, iodine-131, or ytrrium-90. The cumulative mean number of monthly cases was 4.2 (range, 1-34). The majority (56%) of respondents wanted to actively prescribe more RPT; however, many barriers to implementation were identified, most notably treatment infrastructure, interspecialty relations, lack of training, and financial considerations. To our knowledge, this is the first study to specifically evaluate overall and RPT subtype (ie, radium-223, etc) usage, as well as to quantify monthly RPT usage, among domestic ROs.

Our results build upon the recently published ASTRO scope of practice survey,[6] which demonstrated that 31% of ROs prescribed RPTs/theranostics. They found ROs in private practice and nonacademic hospital settings were more likely to prescribe RPTs compared with those in academic settings ($P < .001$ and $P = .0023$, respectively). In addition, generalist ROs were more likely to prescribe RPTs compared with subspecialists ($P = .019$). Among early career ROs, there was significant desire for expanding scope of practice with RPTs. In this study, we also found numerically higher RPT prescribing rates (56% vs 42%) and prescribing interest (60% vs 54%) among nonacademic ROs, though no differences were seen based on number of years in independent practice. Notably, the ASTRO survey was unable to assess specific RPT utilization as in our study.

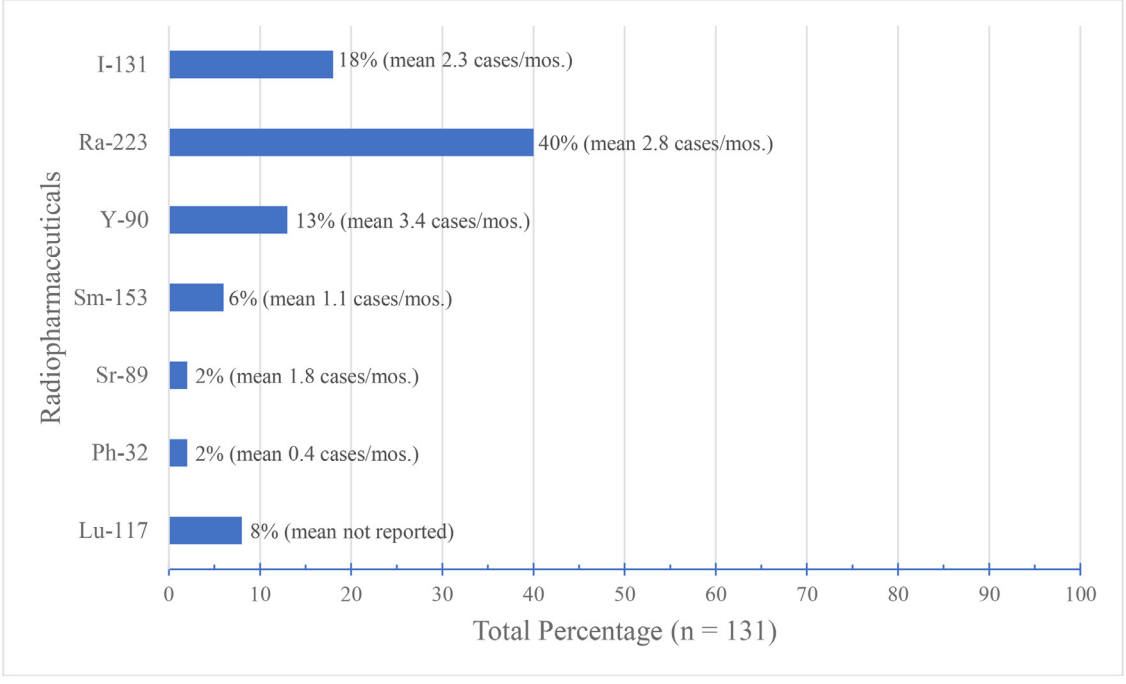

Fig. 1 Specific radiopharmaceutical prescribing patterns.

