March 2023
Volume 12, Number 1

Applied RadiationOncology™

www.appliedradiationoncology.com

Elekta

Hope for everyone dealing with cancer.

At Elekta, we are driven to deliver cutting-edge, precision radiation therapy, to openly collaborate and help clinicians provide the best possible life outcomes for every patient.

We don't just build technology, we build hope.

elekta.com

LADXX220916d

Applied Radiation Oncology™

Anderson Publishing, Ltd.
180 Glenside Avenue,
Scotch Plains, NJ 07076
Tel: 908-301-1995
Fax: 908-301-1997
info@appliedradiology.com
ESSN: 2334-5446 (online)

CIRCULATION, COVERAGE and ADVERTISING RATES: Details regarding circulation, coverage, advertising rates, space sizes, and similar information are available to prospective advertisers. Closing date is 30 days preceding date of issue. View our media planner at appliedradiationoncology.com/advertise.

EDITORIAL CONTRIBUTIONS: *Applied Radiation Oncology* accepts clinical review articles, research papers, and case reports that pertain to radiation oncology and related oncologic imaging procedures that will be of interest to radiation oncologists. Author guidelines are available at https://appliedradiationoncology.com/Author-Guidelines. Every precaution is taken to ensure accuracy, but the publishers cannot accept responsibility for the correctness or accuracy of the information supplied or for any opinion expressed. Before using procedures or treatments discussed or suggested by authors, clinicians should evaluate their patients' conditions, compare the recommendations of other authorities, consider possible contraindications or dangers, and review applicable manufacturer's product information. Review articles and cases should be geared to the practitioner and should reflect practical everyday clinical applications rather than research activity. Articles and cases may pertain to clinical management, administration, fiscal, technical, and medico-legal issues. All review articles, research articles and case reports undergo a double-anonymized peer review process.

Applied Radiation Oncology™

March 2023, Vol 12, No 1

FOCUS: EDUCATION

Applied Radiation Oncology (ISSN: 2334-5446) is published quarterly by Anderson Publishing, Ltd.,180 Glenside Avenue, Scotch Plains, NJ 07076. Subscription is free of charge to all medical professionals. To update your subscription preferences, visit appliedradiationoncology.com/subscribe. Complaints concerning non-receipt of this journal should be made via email to our publisher, Kieran Anderson at kieran@appliedrradiology.com.

Dr. Suh is the editor-in-chief of *Applied Radiation Oncology,* and professor and chairman, Department of Radiation Oncology at the Taussig Cancer Institute, Rose Ella Burkhardt Brain Tumor and Neuro-oncology Center, Cleveland Clinic, Cleveland, OH.

Educational Growth: Seeding a Bright Tomorrow

John Suh, MD, FASTRO, FACR

Welcome to the March issue of *ARO*! As spring ushers in green foliage and longer daylight, we are pleased to focus this edition on another theme of growth and enlightenment: education, which has always been a very keen interest of mine.

Continuous improvement within education is imperative to advance best practices in teaching and, in turn, training a diverse future workforce in evidence-based cancer treatment. These are important take-home messages in the special feature, *Future of Radiation Oncology Education: Transforming Scholarly Teaching Into Medical Education Scholarship*. Offering SA-CME credit, this insightful article delves into gaps and gains surrounding curricula, mentorship, technology-oriented and simulation-based teaching, continuing education, artificial intelligence and other areas that can augment undergraduate, graduate, and continuing medical education, as well as diversity, equity and inclusion efforts within radiation oncology.

Exploring the role of patient education, *Personalizing Approaches to Patient Education Throughout the Radiation Oncology Workflow* offers a pragmatic overview of multiple educational modalities for patients and how to maximize their use. The article reviews costs and benefits, optimal usage, and ways to adapt tools — such as virtual reality, videos, websites, and the role of the medical physicist in patient education — to personalize the educational experience.

On the resident front, *Navigating Radiation Oncology Emergencies: Are We Maximizing Inpatient Call for Residents?* is an excellent column describing optimal formats for inpatient call and how to strengthen what can be a highly educational opportunity for residents.

Please also enjoy this issue's case reports on several unique topics, as well as an interesting research article on proton vs photon stereotactic radiosurgery for vestibular schwannoma.

Beyond these pages, we are excited to share a few updates from *ARO* medical student committees. Anthony Alanis, Bahareh Sharafi, and William Tyree, members of the Future Content Committee, have launched an informative quarterly enewsletter, *RadOnc Student Scan*. Designed to boost awareness and knowledge of radiation oncology among medical students, each issue explains areas of radiation oncology physics, biology, and clinical practice; highlights topical research; offers a radiation oncologist Q&A; and lists opportunities. Visit https://appliedradiationoncology.com/news/ARO-Student-Voice to check out their great work.

In the Podcast and Webinar Committee, members are lining up interviews for the new podcast series, *Beam On*. The first episode is in production as of press time, and features student Ellie Thompson and Dr. Steven Octavianus, MD, discussing radiation therapy in Indonesia. Check our website soon for the exciting debut.

In other news, we are delighted to introduce 3 new members to the *ARO* editorial advisory board: **Bree R. Eaton, MD,** associate professor and pediatric medical director, Emory Proton Therapy Center, Winship Cancer Institute of Emory University; **Austin J. Sim, MD, JD,** assistant professor, James Cancer Hospital, The Ohio State University Comprehensive Cancer Center; and **Meng Xu Welliver, MD, PhD,** associate professor, Mayo Clinic, Rochester. Bringing their respective expertise in pediatrics; advocacy/legislation; and thoracic cancers, soft-tissue sarcomas and blood cancers (among other areas), we are thrilled to welcome them on board.

Rotating off the board are several members who have spent many years aiding the development and expansion of the journal. We are deeply indebted to **Jeffrey C. Buchsbaum, MD, PhD; Daniel J. Indelicato, MD;** and **Mohamed A. Elshaikh, MD**, for their exceptional, dedicated service to *ARO!*

We hope you enjoy the issue and wish you a bright new season of growth in 2023!

Future of Radiation Oncology Education: Transforming Scholarly Teaching Into Medical Education Scholarship

Description

Medical education must develop and adapt through robust education scholarship, applying novel teaching with evidence-based best practices to optimally convey new concepts. Continued growth in undergraduate, graduate and continuing medical education as well as in diversity, equity, and inclusion efforts, are critical for the future of radiation oncology. This review article explores how education scholarship can facilitate these advances in areas from artificial intelligence to technology-oriented teaching.

Learning Objectives

Upon completing this activity:

- Clinicians will be able to identify at least one opportunity for educational innovation at the undergraduate, graduate, and continuing medical education level.
- Clinicians will understand how scholarship in medical education has led to advancement in critical topics in radiation oncology.
- Clinicians will be able to apply Glassick's criteria to transform scholarly activity in radiation oncology into education scholarship.

Authors

Anurag Saraf, MD[1-3]
Graham Boyd, MD[1-3]
Alexandra De Leo, MD[4]
Phylicia D. Gawu, DO[5]
Chelsea C. Pinnix, MD, PhD[6]
Steve Braunstein, MD, PhD[7]
Rachel Jimenez, MD[2]
Idalid Franco, MD, MPH[3]
Lisa Singer, MD, PhD[7]

Affiliations: [1]Harvard Radiation Oncology Program, Boston, MA. [2]Massachusetts General Hospital, Boston, MA. [3]Brigham and Women's Hospital and Dana-Farber Cancer Institute, Boston, MA. [4]University of Florida College of Medicine, Jacksonville, FL. [5]Mayo Clinic Comprehensive Cancer Center, Phoenix, AZ. [6]MD Anderson Cancer Center, Houston, TX. [7]University of California, San Francisco, CA.

Target Audience

- Radiation Oncologists
- Related Oncology Professionals

Commerical Support

None

Accreditation/Designation Statement

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the Institute for Advanced Medical Education (IAME) and Anderson Publishing. IAME is accredited by the ACCME to provide continuing medical education for physicians. IAME designates this activity for a maximum of 1 *AMA PRA Category 1 Credit™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Instructions

To successfully earn credit, participants must complete the activity during the valid credit period.

1. Review this article in its entirety.
2. Visit appliedradiology.org/SAM.
3. Login or create an account.
4. Complete the post test and review the discussion and references.
5. Complete the evaluation.
6. Print your certificate.

Estimated time for completion:
1 hour
Date of release and review:
March 1, 2023
Expiration date:
February 29, 2025

Disclosures

Dr. Pinnix reports research support from Merck. Dr. Braunstein reports honoraria from icotec, International Journal of Radiation Oncology - Biology - Physics, and RadOncQuestions, LLC. He is also co-head of ARO's Education section. Dr. Franco reports research support from NIH/NCI and Brigham Women's Hospital. All other authors disclose no relationships with ineligible companies.

IAME has assessed conflicts of interest with its faculty, authors, editors, and any individuals who were in a position to control the content of this CME activity. Any relevant financial relationships were mitigated with an independent peer review of this activity, and no conflicts or commercial bias were detected. IAME's planners, content reviewers, and editorial staff disclose no relationships with ineligible entities.

Future of Radiation Oncology Education: Transforming Scholarly Teaching Into Medical Education Scholarship

Anurag Saraf, MD;[1-3] Graham Boyd, MD;[1-3] Alexandra De Leo, MD;[4] Phylicia D. Gawu, DO;[5] Chelsea C. Pinnix, MD, PhD;[6] Steve Braunstein, MD, PhD;[7] Rachel Jimenez, MD;[2] Idalid Franco, MD, MPH;[3] Lisa Singer, MD, PhD[7]

Abstract

Medical education is vital in preparing radiation oncologists to care for patients in an ever-changing landscape of new treatments and technologies. Medical education must develop and adapt through robust education scholarship, utilizing novel teaching with evidence-based best practices to optimally teach new concepts. Education scholarship has led to significant advances in several areas of radiation oncology education, spanning undergraduate medical education (UME); graduate medical education (GME); continuing medical education (CME); and diversity, equity, and inclusion (DEI). Continued growth in these domains are critical for the future of our field, and education scholarship can facilitate these advances.

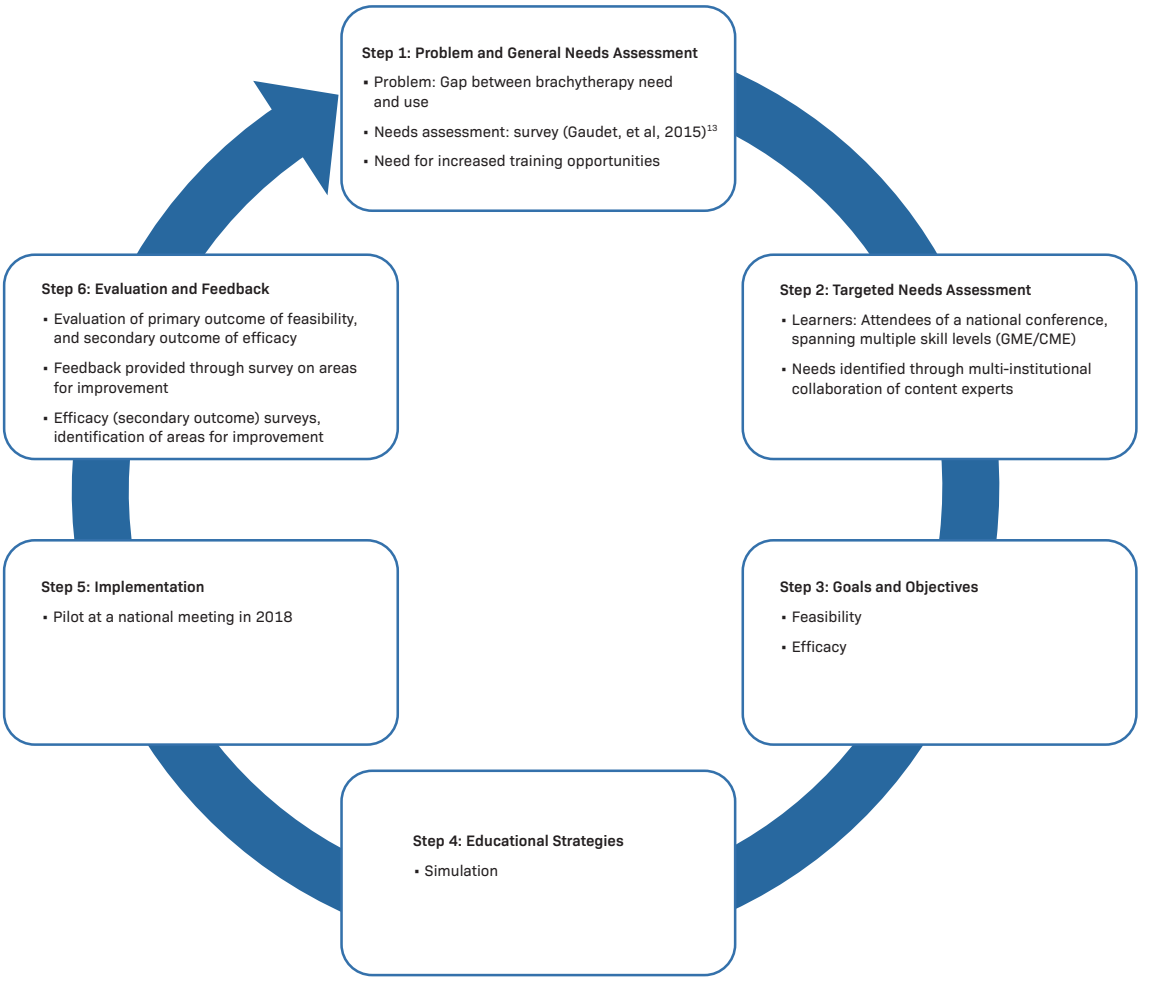
Due to technical advances and changing treatment paradigms, the knowledge required to practice radiation oncology continues to evolve, necessitating a comprehensive and ever-changing set of educational tools to train a spectrum of learners. Over the past two decades, academic medicine, and specifically the field of radiation oncology, has seen an increasing focus on medical education.[1] This is likely multifactorial and attributable in part to an increase in learner's needs, such as the need for high-yield teaching due to time limitations in educational settings, desire for more flexible learning options, and a generally higher standard of education exposure/expectations from a systemically more mature educational community. Increasing attention to vulnerable populations and the importance of diversity, equity, and, inclusion (DEI) in health care and medical training has also fueled educational interventions and innovations.[2-4] In response to this increasing focus on the value of medical education, many US institutions now consider medical education scholarship when evaluating academic faculty for promotion.[5] Here we describe differences between scholarly teaching and the scholarship of teaching before focusing on impactful areas of current and future medical education scholarship within radiation oncology, with a focus on undergraduate medical education (UME); graduate medical education (GME); and continuing medical education (CME); and diversity, equity, and inclusion (DEI). With educational innovation and educational scholarship, the future of radiation oncology education is bright.

Affiliations: [1]Harvard Radiation Oncology Program, Boston, MA. [2]Massachusetts General Hospital, Boston, MA. [3]Brigham and Women's Hospital and Dana-Farber Cancer Institute, Boston, MA.[4] University of Florida College of Medicine, Jacksonville, FL. [5]Mayo Clinic Comprehensive Cancer Center, Phoenix, AZ. [6]MD Anderson Cancer Center, Houston, TX. [7]University of California, San Francisco, CA.
Corresponding Author: *Lisa Singer, MD, PhD; University of California, San Francisco, 1825 Fourth St, First Floor, Room L1101, San Francisco, CA 94158. (Lisa.Singer@ucsf.edu)
Disclosures: Dr. Pinnix reports research support from Merck. Dr. Braunstein reports honoraria from icotec, *International Journal of Radiation Oncology - Biology - Physics*, and RadOncQuestions, LLC. He is also co-head of ARO's Education section. Dr. Franco reports research support from NIH/NCI and Brigham Women's Hospital. No other authors have conflicts of interest to disclose. None of the authors received outside funding for the production of this original manuscript and no part of this article has been previously published elsewhere.
Acknowledgement: The authors acknowledge Daniel W. Golden, MD, for his significant input and guidance on this manuscript.

Defining Medical Education Scholarship

Dissemination of medical education scholarship is needed to synergize efforts across institutions, and to create a foundation upon which future efforts can further advance education.

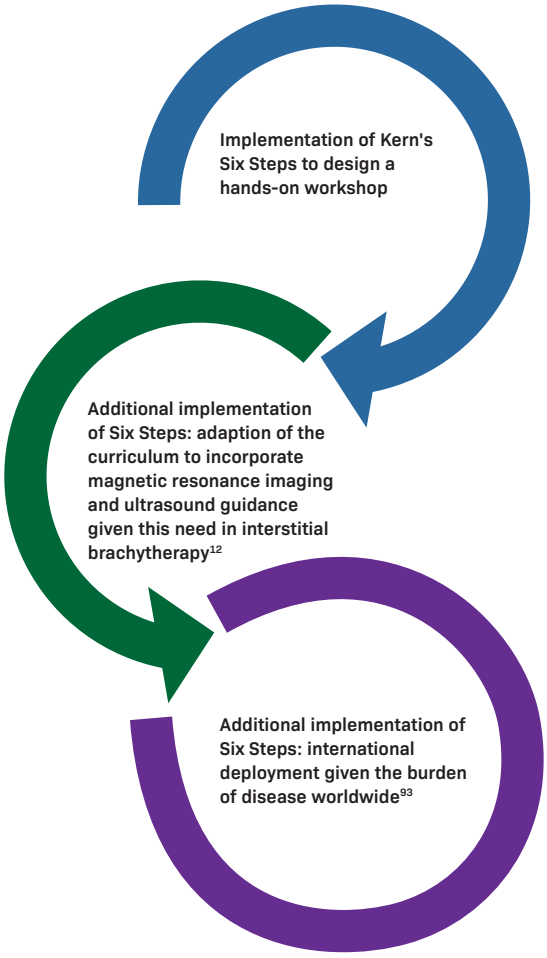
Figure 1A. Kern's Six Steps provide a framework for curricular development. In this example of efforts to improve brachytherapy education, a single research team did not focus on completing all 6 steps independently. Rather, the needs assessment was addressed through surveys and involved Accreditation Council for Graduate Medical Education (ACGME) guidelines, which were written by different authors than those in the simulation-based education project illustrated in steps 2-6.



In this discussion, it is important to differentiate teaching methods within medical education (an umbrella term encompassing multiple practices in teaching hospitals) between those that specifically draw on best practices and evidence-based methods, here referred to as *scholarly teaching*, from nonevidence-based teaching methods. Scholarly teaching is similarly distinct from, though may overlap with, *education scholarship*, the process of moving the field of medical education forward by rigorously measuring, assessing, and reporting on the results of scholarly teaching for publication.[6] These distinctions are important because the advancement of medical education relies on both the development of scholarly teaching methods and the robust assessment and dissemination of the results of these interventions. To ensure that scholarly efforts in medical education qualify as rigorous education scholarship, scholars may look to Glassick's 6 standards for educational scholarship: 1) clear goals, 2) adequate preparation, 3) appropriate methods, 4) significant results, 5) effective presentation, and 6) reflective critique.[7] While interventional studies and prospective trials are a common form of clinical research, impactful educational scholarship can focus on innovative teaching methods, novel educational materials, qualitative survey and focus group assessment, and curriculum design, among other examples.

One of the most common types of medical education scholarship in radiation oncology is curriculum development,[8-10] for which an established framework is Kern's Six Steps (**Figure 1A**).[11] These steps help ensure that Glassick's criteria are met using a structured approach to curriculum development. For example, **Figure 1A** illustrates a needs assessment of a simulation-based educational workshop for GME and CME learners.[12,13] Evaluation of this workshop led to curriculum adjustments and additional implementations of Kern's Six Step Approach (**Figure 1B**),[14] which is

Figure 1B. In Figure 1A, the sixth step of evaluating the curriculum led to multiple new directions and implementation of all of the steps, resulting in multiple scholarly educational efforts. Ongoing assessment motivates educational innovation in multiple directions, but all projects share an overarching goal to improve brachytherapy education. As shown in this example, a single cycle of Kern's Six Steps led to multiple cycles of Kern's Six Steps with additional projects listed in Figure 1B.



cyclical and can be used for continuous educational innovation. Overall, it is important to be methodical and intentional to transform scholarly activity to scholarship.

Undergraduate Medical Education

In the UME setting, medical education can be used to increase exposure to radiation oncology, which is critical for maintaining a workforce as well as preparing those in other specialties to understand when to consult radiation oncology. For students rotating in radiation oncology, an evidence-based national UME curriculum in radiation oncology is also critical given that the field is rapidly evolving, with new technology and management indications growing from year to year. It is documented that UME rarely incorporates information about radiation oncology, while exposure increases medical student interest and affinity for the specialty.[9,15,16]

In UME, most school curricula do not include a dedicated radiation oncology didactic session in their preclinical curricula[17] and some students may not gain exposure to any aspect of radiation oncology throughout their medical school education.[9,18,19] Novel methods of incorporating radiation oncology into the medical school curriculum can include collaborating with preclinical course leaders or integrating radiation oncology into a clinical rotation.[20,21] Radiation oncology can also be incorporated into a general oncology educational curriculum. One example of this is the Scholars in Oncology-Associated Research (SOAR) cancer research education program, a summer research experience for first-year medical students at the University of Chicago, which includes a formalized interdisciplinary and interprofessional oncology curriculum, such as 10 2-hour lectures, tumor board attendance, and half-day shadowing with a pharmacist, therapist, or palliative care advanced practice nurse.[22] This program has demonstrated that preclinical students had an increased understanding of the multidisciplinary nature of oncology, including radiation oncology, after completion of the program.

In the preclinical setting, a single lecture on radiation oncology has been shown to significantly increase medical student knowledge of the field, as well as increase desire to learn more about the field.[23,24] In the clinical setting, the introduction of an optional radiation oncology rotation during a core surgery clerkship for third-year medical students was shown to significantly improve radiation oncology knowledge and usefulness of the knowledge in their careers.[20] Furthermore, a structured didactic curriculum in radiation oncology significantly improved knowledge and clinical competency, suggesting that structured didactics are important to a well-designed clerkship.[25-27]

In addition to novel educational programs in medical school, mentorship initiatives can also promote student interest and engagement in the field of radiation oncology. A large, formalized mentorship program described by Hirsch et al, with both clinical and research tracks,

demonstrated that mentorship significantly impacts specialty selection and productivity in the field.[28,29] This mentorship initiative was associated with high mentee satisfaction and improved confidence in the residency application process.[30] Similar results have been reported from other mentorship pilot programs in recent years.[31,32]

In the COVID era, there has been a new emphasis on creating virtual mentorship and educational opportunities, which allows for expanded access to the field, even for those who attend a school without an associated radiation oncology residency program. The Radiation Oncology Virtual Education Rotation (ROVER) is one example of a novel virtual experience that implemented educational panels and case-based learning, which significantly improved medical student understanding of the role of radiation oncology in a number of disease sites.[33] Other published experiences with virtual clinic, tumor boards, and didactics in the medical student population have yielded similar results with high satisfaction rates.[34] The Radiation Oncology Intensive Shadowing Experience (RISE), a virtual educational and mentorship initiative for under-represented medical students, was recently implemented to help reduce the disparities in access and exposure to radiation oncology during the COVID-19 pandemic; this added to the literature questions on optimal implementation of scholarly teaching for URM students in a virtual environment, as well as reported on experiences of both mentees and mentors in this understudied educational environment.[35] Of the 14 URM students participating in RISE, 100% completed pre- and post-surveys with the majority agreeing strongly that they planned to utilize what they learned for their future practice (93%). This unique program centering equity and inclusion within medical education was not only feasible but desired and highly rated by participants.[36] The above initiatives differ in size and scope, but all provide pathways to drive medical student interest in the field. Future directions should focus on optimizing the design, development, implementation, evaluation, and ongoing sustainability of these educational and mentorship programs as an integral part in the formation of the next generation of radiation oncologists.