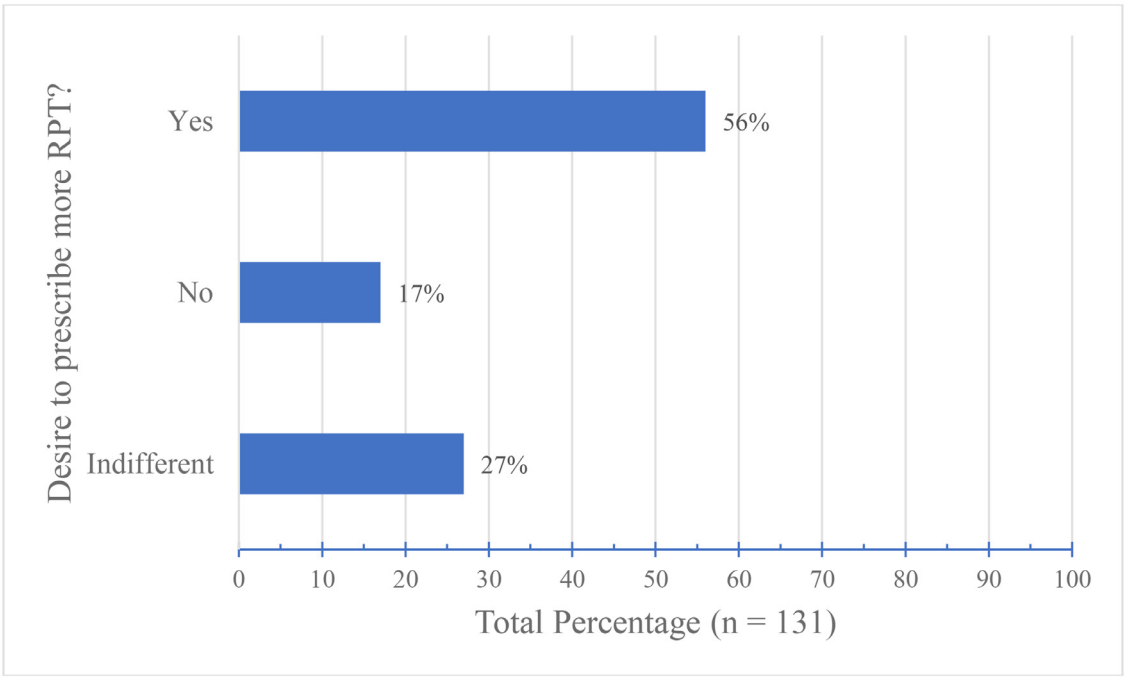

Fig. 2 Interest in prescribing more radiopharmaceuticals.

Treatment infrastructure and financial considerations were identified as significant barriers to RPT utilization among ROs. With many RPTs, the "cold" targeting molecule is centrally manufactured while the radionuclides are formulated for individual patients around the time of administration within so-called "hot" labs of nuclear medicine.[8] Without significant RPT treatment volumes, many RO departments are unable to invest the high financial capital needed to develop their own infrastructure. Additionally, current U.S. nuclear medicine policy requires RPTs to be administered in the inpatient setting where costs are much higher, posing another significant financial restriction.[9] Cooperation with the pharmaceutical industry may present an avenue to overcoming some of these

Fig. 3 Word cloud of perceived barriers to radiopharmaceutical usage.

barriers. Indeed, the increase in approved RPTs[10] as well as the 2017 acquisition of a large nuclear medicine pharmaceutical company (Advanced Accelerator Applications) by the oncology giant Novartis for $3.9 billion, suggests that there may be burgeoning industry interest in RPT.[11]

Another identified common barrier to RPT use was interspecialty relations. There is no 1 dominant user of RPT in the United States, which can lead to confusion and challenges with referral patterns. Recently, the American College of Radiology, American College of Nuclear Medicine, ASTRO, and Society of Nuclear Medicine and Molecular Imaging updated their collaborative practice parameter for RPTs, in which they stressed close cooperation and communication to maximize its efficacious and safe use.[12] Building upon this work, the Theranostic Working Group of ASTRO created a framework for patient-centered pathways of care for RPT.[13] They emphasized unique skillsets that ROs can provide, such as pre- and post-RPT treatment planning. RPT treatment planning[14] allows for more accurate dose delivery as well as potential integration with EBRT, for example, in hepatocellular carcinoma cases receiving both yittrium-90 and stereotactic body radiation therapy. In the past, the lack of availability of standard treatment planning methods and software systems has been an impediment to RPT treatment planning; however, recent joint efforts to create mathematical formalism for RPT dosimetry between National Cancer Institute, Imaging and Radiation Oncology Core Services, and the dosimetry software company may help overcome this barrier.[14,15]