Graduate Medical Education

The national requirements for radiation oncology residency training involve Accreditation Council for Graduate Medical Education (ACGME) case log requirements, American Board of Radiology (ABR) written and oral certification exams, and American College of Radiology (ACR) in-training written exams. However, the overall curriculum is left to individual residency and fellowship training programs. To provide guidance to US training programs with regard to GME curriculum, the Radiation Oncology Education Collaborative Study Group (ROECSG) formed a Core Curriculum Leadership Committee utilizing the Delphi method to identify and develop content domains (CDs) and entrustable professional activities (EPAs) to formalize a curricular framework for radiation oncology GME in the United States.[37] A strength of this process is the inclusion of numerous radiation oncology GME stakeholders, including academic and private practice physicians, residents, physicists, dosimetrists, nurses, therapists, and others to ensure a well-balanced curriculum.

Novel educational initiatives that leverage technology to facilitate learning in residency also have the potential to improve medical education. Recent work on web-based educational tools for residents focusing on anatomy and contouring guidelines has improved resident confidence and competence in these areas.[38,39] A case bank learning tool on radiation treatment plan evaluation from Princess Margaret Cancer Centre has also been shown to improve resident competency, with a pilot study demonstrating that a high-fidelity simulation platform was associated with increased learning and competency attainment.[40] A common limitation in these studies utilizing web-based or technology-oriented teaching is the reproduction of these tools outside of the institution, whether due to intellectual property concerns or resource concerns (ie, when an institution may not have the same software available to their learners). Another concern was the need for continuous information technology upkeep and maintenance that may require funding and resources. Finally, specialty curricula in radiation oncology residency have been developed in several niche areas such as global oncology[41] and quality and safety,[42] among others, with the intent that more robust education will increase career interest and progress in areas of critical need. With the increasing field complexity and growing knowledge required to be a radiation oncologist, work on innovative learning tools should be prioritized.

Future GME efforts can also focus on transition to practice. Although residency is ultimately intended to prepare physicians for independent practice, the transition from resident to attending physician is often challenging, especially in areas of limited exposure during training. Within radiation oncology, multiple surveys, editorials, and focus groups have described the encountered or anticipated obstacles involved in adjusting to unsupervised clinical care during transition to independent practice.[43-47] Commonly cited issues include inadequate exposure to certain clinical competencies, such as treatment plan review and image verification, and limited guidance about nonclinical responsibilities, including leadership,[48,49]

mentorship,[31] and education.[50] Currently, there are few widely available resources to develop proficiencies in plan review[51,52] or image verification, while resources provided by individual programs can vary significantly, or more often are lacking altogether.[53] Scholarship of simulation-based teaching has shown substantial impact in acquisition of practical skills and, to date in radiation oncology, simulation-based teaching has been created for plan review[40] and image verification,[54] although it has broad applicability for other radiation oncology skills, including treatment planning and toxicity management. As part of a collective effort through ROECSG, a series of workshops to structure the teaching of the basic components of plan evaluation – called the Radiation Oncology Plan Evaluation School (ROPES) – is in progress.[55] This project draws on expert consensus from multiple institutions to develop a practical educational tool to evaluate several acceptable plans in the same patient scenario. Likewise, select programs are aimed at enhancing leadership[56-58] and teaching[59] skills to utilize best practices in individual environments. Another ongoing ROECSG effort is the Teaching Mentoring in Radiation Oncology (TEAMRO) program designed to develop mentoring talents among residents,[60] with a multi-institutional pilot program underway investigating whether formalized mentoring of students by residents can impact a resident's mentorship relations and education overall.

In addition to individual interventions targeting specific deficiencies, another approach would be to augment resident autonomy overall. For example, continuity clinics and "transition-to-practice" services are experiences designed to position residents as the primary care provider with appropriate supervision. While these are common across the medical field,[61-64] few programs in radiation oncology have been described. Of the published experiences, the most comprehensive resident-led rotations include the senior resident rotation at Mayo Clinic[65] and the Veterans Affairs Medical Center rotation in Duke's radiation oncology residency training program;[66] however; there is a need for more robust and longitudinal scholarship demonstrating beneficial translation of these experiences into clinical practice. Both programs facilitate autonomy by allowing the resident to assume responsibility for most patient care tasks, including clinical encounters, management recommendations, documentation, directing radiation therapy planning and delivery (ie, simulation, contouring, plan evaluation, image verification), and interdisciplinary communication and collaboration. While there is attending oversight, the attending assumes a consultant role for the trainee, allowing the resident greater independence and responsibility, mimicking independent practice. Another option to promote autonomy is a continuity clinic for follow-up visits, as at the University of Southern California.[67] These clinics have been reported to improve resident confidence while addressing core issues during early independent practice.[67] Widespread use of resident-led follow-up clinics may be limited because of institutional and ACGME supervision policies but warrant additional consideration.

Continuing Medical Education

With the continuing technical advances and evidence-based clinical practice shifts in radiation oncology, the need for education does not end after residency training. With practice-changing clinical trials in radiation oncology, medical oncology, and surgery, the standard of care in any disease site continues to evolve. Although states differ in the number and type of CME credits required (for example AMA category 1, vs AMA category 2, vs self-assessment or SA-CME), CME credits are required for state licensing, American Board of Radiology (ABR) certification and maintenance of certification (MOC). AMA Category 2 credit is self-designated, allowing physicians to claim credit for educational activities such as peer review, provided the activity meets AMA standards. Radiation oncologists may already engage in these activities at their practices. Self-assessment CME (SA-CME) is a subtype of CME that includes content followed by related questions. SA-CME has been historically required for physicians to maintain certification with ABR. Recently, the ABR announced that participation in MOC and online longitudinal assessment (OLA) would fulfill the SA-CME requirement, removing the need to complete additional self-assessment modules to meet ABR requirements.[68] It is unknown if this change will impact quality or utility of CME. Outside of self-assessment, CME enables radiation oncologists to stay current on treatments, planning techniques, and toxicity management. Annual meetings for radiation oncology professional societies provide CME opportunities. In addition, many institutions offer oncology-specific CME courses. Virtual access to these meetings during the COVID-19 pandemic enabled learning without travel, and continued virtual opportunities may improve future CME access.

Educational needs for practicing radiation oncologists also may be driven by changes in practice throughout a career, such as treating new disease sites, or by a practice acquiring new technology. Web-based contouring tools such as eContour provide a resource for ongoing contouring education for radiation oncologists across the world.[69,70] On-the-job mentorship in brachytherapy was encouraged through the American Brachytherapy Society #NextGenBrachy initiative.[71]

Novel simulation-based workshops in brachytherapy have also been beneficial, and simulation-based education may enhance CME in other areas in the future.[12,72] Currently, the ACR offers a number of multiday hands-on educational experiences for practicing radiologists focusing on topics such as breast MRI and nuclear medicine. In the future, similar courses for radiation oncologists could facilitate practice transitions or vendor-neutral understanding of new technology in a practice.

Technological advances in radiation oncology will also drive new CME needs, such as with online adaptive planning for external-beam radiation therapy. Both CT- and MR-based systems are now widely available for commercial use, necessitating the development of new physician workflows and education for clinicians unfamiliar with this technology.[73,74] Future work in the medical education space should also focus on artificial intelligence (AI) in clinical practice, such as AI-based contouring and treatment planning.[75] As multiple recent studies have demonstrated, auto segmentation with AI and machine learning models can delineate some target volumes and organs at risk while significantly improving efficiency across disease sites.[76-80] Multiple recent studies have also shown a potential role for AI-based treatment planning and optimization.[81-83] Better understanding of AI could also facilitate radiation oncology research in optimizing clinical workflow, prognosticating patient and personalization of management decisions, and identifying patients at risk of toxicity who require greater clinical attention, among other areas. Finally, AI-based tools may also be introduced into medical education to optimize teaching the next generation of learners.[84] One example is a study that found deep-learning models could take full videos of surgeons performing surgical techniques for assessment, categorize them into individual surgical steps, and assess performance levels, suggesting a framework for assessing technical skills that may be difficult to quantify with examinations.[85] CME scholarship in adaptive radiation therapy, AI, and other areas of growth will facilitate future medical education needs for radiation oncologists in practice.

Advancement of Diversity, Equity, and Inclusion

Integration of diversity, equity and inclusion (DEI) principles and practices throughout all aspects of medical education (UME, GME, and CME) are critical to workforce training. Ultimately, the creation of clinically applicable and sustainable education solutions that advance diversity require strategies that involve all aspects of medical education and include not only underrepresented-in-medicine (UIM) physicians, but also non-UIM physicians, patients, and hospital systems.

In radiation oncology, a virtual away rotation is a medical education initiative that addresses DEI issues in clinical learning environments.[86,87] RISE is one such example of intentionally targeting opportunities to learn about radiation oncology and UIM medical students.[35] The RISE program demonstrates an example of transforming education research in DEI from scholarly teaching to scholarship, as authors utilize pre- and post-surveys to investigate how scholarly teaching impacted both teachers and learners in a novel environment, with results serving to improve future iterations of scholarly teaching in the virtual environment. There are also in-person opportunities, such as in the Department of Radiation Oncology at the Washington University School of Medicine in St. Louis, which offers a 1-month medical student rotation for fourth-year medical students from diverse backgrounds through the Diversity & Inclusion Clerkship Opportunity for Underrepresented Medical Students (D.I.C.O.M.S.) program. The rotation includes a $2000 stipend to help offset the cost of travel, housing, Visiting Student Application Service (VSAS), and incidental expenses. National radiation oncology organizations, such as the American Society for Radiation Oncology (ASTRO), also have dedicated opportunities for medical students and early career faculty from underrepresented groups. Two examples are the ASTRO Minority Summer Fellowship Award, which exposes medical students to clinical, basic and translational research questions in radiation oncology, and the ASTRO Leadership Pipeline Program (formerly known as the Pipeline Protégé Program), a career development program aimed at increasing diversity among ASTRO leadership. Overall, as examples of scholarly teaching in DEI for radiation oncology grow, so does the need for medical education scholarship of such initiatives, highlighting the importance of evaluating and reporting on the impact of scholarly teaching on URM students, and radiation oncology trainees and practitioners, to inform and advance the field for our colleagues, patients, communities, and ourselves.

Radiation oncology residents have also addressed the need for DEI training by establishing the Subcommittee on Equity and Inclusion as part of the Association of Residents in Radiation Oncology (ARRO). The goal of the subcommittee is to foster a supportive environment for trainees, systematically assessing and reporting trends in workforce diversity, and initiating and fostering ongoing dialogue on issues of DEI and social justice.[88] With studies demonstrating ongoing workforce disparities[89] and the subsequent impact on health equity,[90] it is critical that we move toward implementation and assessment of these and

other DEI-centered interventions[91] to foster sustainability and reproducibility across specialties.[92]

Conclusion

Radiation oncology medical education is at an important inflection point where a heightened interest in educational innovation is meeting increased needs for research and innovation in critical topics across UME, GME, CME, and DEI. This article has noted several examples of education scholarship that have increased opportunity for further research into critical areas. Scholarship on mentorship with medical students has improved mentorship practices in other areas of radiation oncology. Curriculum design on special topics such as simulation-based education in brachytherapy at the GME level has led to robust curriculum design of other special topics of critical need in early training and education of other technological advances, including simulation-based training in online adaptive radiation therapy at the CME level. Results in pilot studies investigating educational approaches for UIM students suggest that DEI education can improve training and patient care. Continued efforts in education and educational scholarship can advance best practices and evidence-based approaches for teaching, both of which are essential to train a diverse future workforce in evidence-based cancer treatment.

References

1) Rosenberg DM, Braunstein SE, Fields EC, et al. Radiation oncology education collaborative study group annual spring symposium: initial impact and feedback. *J Cancer Educ*. Published online March 16, 2021. doi:10.1007/s13187-021-01990-8

2) Daniel M, Gordon M, Patricio M, et al. An update on developments in medical education in response to the COVID-19 pandemic: A BEME scoping review: BEME Guide No. 64. *Med Teach*. 2021;43(3):253-271. doi:10.1080/0142159X.2020.1864310

3) Eva KW. Publishing during COVID-19: Lessons for health professions education research. *Med Educ*. 2021;55(3):278-280. doi:10.1111/medu.14450

4) Fernandez A. Further incorporating diversity, equity, and inclusion into medical education research. *Acad Med*. 2019;94(11S):S5. doi:10.1097/ACM.0000000000002916

5) Lubitz RM. Guidelines for promotion of clinician-educators. *J Gen Intern Med*. 1997;12(Suppl 2):S71-S78. doi:10.1046/j.1525-1497.12.s2.10.x

6) Fincher RM, Simpson DE, Mennin SP, et al. Scholarship in teaching: an imperative for the 21st century. *Acad Med*. 2000;75(9):887-894. doi:10.1097/00001888-200009000-00009

7) Glassick CE. Boyer's expanded definitions of scholarship, the standards for assessing scholarship, and the elusiveness of the scholarship of teaching. *Acad Med*. 2000;75(9):877-880. doi:10.1097/00001888-200009000-00007

8) Christensen MT, Kumar KA, Wang WS, Dharmarajan KV, Siropaides CH. Development of patient-centered communication curriculum for radiation oncology residents. *Int J Radiat Oncol Biol Phys*. 2022;114(1):e12. doi:10.1016/j.ijrobp.2022.06.021

9) Oskvarek J, Braunstein S, Farnan J, et al. Medical student knowledge of oncology and related disciplines: a targeted needs assessment. *J Cancer Educ*. 2016;31(3):529-532. doi:10.1007/s13187-015-0876-2

10) Buckley L, Bacha B, Gaudet M, et al. Development of a curriculum for the implementation of stereotactic radiation therapy programs in middle-income countries. *JCO Glob Oncol*. 2022;8:e2100389. doi:10.1200/GO.21.00389

11) Thomas PA, Kern DE, Hughes MT, Chen BY. *Curriculum Development for Medical Education: A Six-Step Approach*. J. Hopkins Uni. Press; 2015. Accessed September 29, 2022. https://jhu.pure.elsevier.com/en/publications/curriculum-development-for-medical-education-a-six-step-approach

12) Singer L, Braunstein S, Klopp A, Joyner M. Development and implementation of a simulation-based educational workshop on gynecological brachytherapy: pilot study at a national meeting. *Pract Radiat Oncol*. 2019;9(5):e465-e472. doi:10.1016/j.prro.2019.05.006

13) Gaudet M, Jaswal J, Keyes M. Current state of brachytherapy teaching in Canada: a national survey of radiation oncologists, residents, and fellows. *Brachytherapy*. 2015;14(2):197-201. doi:10.1016/j.brachy.2014.11.004

14) Fields EC, Joyner MM, Singer L, Todor D. A new development in ultrasound-compatible gynecologic brachytherapy simulators. *Brachytherapy*. 2020;19(6):783-786. doi:10.1016/j.brachy.2020.09.011

15) Mattes MD, Patel KR, Burt LM, Hirsch AE. A nationwide medical student assessment of oncology education. *J Cancer Educ*. 2016;31(4):679-686. doi:10.1007/s13187-015-0872-6

16) Agarwal A, Shah A, Shah B, Koottappillil B, Hirsch AE. The impact of a radiation oncologist led oncology curriculum on medical student knowledge. *J Cancer Educ*. 2018;33(6):1176-1180. doi:10.1007/s13187-017-1227-2

17) Zaorsky NG, Shaikh T, Handorf E, et al. What are medical students in the United States learning about radiation oncology? Results of a multi-institutional survey. *Int J Radiat Oncol Biol Phys*. 2016;94(2):235-242. doi:10.1016/j.ijrobp.2015.10.008

18) Arbab M, Holmes JA, Olivier KR, et al. Integrating radiation oncology into undergraduate medical education. *Adv Radiat Oncol*. 2021;6(6):100765. doi:10.1016/j.adro.2021.100765

19) Mattes MD, Deville C, Vega RBM, et al. Demographics of ASTRO student members and potential implications for future U.S. radiation oncology workforce diversity. *Adv Radiat Oncol*. 2022;7(2):100834. doi:10.1016/j.adro.2021.100834

20) Zaorsky NG, Malatesta TM, Den RB, et al. Assessing the value of an optional radiation oncology clinical rotation during the core clerkships in medical school. *Int J Radiat Oncol Biol Phys*. 2012;83(4):e465-e469. doi:10.1016/j.ijrobp.2012.01.058

21) Zaorsky NG, Malatesta TM, Showalter TN, et al. Impact of a radiation oncology elective on the careers of young physicians: update on a prospective cohort study. *Int J Radiat Oncol Biol Phys*. 2013;86(2):214-215. doi:10.1016/j.ijrobp.2013.02.001

22) McKillip RP, Hahn OM, Bartkowiak B, et al. Implementation of a novel medical school multidisciplinary and interprofessional oncology curriculum: a mixed method study. *J Cancer Educ*. 2019;34(1):50-55. doi:10.1007/s13187-017-1264-x

23) Hirsch AE, Bishop PM, Dad L, Singh D, Slanetz PJ. An increase in medical student knowledge of radiation oncology: a pre–post examination analysis of the oncology education initiative. *Int J Radiat Oncol Biol Phys*. 2009;73(4):1003-1008.e2. doi:10.1016/j.ijrobp.2008.12.012

24) Hirsch AE, Handal R, Daniels J, et al. Quantitatively and qualitatively augmenting medical student knowledge of oncology and radiation oncology: an update on the impact of the oncology education initiative. *J Am Coll Radiol*. 2012;9(2):115-120. doi:10.1016/j.jacr.2011.07.001

25) Golden DW, Kauffmann GE, McKillip RP, et al. Objective evaluation of a didactic curriculum for the radiation oncology medical student clerkship. *Int J Radiat Oncol Biol Phys*. 2018;101(5):1039-1045. doi:10.1016/j.ijrobp.2018.04.052

26) Golden DW, Spektor A, Rudra S, et al. Radiation oncology medical student clerkship: implementation and evaluation of a bi-institutional pilot curriculum. *Int J Radiat Oncol Biol Phys*. 2014;88(1):45-50. doi:10.1016/j.ijrobp.2013.10.041

27) Jagadeesan VS, Raleigh DR, Koshy M, Howard AR, Chmura SJ, Golden DW. A national radiation oncology medical student clerkship survey: didactic curricular components increase confidence in clinical competency. *Int J Radiat Oncol Biol Phys*. 2014;88(1):51-56. doi:10.1016/j.ijrobp.2013.11.206

28) Hirsch AE, Agarwal A, Rand AE, et al. Medical student mentorship in radiation oncology at a single academic institution: a 10-year analysis. *Pract Radiat Oncol*. 2015;5(3):e163-e168. doi:10.1016/j.prro.2014.08.005

29) Huang D, Qureshi MM, Sarfaty S, et al. Longitudinal outcomes of medical student research mentorship: a 15-Year analysis of the radiation oncology mentorship initiative. *J Cancer Educ*. Published online September 24, 2021. doi:10.1007/s13187-021-02091-2

30) Boyd GH, Rand AE, DeNunzio NJ, Agarwal A, Hirsch AE. The radiation oncology mentorship initiative: analysis of a formal mentoring initiative for medical students interested in radiation oncology. *J Cancer Educ*. 2020;35(5):893-896. doi:10.1007/s13187-019-01539-w

31) Marsiglio JA, Rosenberg DM, Rooney MK, et al. Mentorship initiatives in radiation oncology: a scoping review of the literature. *Int J Radiat Oncol Biol Phys*. 2021;110(2):292-302. doi:10.1016/j.ijrobp.2020.12.049

32) Rallis KS, Wozniak A, Hui S, et al. Mentoring medical students towards oncology: results from a pilot multi-institutional mentorship programme. *J Cancer Educ*. 2022;37(4):1053-1065. doi:10.1007/s13187-020-01919-7

33) Kahn JM, Sandhu N, von Eyben R, et al. Radiation oncology virtual education rotation (ROVER) for medical students. *Int J Radiat Oncol Biol Phys*. 2021;111(1):29-35. doi:10.1016/j.ijrobp.2021.03.057

34) Sandhu N, Frank J, von Eyben R, et al. Virtual radiation oncology clerkship during the COVID-19 pandemic and beyond. *Int J Radiat Oncol Biol Phys*. 2020;108(2):444-451. doi:10.1016/j.ijrobp.2020.06.050

35) Franco I, Oladeru OT, Saraf A, et al. Improving diversity and inclusion in the post–coronavirus disease 2019 era through a radiation oncology intensivesShadowing experience (RISE). *Adv Radiat Oncol*. 2020;6(1):100566. doi:10.1016/j.adro.2020.09.006

36) Franco I, Oladeru OT, Saraf A, et al. RISE: an equity and inclusion-based virtual pipeline program for medical students underrepresented in medicine. *Int J Radiat Oncol Biol Phys*. 2021;111(1):e8. doi:10.1016/j.ijrobp.2021.05.149

37) Jeans EB, Brower JV, Burmeister J, et al. Radiation oncology deliberative curriculum inquiry: feasibility of a national delphi process. *Int J Radiat Oncol Biol Phys*. 2021;111(1):e7. doi:10.1016/j.ijrobp.2021.05.147

38) Gillespie EF, Panjwani N, Golden DW, et al. Multi-institutional randomized trial testing the utility of an interactive three-dimensional contouring atlas among radiation oncology residents. *Int J Radiat Oncol Biol Phys*. 2017;98(3):547-554. doi:10.1016/j.ijrobp.2016.11.050

39) Eansor P, Norris ME, D'Souza LA, et al. Is remote learning as effective as in-person learning for contouring education? A prospective comparison of face-to face versus online delivery of the anatomy and radiology contouring bootcamp. *Int J Radiat Oncol Biol Phys*. 2022;112(3):590-599. doi:10.1016/j.ijrobp.2021.10.011

40) Winter JD, Adleman J, Purdie TG, Heaton J, McNiven A, Croke J. An innovative learning tool for radiation therapy treatment plan evaluation: implementation and evaluation. *Int J Radiat Oncol Biol Phys*. 2020;107(4):844-849. doi:10.1016/j.ijrobp.2020.03.018

41) Li BC, Chew J, Wakefield DV, Agarwal A, Jhingran A. Frameworks for radiation oncology global health initiatives in US residency programs. *JCO Global Oncology*. 2021;(7):233-241. doi:10.1200/GO.20.00315

42) Yeung A, Greenwalt J. A framework for quality improvement and patient safety education in radiation oncology residency programs. *Pract Radiat Oncol*. 2015;5(6):423-426. doi:10.1016/j.prro.2015.07.008

43) Brower JV, Chen S, Ritter A, et al. Comfort level of US radiation oncology graduates: assessment of transition to independent clinical practice. *J Cancer Educ*. 2021;36(2):278-283. doi:10.1007/s13187-019-01625-z

44) Kahn JM, DiazGranados D, Fields EC. Transitioning roles from residency to attending physician in radiation oncology. *J Cancer Educ*. 2022;37(4):1179-1185. doi:10.1007/s13187-020-01936-6

45) Nabavizadeh N, Burt LM, Mancini BR, et al. Results of the 2013-2015 association of residents in radiation oncology survey of chief residents in the United States. *Int J Radiat Oncol Biol Phys*. 2016;94(2):228-234. doi:10.1016/j.ijrobp.2015.10.014

46) Samuels S. First-year fears and fundamentals: an open letter to new radiation oncologists. *App Radiat Oncol*. 2019;8(1):31-36.