We identified lack of RPT training among ROs as a major barrier in both our survey and the ASTRO Scope of Practice Survey. Historically, enthusiasm for RPT within RO has waxed and waned. In 2003, ASTRO developed the Systemic Targeted Radionuclide Therapy initiative, aimed to stimulate clinical interest and research in RPT. Initial research efforts were funded in conjunction with the National Cancer Institute to investigate the molecular aspects of isolating and developing radiolabeled targeted monoclonal antibodies and receptor peptides; however, this project ultimately failed and was discontinued in 2007 owing to lack of interest.[16,17] ASTRO has recently begun offering "master classes" specific to RPT training at the 2019 to 2021 annual meetings to allow members to expand their practices.[18] These classes include introduction to RPTs, basics of physics, and in-depth practical training for multiple RPTs. In addition, the Accreditation Counsel for Graduate Medical Education RO residency committee increased the minimum case requirement of RPTs/unsealed sources from 6 to 8 procedures, effective July 2020.[19] Although this is a good first step, it is imperative to ensure that RO residents are not simply observers fulfilling case requirements, but rather active participants in the RPT process from consultation to follow-up. Without adequate training of all radiation-related therapeutic modalities, patients will be lacking potentially life-prolonging therapies[24,25] or other specialties will enter the void, potentially leaving ROs as technicians fixed with their machines.

There are some limitations to this study. We cannot define a response rate given our distribution method; however, our methodology is consistent with web-based survey sampling methodology[7] and recent published web-based surveys.[20,21] Notably, the total responses in this study are greater than published studies with high response rates,[22,23] which highlights how strongly response rate is affected by sample size (ie, 80% response rate but only a 60-person sample). Nonetheless, we acknowledge our overall number is still limited relative to the total number of practicing domestic ROs. Our findings are subject to response bias. It is important to note that the percentage of respondents self-reporting as "academic" was higher than expected based on prior publications. Respondents with interest or who are actively engaging in RPT administration are also more likely to respond to our survey. Therefore, true estimates of RPT utilization are likely lower than what was found in our study. This does, however, come with the advantage of learning from those that are highly informed regarding RPT prescribing challenges.

Conclusions

In this study, almost half of surveyed domestic ROs actively prescribe at least 1 RPT (mean 4.5 cases/mo), of which radium-223 was the most common. The majority expressed interest in prescribing additional RPTs. Barriers to RPT implementation were identified, including treatment infrastructure, interspecialty relations, lack of training, and financial considerations. A multifaceted approach is needed to make RPTs a routine part of an RO's toolbox.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.adro.2021.100827.

References

1. Parker C, Nilsson S, Heinrich D, et al. Alpha emitter radium-223 and survival in metastatic prostate cancer. *N Engl J Med.* 2013;369:213–223.
2. Sartor O, de Bono J, Chi KN, et al. Lutetium-177–PSMA-617 for metastatic castration-resistant prostate cancer. *N Engl J Med.* 2021;385:1091–1103.