47) Best LR, Sengupta A, Murphy RJL, et al. Transition to practice in radiation oncology: mind the gap. *Radiother Oncol*. 2019;138:126-131. doi:10.1016/j.radonc.2019.06.012

48) Turner SL, Tesson S, Butow P, Vachan B, Chan MK, Shaw T. Integrating leadership development into radiation oncology training: a qualitative analysis of resident interviews. *Int J Radiat Oncol Biol Phys*. 2022;113(1):26-36. doi:10.1016/j.ijrobp.2021.09.051

49) Akthar AS, Hellekson CD, Ganai S, et al. Interdisciplinary oncology education: a national survey of trainees and program directors in the United States. *J Cancer Educ*. 2018;33(3):622-626. doi:10.1007/s13187-016-1139-6

50) Ni L, Thomas HR, Raleigh DR, Boreta LC, Park CC, Braunstein SE. Residents-as-teachers curriculum for radiation oncology: a targeted needs assessment. *Int J Radiat Oncol Biol Phys*. 2021;111(3):638-642. doi:10.1016/j.ijrobp.2021.06.024

51) American Society for Radiation Oncology. ASTRO-ARRO meet me in treatment planning webinars. Published online November 19, 2019. Accessed August 29, 2022. https://www.astro.org/Affiliate/ARRO/Resident-Resources/Educational-Resources/Webinars/ASTRO-ARRO-Meet-Me-in-Treatment-Planning-Webinars

52) Dean M, Jimenez R, Mellon E, Fields E, Yechieli R, Mak R. CB-CHOP: a simple acronym for evaluating a radiation treatment plan. *Appl Radiat Oncol*. 2017;6(4):28-30.

53) Wu SY, Sath C, Schuster JM, et al. Targeted needs assessment of treatment planning education for United States radiation oncology residents. *Int J Radiat Oncol Biol Phys*. 2020;106(4):677-682. doi:10.1016/j.ijrobp.2019.11.023

54) Padilla L, Burmeister JW, Burnett OL, et al. Interprofessional image verification workshop for physician and physics residents: a multi-institutional experience. *Int J Radiat Oncol Biol Phys*. 2021;111(4):1058-1065. doi:10.1016/j.ijrobp.2021.07.1706

55) Leo AND, Ryckman JM, Fields EC, et al. Treatment plan evaluation workshops for residents: learning the ROPES (radiation oncology plan evaluation school). *Int J Radiat Oncol Biol Phys*. 2022;114(1):e8. doi:10.1016/j.ijrobp.2022.06.012

56) Song EY, Chuang J, Frakes JM, et al. Developing a dedicated leadership curriculum for radiation oncology residents. *J Cancer Educ*. Published online February 22, 2021. doi:10.1007/s13187-021-01980-w

57) Berriochoa C, Amarnath S, Berry D, Koyfman SA, Suh JH, Tendulkar RD. Physician leadership development: a pilot program for radiation oncology residents. *Int J Radiat Oncol Biol Phys*. 2018;102(2):254-256. doi:10.1016/j.ijrobp.2018.05.073

58) Turner S, Janssen A, Chan MK, et al. Can radiation oncologists learn to be better leaders? Outcomes of a pilot foundations of leadership in radiation oncology program for trainees delivered via personal electronic devices. *J Med Imaging Radiat Oncol*. 2018;62(6):847-853. doi:10.1111/1754-9485.12793

59) Ni L, Thomas H, Sinha S, Braunstein S, et al. Determining the feasibility and effectiveness of a virtual interactive residents-as-teachers curriculum: a proposed pilot study. *Int J Radiat Oncol Biol Phys*. 2022;114(1):e10. doi:10.1016/j.ijrobp.2022.06.017

60) Saraf A, Sim AJ, DeLeo AN, et al. Teaching mentoring in radiation oncology (TEAMRO): a ROECSG GME multi-institutional pilot study on teaching mentorship skills to residents. *Int J Radiat Oncol Biol Phys*. 2022;114(1):e7-e8. doi:10.1016/j.ijrobp.2022.06.011

61) Stepczynski J, Holt SR, Ellman MS, Tobin D, Doolittle BR, et al. Factors affecting resident satisfaction in continuity clinic-a systematic review. *J Gen Intern Med*. 2018;33(8):1386-1393. doi:10.1007/s11606-018-4469-8

62) Gangat M, Klein GW, Cohen HW, Heptulla RA. National study of continuity clinic satisfaction in pediatric fellowship training. *Adv Med Educ Pract*. 2013;4:165-169. doi:10.2147/AMEP.S51069

63) Witherspoon L, Jalali S, Roberts MT, et al. Resident-run urology clinics: a tool for use in competency-based medical education for teaching and assessing transition-to-practice skills. *Can Urol Assoc J*. 2019;13(9):E279-E284. doi:10.5489/cuaj.5710

64) Lister JR, Friedman WA, Murad GJ, Dow J, Lombard GJ, et al. Evaluation of a transition to practice program for neurosurgery residents: creating a safe transition from resident to independent practitioner. *J Grad Med Educ*. 2010;2(3):366-372. doi:10.4300/JGME-D-10-00078.1

65) Jeans EB, Beard TB, Boon AL, et al. Empowering residents into independent practice: a single-institutional endeavor aimed at developing resident autonomy through implementation of a chief resident service in radiation oncology. *Int J Radiat Oncol Biol Phys*. 2020;107(1):23-26. doi:10.1016/j.ijrobp.2020.01.001

66) Price JG, Moravan MJ, Boyer MJ, et al. Facilitating the transition to independent radiation oncology practice through a resident-led, veterans affairs teaching hospital service. *Pract Radiat Oncol*. 2021;11(6):441-447. doi:10.1016/j.prro.2021.08.006

67) Yoo SK, Bian SX, Lin E, et al. Development of a radiation oncology resident continuity clinic to improve clinical competency and patient compliance. *Int J Radiat Oncol Biol Phys*. 2018;100(3):551-555. doi:10.1016/j.ijrobp.2017.11.034

68) American Board of Radiology. ABR eliminating SA-CME requirement for OLA participants. theabr.org. Published March 29, 2022. Accessed September 29, 2022. https://www.theabr.org/blogs/abr-eliminating-sa-cme-requirement-for-ola-participants

69) Sherer MV, Lin D, Puri K, et al. Development and usage of eContour, a novel, three-dimensional, image-based website to facilitate access to contouring guidelines at the point of care. *JCO Clin Cancer Inform*. 2019;3:1-9. doi:10.1200/CCI.19.00041

70) McClelland S, Chernykh M, Dengina N, et al. Bridging the gap in global advanced radiation oncology training: impact of a web-based open-access interactive three-dimensional contouring atlas on radiation oncologist practice in russia. *J Cancer Educ*. 2019;34(5):871-873. doi:10.1007/s13187-018-1388-7

71) Franco I, Petereit DG, Mourtada F, Singer L, et al. Increasing brachytherapy mentorship and representation through #NextGenBrachy. *Int J Radiat Oncol Biol Phys*. 2021;111(1):e15. doi:10.1016/j.ijrobp.2021.05.163

72) Brenneman RJ, Goddu SM, Andruska N, et al. Feasibility of same-day prostate fiducial markers, perirectal hydrogel spacer placement, and computed tomography and magnetic resonance imaging simulation for external beam radiation therapy for low-risk and intermediate-risk prostate cancer. *Pract Radiat Oncol*. 2022;12(2):e117-e122. doi:10.1016/j.prro.2021.09.015

73) Green OL, Henke LE, Hugo GD, et al. Practical clinical workflows for online and offline adaptive radiation therapy. *Semin Radiat Oncol*. 2019;29(3):219-227. doi:10.1016/j.semradonc.2019.02.004

74) Lamb J, Cao M, Kishan A, et al. Online adaptive radiation therapy: implementation of a new process of care. *Cureus*. 2017;9(8):e1618. doi:10.7759/cureus.1618

75) Kang J, Thompson RF, Aneja S, et al. National cancer institute workshop on artificial intelligence in radiation oncology: training the next generation. *Pract Radiat Oncol*. 2021;11(1):74-83. doi:10.1016/j.prro.2020.06.001

76) Hosny A, Bitterman DS, Guthier CV, et al. Clinical validation of deep learning algorithms for radiotherapy targeting of non-small-cell lung cancer: an observational study. *Lan Dig Heal*. 2022;4(9):e657-e666. doi:10.1016/S2589-7500(22)00129-7

77) Wong J, Huang V, Wells D, et al. Implementation of deep learning-based auto-segmentation for radiotherapy planning structures: a workflow study at two cancer centers. *Radiat Oncol*. 2021;16(1):101. doi:10.1186/s13014-021-01831-4

78) van der Veen J, Willems S, Deschuymer S, et al. Benefits of deep learning for delineation of organs at risk in head and neck cancer. *Radiother Oncol*. 2019;138:68-74. doi:10.1016/j.radonc.2019.05.010

79) Ma C, Zhou J, Xu X, et al. Deep learning-based auto-segmentation of clinical target volumes for radiotherapy treatment of cervical cancer. *J Appl Clin Med Phys*. 2021;23(2):e13470. doi:10.1002/acm2.13470

80) Duan J, Bernard M, Downes L, et al. Evaluating the clinical acceptability of deep learning contours of prostate and organs-at-risk in an automated prostate treatment planning process. *Med Phys*. 2022;49(4):2570-2581. doi:10.1002/mp.15525

81) Li X, Zhang J, Sheng Y, et al. Automatic IMRT planning via static field fluence prediction (AIP-SFFP): a deep learning algorithm for real-time prostate treatment planning. *Phys Med Biol*. 2020;65(17):175014. doi:10.1088/1361-6560/aba5eb

82) Li X, Wang C, Sheng Y, et al. An artificial intelligence-driven agent for real-time head-and-neck IMRT plan generation using conditional generative adversarial network (cGAN). *Med Phys*. 2021;48(6):2714-2723. doi:10.1002/mp.14770

83) Kiser KJ, Fuller CD, Reed VK, et al. Artificial intelligence in radiation oncology treatment planning: a brief overview. *J Med Artif Intel*. 2019;2(0). doi:10.21037/jmai.2019.04.02

84) Carin L. On Artificial intelligence and deep learning within medical education. *Acad Med*. 2020;95(11S):S10. doi:10.1097/ACM.0000000000003630

85) Khalid S, Goldenberg M, Grantcharov T, Taati B, Rudzicz F. Evaluation of deep learning models for identifying surgical actions and measuring performance. *JAMA Netw Open*. 2020;3(3):e201664. doi:10.1001/jamanetworkopen.2020.1664

86) Janopaul-Naylor J, Qian D, Khan M, et al. Virtual away rotations increase access to radiation oncology. *Pract Radiat Oncol*. 2021;11(5):325-327. doi:10.1016/j.prro.2021.06.002

87) Kahn JM, Fields EC, Pollom E, et al. Increasing medical student engagement through virtual rotations in radiation oncology. *Adv Radiat Oncol*. 2021;6(1):100538. doi:10.1016/j.adro.2020.07.015

88) Tye KE, Williams VM, Franco I, et al. Filling a void: the creation of the ARRO equity and inclusion subcommittee. *App Radiat Oncol*. 2020;9(3):4.

89) Kamran SC, Niemierko A, Deville C, Vapiwala N, et al. Diversity trends by sex and underrepresented in medicine status among US radiation and medical oncology faculty over 5 decades. *JAMA Oncol*. 2022;8(2):221-229. doi:10.1001/jamaoncol.2021.6011

90) Beltrán Ponce SE, Thomas CR, Diaz DA, et al. Social determinants of health, workforce diversity, and financial toxicity: a review of disparities in cancer care. *Curr Probl Cancer*. Published online August 6, 2022:100893. doi:10.1016/j.currproblcancer.2022.100893

91) Mattes MD, Deville C, et al. A survey to assess and delineate approaches to medical student outreach to promote diversity at academic radiation oncology programs. *Int J Radiat Oncol Biol Phys*. 2022;112(5):1083-1089. doi:10.1016/j.ijrobp.2021.12.165

92) Powell C, Yemane L, Brooks M, et al. Outcomes from a novel graduate medical education leadership program in advancing diversity, equity, and inclusion. *J Grad Med Educ*. 2021;13(6):774-784. doi:10.4300/JGME-D-21-00235.1

93) Damast S, Felder S, Fields E, Singer L. Feasibility of deploying a U.S. simulation-based gynecological brachytherapy educational workshop to an international setting. *Brachytherapy*. 2020;19(6):777-782. DOI:10.1016/j.brachy.2020.09.015. Epub 2020 Nov 19.

Personalizing Approaches to Patient Education Throughout the Radiation Oncology Workflow

Jodi Goldman, BS;[1] Keldon K. Lin, BA;[2] Valeria Londoño, BS;[3] Sarah E. Hoffe, MD[4*]

Abstract

For cancer patients who undergo radiation therapy (RT) at some part of their treatment journey, new knowledge regarding the principles underlying RT, workflow, and side effects can become overwhelming and lead to patient fear and anxiety. Various patient education tools have been implemented in radiation oncology clinics internationally including virtual reality, educational videos, educational sessions, websites, and pamphlets. Although studies have demonstrated that such tools can increase patient knowledge regarding RT and its side effects while also decreasing patient anxiety, it is unclear how best to personalize each patient's education. Similarly, patient characteristics such as age, gender, literacy level, and cultural considerations can also impact a patient's need or desire for specific educational tools. Barriers to optimization include cost and resource availability with virtual reality, online misinformation, and pamphlets that may be written at an educational level higher than the average population reading level. The efficacy of different educational methods has been studied at various time points throughout the radiation oncology workflow. Overall, early educational intervention with continued reinforcement throughout the treatment course through an individualized multimodal learning approach is likely to be most effective.

Keywords: patient education, direct patient care, medical physicists, virtual reality

Approximately half of patients diagnosed with cancer will receive radiation therapy (RT) as part of their treatment course.[1] Receiving a cancer diagnosis can instill fear and anxiety in patients, particularly regarding the uncertainty of what to expect during treatment. Specific to RT, most patients and caregivers do not possess a sound understanding of treatment and often present with misconceptions about its effects, such as treatment-induced radioactivity.[2] Providing effective education to patients upon consultation is challenging. Up to 30% of words used during an initial RT consultation can be identified as medical jargon, potentially compromising knowledge retention following an RT consultation.[3,4] This can be problematic for patients emotionally, and can disrupt the consent process and treatment compliance.[5] Providing education on RT terminology, logistics, and workflow plays an important role in achieving successful treatment outcomes. Patients who receive education show higher levels of understanding and lower levels of anxiety surrounding their radiation treatment.[6-9]

Although supplementary educational materials are valuable, they should not replace interactions and relationships between patients and health care providers during which patients' unique needs and learning styles can be individualized. Demographic characteristics including male gender and older age have been associated with lower requests for information during RT consultation.[10]

Affiliations: [1]Texas Tech University Health Science Center School of Medicine, Lubbock, TX. [2]Mayo Clinic Alix School of Medicine, Scottsdale, AZ. [3]Georgetown University School of Medicine, Washington DC. [4]Moffitt Cancer Center, Tampa, FL.
Corresponding author: *Sarah E. Hoffe, MD, Department of Radiation Oncology, Moffitt Cancer Center, 12902 Magnolia Drive, Tampa, FL 33612, (Sarah.Hoffe@moffitt.org)
Disclosures: Ms. Goldman, Mr. Lin, and Ms. Londoño are members of the *Applied Radiation Oncology* (ARO) Future Content Medical Student Committee. Dr. Hoffe is an editorial board member for ARO and faculty advisor for ARO's medical student committees. None of the authors received outside funding for the production of this original manuscript and no part of this article has been previously published elsewhere.

As this suggests, there is no one-size-fits-all approach to patient education within radiation oncology; rather, each patient has different educational needs depending on age, gender, and educational level. Similarly, cultural differences including language may be a barrier to providing patients with generalized information. Radiation oncologists and allied health care staff should consider implementing individualized patient-centered educational tools into the clinical workflow to enhance patients' understanding of their radiation treatment. The purpose of the current PubMed literature review is to present an overview of multiple educational modalities within radiation oncology patient education, their costs and benefits, where each technology may be best utilized within the RT treatment course, and how to adapt different tools to personalize the educational experience.

Patient Education Methods

Virtual Reality

Virtual reality (VR) is a more recently instituted technology for educating patients about RT. One example of its use is Virtual Environment for Radiotherapy Training (VERT).[5,11] VERT is displayed via a projection screen and serves to create an interactive 3-dimensional (3D) RT treatment room environment consisting of clinical tools such as a linear accelerator, patient couch, and radiation fields.[5] RT treatment plans in Digital Imaging and Communication in Medicine (DICOM) can be uploaded to display patient-specific anatomy, doses, tumor and target volumes, and therapy techniques.[11] Additional studies have used VR headsets and 360-degree video tours to show patients a virtual version of themselves undergoing RT.[9,12]

Overall, studies have demonstrated that VERT provides a basis for treatment expectations and therapy precision.[5] VERT has also lowered patient anxiety, likely by enabling patients to directly envision the clinical experience in a nonclinical environment.[13] The 3D environment creates a bridge that closes the gap between written educational materials and the treatment experience. This form of learning may be well-suited for patients who are visuospatial learners and those who prefer interactive learning. However, virtual reality is not without its challenges. For example, displaying DICOM images with treatment parameters may unnecessarily overwhelm and distress patients.[5] Logistically, VERT requires a high volume of resources upfront that may rely on institutional budgets, leading to inequality in access to care.[5]

Educational Video

Verbal communication regarding the RT process, including discussion of face masks and equipment, can increase fear during a patient's consultation.[6] By visually describing the RT workflow, educational videos provide a realistic image of what to expect during treatment. Videos are advantageous because patients can view them prior to a consultation, reducing time on basic explanation and increasing time for specific patient questions during an appointment.[14] Videos can also be effective for a wider variety of patient populations, including audiovisual learners or those with reduced literary skill. Additionally, patients can watch educational videos multiple times for longitudinal reinforcement. Given the significant logistical barriers to undergoing a lengthy radiation treatment process, many patients rely on their support network while undergoing RT. Another benefit of educational videos is that patients can easily share them with family and friends, improving understanding of the treatment process.

Studies have demonstrated an increase in patient knowledge of RT side effects and workflow after watching an approximately 20-minute educational video, demonstrating its value as a tool to educate a diverse patient population.[2,6,15] Although online and video-based education can be a powerful tool, some patients may have limited ability to benefit from these modalities due to limited technological literacy or access. Those without reliable access to technology or who lack the basic skills to navigate online video platforms may have difficulty taking full advantage of online and video-based education. Those not comfortable using technology may be overwhelmed by video-based education, making learning more difficult.

Online Information

Due to the general lack of knowledge surrounding RT, patients and caregivers may search the internet to learn more about their treatment, leading them to departmental websites and social media outlets such as YouTube, Twitter, and TikTok.[6]

A major benefit to these sites as educational tools is the increasing internet accessibility and flexibility of use. Some patients may read web-based content before their initial RT appointment to help guide expectations and foster understanding of treatment options prior to physician recommendations.[16] This can lead to thoughtful discussion and help build a patient-physician relationship, but could also lead to misinformation, especially since it is difficult to discern accurate from inaccurate information online.[17] Misinformation online can generate negative consequences, such as patients believing they will emit radiation to loved ones after treatment or viewing their disease as an impending death.[17] With increased patient anxiety, health care providers are forced to spend more appointment time counteracting and refuting misinformation read online.[17]

An analysis of academic radiation oncology department websites

Table 1. Advantages and Disadvantages Associated With Various Patient Education Tools Utilized in Radiation Oncology

MODALITY	ADVANTAGES	DISADVANTAGES
Virtual reality	▪ Closest replication to actual treatment experience ▪ Can help ease patient anxiety surrounding treatment experience ▪ Can be personalized for each patient	▪ High cost ▪ High resource volume ▪ Potential for unequal access to care ▪ Requires patient to be physically present in clinic ▪ May require digital literacy above the patient's level
Educational videos	▪ Beneficial for patients with reduced literacy level ▪ Effective for audiovisual learners ▪ Can be built into department websites ▪ Easily disseminated to patients' support systems	▪ Cost and resources necessary for video production ▪ May not be as helpful for patients who have nonvisual learning styles ▪ Challenging to personalize
Online information	▪ Relatively easy accessibility and usability ▪ Can be incorporated into existing department website ▪ Low-cost or free for patients to access	▪ Potential risk for misinformation ▪ Difficult to comprehend based on literacy level ▪ Challenging to personalize according to patients' unique questions ▪ Requires IT expertise to produce and update content
Medical physicist consultation	▪ Improved technical aspect education ▪ Provides additional opportunity to directly address patient questions ▪ Can be conducted remotely	▪ Need for increased patient-simulation and communication training implementation at medical physics residency ▪ Requires increased time commitment for medical physicists ▪ Physicists may not be able to answer all questions relating to clinical care
Education sessions	▪ One-on-one patient education with more time for discussion ▪ Allows for personalization according to patients' unique concerns ▪ Can be conducted remotely	▪ Increased time requirement for providers ▪ Potential for redundancy in patient questions ▪ May not be effective if not tailored to specific patient needs
Pamphlets	▪ Relatively inexpensive to produce and distribute ▪ Common in clinical practice ▪ Can be produced in paper and electronic format	▪ Can be difficult to understand ▪ Challenging to personalize ▪ May not be up to date with the latest medical advances and research