3. Zietman A. The future of radiation oncology: The evolution, diversification, and survival of the specialty. *Semin Radiat Oncol*. 2008;18:207–213.
4. Shah C, Royce TJ. Chicken little or goose-is-cooked? The state of the US radiation oncology workforce: Workforce concerns in US radiation oncology. *Int J Radiat Oncol Biol Phys*. 2021;110:268–271.
5. Royce TJ, Qureshi M, Tam Truong M. Radiotherapy utilization and fractionation patterns during the first course of cancer treatment in the United States from 2004 to 2014. *J Am Coll Radiol*. 2018;15:1558–1564.
6. Fung CY, Vapiwala N, Mattes MD, et al. US radiation oncologists (re)defined: An American Society for Radiation Oncology scope of practice study. *Int J Radiat Oncol Biol Phys*. 2021;109:335–343.
7. Fricker RD. Sampling Methods for Web and E-mail Surveys. *The SAGE Handbook of Online Research Methods*. London: SAGE Publications, Ltd; 2008.
8. Turck R. Radio-pharmaceuticals for cancer treatment: Are they ready for prime time yet? *Ann Oncol*. 2018;29:1594–1597.
9. Divgi C, Carrasquillo JA, Meredith R, et al. Overcoming barriers to radiopharmaceutical therapy (RPT): An overview from the NRG-NCI working group on dosimetry of radiopharmaceutical therapy. *Int J Radiat Oncol Biol Phys*. 2021;109:905–912.
10. Sgouros G, Bodei L, McDevitt MR, Nedrow JR. Radiopharmaceutical therapy in cancer: Clinical advances and challenges. *Nat Rev Drug Discov*. 2020;19:589–608.
11. Miller J. Novartis to buy French cancer specialist AAA for $3.9 billion. *Reuters*. October. 2017;30.
12. American College of Radiology, American College of Nuclear Medicine, American Society for Radiation Oncology, Society of Nuclear Medicine and Molecular Imaging. ACR−ACNM−ASTRO−SNMMI practice parameter for the performance of therapy with unsealed radiopharmaceutical sources. Available at: https://www.acr.org/-/media/ACR/Files/Practice-Parameters/unsealedsources.pdf. Accessed June 1, 2021.
13. Buatti JM, Pryma DA, Kiess AP, et al. A framework for patient-centered pathways of care for radiopharmaceutical therapy: An ASTRO consensus document. *Int J Radiat Oncol Biol Phys*. 2021;109:913–922.
14. Xiao Y, Roncali E, Hobbs R, et al. Toward individualized voxel-level dosimetry for radiopharmaceutical therapy. *Int J Radiat Oncol Biol Phys*. 2021;109:902–904.
15. Goetz TI, Lang EW, Prante O, et al. Three-dimensional Monte Carlo-based voxel-wise tumor dosimetry in patients with neuroendocrine tumors who underwent (177)Lu-DOTATOC therapy. *Ann Nucl Med*. 2020;34:244–253.
16. Wong RSL, Brechbiel MW. National Cancer Institute perspectives. *Int J Radiat Oncol Biol Phys*. 2006;66(2 Suppl):S96–S99.
17. Wallner PE. Systemic radionuclide therapy: What's old is new again!. *ASTROnews*. 2019:19–21.
18. Your guide to the ASTRO 2020 annual meeting. *ASTRONews*. 2020:19.
19. American College of Graduate Medical Education. ACGME program requirements for graduate medical education in radiation oncology. Available at: https://www.acgme.org/Portals/0/PFAssets/ProgramRequirements/430_RadiationOncology_2020.pdf. Accessed June 1, 2021.
20. Pendergrast TR, Jain S, Trueger NS, Gottlieb M, Woitowich NC, Arora VM. Prevalence of personal attacks and sexual harassment of physicians on social media. *JAMA Intern Med*. 2021;181:550–552.
21. Berkowitz MJ, Thompson CK, Zibecchi LT, et al. How patients experience endocrine therapy for breast cancer: An online survey of side effects, adherence, and medical team support. *J Cancer Surviv*. 2021;15:29–39.
22. Zhang H, Cha EE, Lynch K, et al. Radiation oncologist perceptions of telemedicine from consultation to treatment planning: A mixed-methods study. *Int J Radiat Oncol Biol Phys*. 2020;108:421–429.
23. Kang S, Caissie A, Kassam Z, et al. Promoting career selection through a comprehensive enrichment experience: A review of the Canadian Radiation Oncology Summer Studentship. *Int J Radiat Oncol Biol Phys*. 2020;107:27–32.