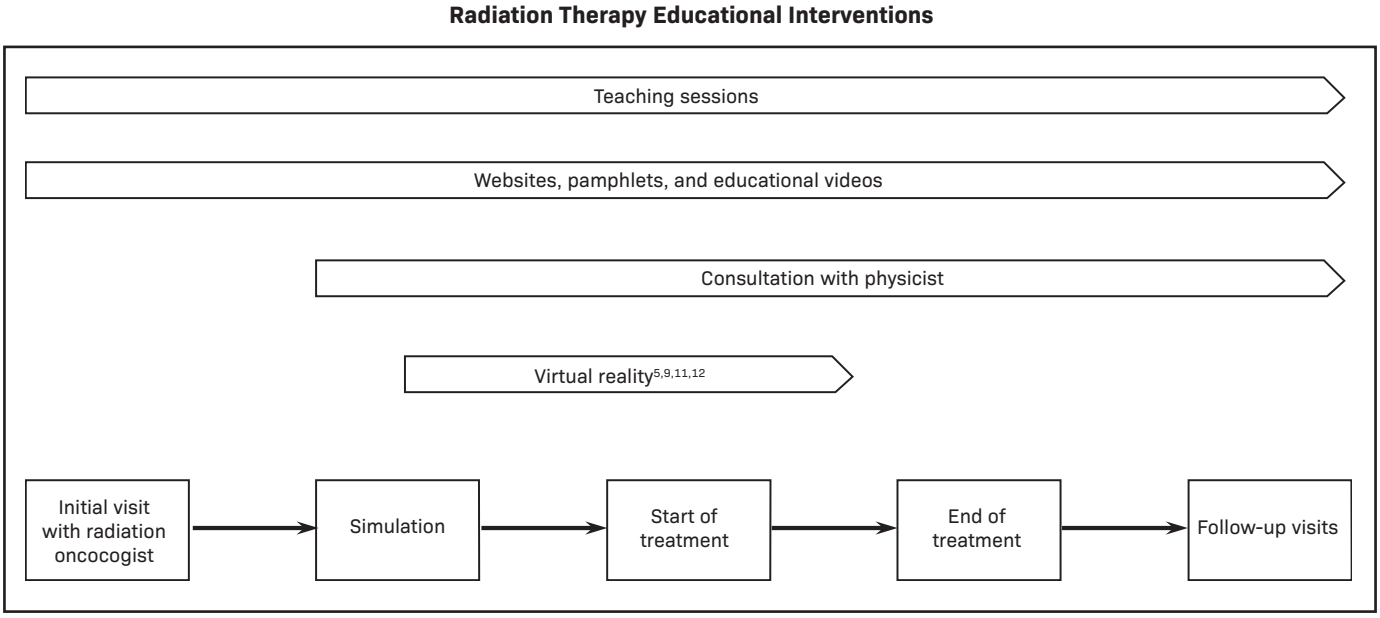
demonstrated that website language reached far above the reading level of an average adult, or the seventh to ninth grade reading level.[16] Similarly, information presented on academic departmental websites may be intended for physicians, residents, medical students, or others who might have an advanced baseline knowledge of the associated medical topic.[16] The National Assessment of Adult Literacy study demonstrated that most US adults lack the health literacy to understand most information provided through different educational modalities.[18]

Although most studies analyzing online health care language readability involve the English language, more recent studies have compared online English and Spanish content.[19,20] One study comparing online pancreatic cancer treatment information found that English content was written at a university level while Spanish content was written at a high school level.[19] Both English and Spanish content exceeded the average reading level for an adult.[19,21] These findings suggest that readability issues with online materials span across languages and cultures.[19] It is imperative that educational materials such as academic websites should aim to best align to the literacy level and the language/linguistic needs of the general population, to ensure patients are appropriately informed in their search for RT educational content. Strategies to reduce the challenge of readability of online information include incorporating less complex language and acronyms, shortening sentences, and providing links to audiovisual material.[20]

Medical Physicist Clinical Role

As technical experts, medical physicists play an integral role in treatment planning and patient quality assurance measurements. Their educational training and expertise facilitate patient discussions of technical details of radiation treatment (eg, type of radiation, dose,

Figure 1. Timeline displaying the point during radiation therapy consultation and treatment at which various educational interventions may occur.



and delivery method). Confusion and concerns about complex imaging and treatment modalities often arise. Clinical trials have suggested that medical physicists, with their relevant training and knowledge, have potential to fill the gap on technology education.[22,23]

Studies reviewing one-on-one physicist-patient consults have demonstrated a unique avenue for patient education and anxiety reduction.[22,23] In studies where the intervention-arm patients met with a medical physicist, the patients were surveyed for anxiety and distress levels.[22,24] The medical physicists addressed technical aspects and questions at multiple points of treatment (eg, at treatment simulation, before the first treatment, and before completion). Anxiety was significantly reduced in patients who met with a medical physicist throughout treatment, demonstrating a unique and beneficial role of physicist-patient consults.[22,24] Furthermore, the consults also enabled patients to develop a more robust understanding of what to expect during treatment.[25]

Education Sessions

Preparing patients for RT includes addressing their complex emotions and distress. Educational sessions specifically aimed at minimizing psychological distress while expanding patient understanding have shown to be effective in a number of studies.[26] Both one-on-one video conferencing and face-to-face individualized consultations have demonstrated increased patient satisfaction.[27,28] Although the additional intervention varied along the RT workflow in these studies, the educational framework incorporated individualized written and verbal information at additional education-focused appointments. This material was presented by multiple members of the interdisciplinary team, including nurses, radiation therapists, physicists, and physicians, each bringing unique perspectives to the patient. Along with time for additional questions, information included general RT materials, side effects and management, and anticipated stressors.[27-29]

Education sessions significantly reduced in anxiety scores in patients who received 2 consultations with a radiation therapist prior to planning and treatment in addition to decreased depression scores in patients receiving a teaching session by a clinical nurse.[27,29] Video conferencing with visual tele-education materials prior to simulation also demonstrated high patient satisfaction with preparation and education.[28]

Providers should take special considerations when conducting education sessions with patients whose primary language is one other than English, using certified medical interpreters. In-person interpretation may offer greater personalization during the treatment visit as opposed to phone interpretation, although availability may be limited throughout the entire treatment workflow.[30] Family members often accompany patients, but should not be used as primary interpreters given the risk for biased interpretation.[30] Educational sessions could provide an opportune setting for providers to learn how their patients' cultural values may affect their beliefs about cancer and preferences regarding their treatment.[30]

Pamphlets

The use of informational pamphlets can also be an effective method of patient education for those undergoing RT. These can provide

concise and detailed information about radiation treatment and side effects in a medium that can be distributed quickly and relatively inexpensively. Although certain patients may prefer printed materials, pamphlets can also be produced electronically and sent to patients via email or uploaded to their patient portal, allowing for decreased environmental impact, greater reach, and faster delivery compared with printed materials.[31]

A significant drawback of pamphlets is that they can be difficult for some patients to understand, particularly those with literacy limitations. Furthermore, pamphlets cannot offer the same level of personalization that an interactive discussion with a radiation oncologist, physicist, or therapist can provide. As a result, it can be difficult for patients to gain a full understanding of the risks and benefits of their treatment from pamphlets alone. **Table 1** discusses advantages and disadvantages associated with each education modality discussed.

Clinical Application

RT is a complex process that requires a multidisciplinary team for safe, effective execution. After the initial visit with a radiation oncologist, and once patients decide to pursue radiation treatment, they undergo simulation imaging with unique positioning considerations for optimal treatment. Planning may be modified and reassessed due to anatomic shifts. Once the planning and quality assurance process is complete, RT delivery begins.[32] Patient education intervention has been implemented in many instances throughout the patient's experience with the RT team. Physicist-patient consults, educational sessions with providers, and informational pamphlets have been provided directly before or after simulation sessions and before beginning treatment.[22,28,29] Other educational modalities, such as videos, have been utilized prior to initial visits to establish a baseline understanding for patients.[14]

Figure 1 depicts at what point during the radiation oncology workflow various patient education modalities have been studied and found to be effective.

Conclusion

Patients receiving RT often experience emotional distress and anxiety.[33] These emotions can be exacerbated by unfamiliarity and lack of understanding about RT. To address patient concerns and improve quality of care, a multimodal approach to education should be used throughout the RT workflow. The modalities should be directed toward patient-specific needs while considering demographics, health literacy, and baseline knowledge. A multidisciplinary approach may also be implemented with the radiation oncologists, physicists, and nurses at different time points in the treatment plan. Studies have suggested that effective teaching must occur early and throughout the course of radiation.[29]

Accessibility can be improved for many methods addressing RT patient education. Despite their ongoing efforts, education modalities often do not conform to the patient's health literacy.[34] Tools such as websites and pamphlets should be revised at a seventh-ninth grade reading level to be accessible and effective for the general population. Furthermore, patients who do not primarily speak English will also have additional language barriers when applying the multiple education modalities. To increase accessibility, future work should include creating opportunities for language translation, whether that be provided by the modality itself (eg, a website presented in multiple languages) or by an interpreter for tools such as educational sessions. Patient preferences and convenience should also be considered when incorporating increased technological modalities (eg, an elderly patient meeting for an education session in person instead of via videoconferencing). To improve and advance education sessions and medical physicist participation in consultations, direct patient care experience is also necessary for providers.[35] Specific tracks or programming can be implemented in health care training programs to educate radiation oncology providers on various patient education modalities.

Ultimately, the goal of patient education technologies is to improve patient understanding of radiation treatment and reduce anxiety. As modalities improve and diversify, more patients will gain access to tools best suited for their unique preferences and physical needs.

References

1) Jaffray DA, Gospodarowicz MK. Radiation therapy for cancer. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, eds. *Cancer: Disease Control Priorities, Third Edition (Volume 3)*. The International Bank for Reconstruction and Development / The World Bank; November 1, 2015.

2) Matsuyama RK, Lyckholm LJ, Molisani A, Moghanaki D. The value of an educational video before consultation with a radiation oncologist. *J Cancer Educ.* 2013;28(2):306-313. doi:10.1007/s13187-013-0473-1

3) Schnitzler L, Smith SK, Shepherd HL, et al. Communication during radiation therapy education sessions: the role of medical jargon and emotional support in clarifying patient confusion. *Pat Educ Couns.* 2017;100(1):112-120. doi:10.1016/j.pec.2016.08.006

4) Arya R, Ichikawa T, Callender B, et al. Communicating the external beam radiation experience (CEBRE): perceived benefits of a graphic narrative patient education tool. *Pract Radiat Oncol.* 2020;10(4). doi:10.1016/j.prro.2019.09.001

5) Jimenez YA, Cumming S, Wang W, Stuart K, Thwaites DI, Lewis SJ. Patient education using virtual reality increases knowledge and positive experience for breast cancer patients undergoing radiation therapy. *Supp Care Cancer.* 2018;26(8):2879-2888. doi:10.1007/s00520-018-4114-4

6) Kumar KA, Balazy KE, Gutkin PM, et al. Association between patient education videos and knowledge of radiation treatment. *Int J Radiat Oncol Biol Phys.* 2021;109(5):1165-1175. doi:10.1016/j.ijrobp.2020.11.069

7) Schuller BW, Burch C, Casterton T, Crowther C, Fowler J, Stenmark MH. Precision patient education using a "flipped classroom" approach. *J Appl Clin Med Phys.* 2022;23(5)e13601. doi:10.1002/acm2.13601

8) Pembroke M, Bradley J, Mueller M, Mollica M, Nemeth LS. Feasibility of breast radiation therapy video education combined with standard radiation therapy education for patients with breast cancer. *Oncol Nurs Forum.* 2021;48(3):279-290. doi:10.1188/21.ONF.279-290

9) Wang LJ, Casto B, Luh JY, Wang SJ. Virtual reality-based education for patients undergoing radiation therapy. *J Cancer Educ.* 2022;37(3):694-700. doi:10.1007/s13187-020-01870-7

10) Zeguers M, de Haes HCJM, Zandbelt LC, et al. The information needs of new radiotherapy patients: How to measure? Do they want to know everything? And if not, why? *Int J Radiat Oncol Biol Phys.* 2012;82(1):418-424. doi:10.1016/j.ijrobp.2010.09.032

11) Sulé-Suso J, Finney S, Bisson J, et al. Pilot study on virtual imaging for patient information on radiotherapy planning and delivery. *Radiography.* 2015;21(3):273-277. doi:10.1016/j.radi.2015.02.002

12) Galvez J, Eisenhower M, England W, et al. An interactive virtual reality tour for adolescents receiving proton radiation therapy: proof-of-concept study. *JMIR Perioper Med.* 2019;2(1):e11259. Published 2019 Mar 5. doi:10.2196/11259

13) Flockton A. Men's experience of virtual simulation to aid patient education for radiation treatment to the prostate. *J Med Imag Radiat Sci.* 2017;48(1). doi:10.1016/j.jmir.2017.02.021

14) Brock TP, Smith SR. Using digital videos displayed on personal digital assistants (PDAs) to enhance patient education in clinical settings. *Int J Med Inform.* 2007;76(11-12):829-835. doi:10.1016/j.ijmedinf.2006.09.024

15) Hahn CA, Fish LJ, Dunn RH, Halperin EC. Prospective trial of a video educational tool for radiation oncology patients. *Am J Clin Oncol.* 2005;28(6):609-612. doi:10.1097/01.coc.0000182417.94669.a0

16) Rosenberg SA, Francis DM, Hullet CR, et al. Online patient information from radiation oncology departments is too complex for the general population. *Pract Radiat Oncol.* 2017;7(1):57-62. doi:10.1016/j.prro.2016.07.008

17) Teplinsky E, Ponce SB, Drake EK, et al. Online medical misinformation in cancer: distinguishing fact from fiction. *JCO Oncol Pract.* 2022;18(8):584-589. doi:10.1200/op.21.00764

18) Cutilli CC, Bennett IM. Understanding the health literacy of America. *Orthop Nurs.* 2009;28(1):27-32. doi:10.1097/01.nor.0000345852.22122.d6

19) Garland ME, Lukac D, Contreras P. A brief report: comparative evaluation of online Spanish and English content on pancreatic cancer treatment. *J Cancer Educ.* 2022. doi:10.1007/s13187-022-02171-x

20) Villa Camacho JC, Pena MA, Flores EJ, et al. Addressing linguistic barriers to care: evaluation of breast cancer online patient educational materials for Spanish-speaking patients. *J Am Coll Radiol.* 2021;18(7):919-926. doi:10.1016/j.jacr.2021.02.001

21) Kutner M, Greenberg E, Baer J. A first look at the literacy of America's adults in the 21st Century. Accessed February 12, 2023. https://nces.ed.gov/NAAL/PDF/2006470.PDF

22) Atwood TF, Brown DW, Murphy JD, et al. Examining the effect of direct patient care for medical physicists: a randomized prospective phase III trial. *Int J Radiat Oncol Biol Phys.* 2023;115(1):224-232. https://doi.org/10.1016/j.ijrobp.2022.05.014

23) Atwood TF, Brown DW, Juang T, et al. A review of patient questions from physicist-patient consults. *J App Clin Med Phys.* 2020;21(8):305-308. https://doi.org/10.1002/acm2.12942

24) Burmeister J, Dominello MM, Soulliere R, et al. A direct patient-provider relationship with the medical physicist reduces anxiety in patients receiving radiation therapy. *Int J Radiat Oncol Biol Phys.* 2023;115(1):233-243. https://www.sciencedirect.com/science/article/pii/S036030162203437X. doi:10.1016/j.ijrobp.2022.10.011

25) Hyun M, Hyun A. Respecting patient autonomy in radiation oncology and beyond. In: *Ethics and Error in Medicine.* Routledge; 2019:103-117.

26) Halkett G, O'Connor M, Jefford M, et al. RT prepare: a radiation therapist-delivered intervention reduces psychological distress in women with breast cancer referred for radiotherapy. *Br J Cancer.* 2018;118(12):1549-1558. doi:10.1038/s41416-018-0112-z

27) Halkett GKB, O'Connor M, Aranda S, et al. Pilot randomised controlled trial of a radiation therapist-led educational intervention for breast cancer patients prior to commencing radiotherapy. *Sup Care Cancer.* 2013;21(6):1725-1733. doi:10.1007/s00520-013-1719-5

28) Magliozzi M, Cashell A, Ishmail N, Hill C, Velec M. Virtual integration of patient education in radiotherapy (VIPER). *Tech Innov Patient Support Radiat Oncol.* 2022;23:47-57. doi:10.1016/j.tipsro.2022.08.008

29) Zaheer S, Gul RB, Bhamani SS, Memon MA. The effect of individualized education with support on breast cancer patients' anxiety and depression during radiation therapy: a pilot study. *Eur J Oncol Nurs.* 2020;48:101826. https://www.sciencedirect.com/science/article/pii/S146238892030106X. doi:10.1016/j.ejon.2020.101826

30) Chou F-Y, Kuang LY, Lee J, Yoo GJ, Fung L-C. Challenges in cancer self-management of patients with limited English proficiency. *Asia-Pacific J Oncol Nurs.* 2016;3(3):259-265. doi:10.4103/2347-5625.189815

31) Jewitt N, Hope AJ, Milne R, et al. Development and evaluation of patient education materials for elderly lung cancer patients. *J Cancer Educ.* 2016;31(1):70-74. doi:10.1007/s13187-014-0780-1

32) Green OL, Henke LE, Hugo GD. Practical clinical workflows for online and offline adaptive radiation therapy. *Semin Radiat Oncol.* 2019;29(3):219-227. doi:10.1016/j.semradonc.2019.02.004

33) Canil T, Cashell A, Papadakos J, Abdelmutti N, Friedman AJ. Evaluation of the effects of pre-treatment education on self-efficacy and anxiety in patients receiving radiation therapy: a pilot study. *J Med Imag Radiat Sci.* 2012;43(4):221-227. doi:10.1016/j.jmir.2012.05.002

34) Giannopoulos E, McBain S, Giuliani M, et al. Health literacy and radiation therapy: a current state assessment of patient education materials. *J Cancer Educ.* 2022. doi:10.1007/s13187-022-02208-1

35) Brown DW, Atwood TF, Moore KL, et al. A program to train medical physicists for direct patient care responsibilities. *J Appl Clin Med Phys.* 2018;19(6):332-335. doi:10.1002/acm2.12472.

Dosimetric Comparison of Proton Versus Photon Stereotactic Radiosurgery for Treatment of Vestibular Schwannoma

Shivani Sud, MD;[1] Marc Bussiere, MSc;[2] Thomas Botticello, BS, CMD;[2] Andrzej Niemierko, PhD;[3] Adam Schwartz, MS, CMD;[2] Helen A. Shih, MD, MS, MPH[2]

Abstract

Objective: To evaluate the dosimetric advantages and limitations of protons compared with photons in stereotactic radiosurgery for vestibular schwannoma.

Methods and Materials: Nine patients with vestibular schwannoma were selected among those receiving single-fraction proton stereotactic radiation therapy (PSRS) via a dedicated, passive, single-scattering stereotactic proton unit at a single institution between 2015 and 2018. These cases were re-planned with photon (X-ray) SRS (XSRS) volumetric-modulated arc therapy (VMAT) with 2.5- and 5-mm multileaf collimators (2.5 XSRS and 5 XSRS), respectively. Plans were constructed using the original total treatment dose of 12 Gy relative biological effectiveness (RBE) delivered in 1 fraction.

Results: Treatment plans were compared based on target volume dosimetry and estimated clinical toxicity. Average target volume was 0.71 cc (range, 0.2-1.8). There were no significant differences in V100%, homogeneity index or Dmax% between treatment modalities. However, 5 XSRS and 2.5 XSRS offered equal or superior V90% and V95% compared with PSRS for all 9 cases. Gradient and conformity indices were most optimal for 2.5 XSRS. Dmax in Gy (RBE) to ipsilateral temporal lobe (7.7, 9.5, 8.2), cochlea (9.6, 10.9, 10.6) and vestibule (7.7, 8.7, 8.5) was lower with 2.5 XSRS vs PSRS and 5 XSRS, $P < 0.05$. Dmax to brainstem was 8.8, 8.6, 9.2 for 2.5 XSRS, PSRS, 5 XSRS, respectively. Mean equivalent uniform dose (EUD) in Gy (RBE) to the ipsilateral temporal lobe, cochlea and vestibule was lower with 2.5 XSRS vs PSRS and 5 XSRS, $P < 0.05$. The projected risk of secondary tumors in excess of baseline was lowest for PSRS (PSRS - 2.8, 5 XSRS - 6.6, 2.5 XSRS - 5.5 cases per 10,000 patient-years; $P < 0.008$ for all comparisons).

Conclusions: This study compared the dosimetric advantages and limitations of PSRS, 5 XSRS and 2.5 XSRS for vestibular schwannoma. Target volume coverage and organ at risk (OAR) dose is similar between XSRS and PSRS; 2.5 XSRS offers greater target conformality and lower dose to OAR than 5 XSRS. PSRS offers significantly lower excess risk of secondary tumor than 2.5 XSRS and 5 XSRS although the absolute risk of secondary tumors is low across modalities.

Keywords: vestibular schwannoma, radiosurgery, proton therapy, acoustic neuroma

Affiliations: [1]Department of Radiation Oncology, University of North Carolina Hospitals, Chapel Hill. [2]Department of Radiation Oncology, Massachusetts General Hospital, Boston. [3]Division of Biostatistics, Department of Radiation Oncology, Massachusetts General Hospital, Boston.
Corresponding author: *Helen A. Shih, MD, MS, MPH, Massachusetts General Hospital, Department of Radiation Oncology, 30 Fruit St, Boston, MA 02114 (hshih@mgh.harvard.edu)
Disclosure: Dr. Shih: UpToDate, writer and section editor; The Radiosurgery Society, board of directors; Advanced Accelerator Applications, advisory board; Servier Pharmaceuticals, consultant. The remaining authors have no conflicts of interest to disclose. None of the authors received outside funding for the production of this original manuscript. A subset of this data was presented at the 2020 Radiosurgery Society Virtual Scientific Meeting, March 18, 2020. Reference: Sud S, Botticello T, Schwartz AM, et al. Dosimetric comparison of protons versus photons for treatment of vestibular schwannoma. *Cureus.* 2020;12(4):a461.
Data sharing: Research data are stored in an institutional repository and will be shared upon request to the corresponding author. Authors responsible for statistical analysis are Andrzej Niemierko, PhD, aniemierko@mgh.harvard.edu, and Shivani Sud, MD, shivani_sud@med.unc.edu.

Vestibular schwannomas are benign cerebellopontine angle tumors arising from myelin sheath forming Schwann cells of the vestibular division of cranial nerve VIII. Common presentations include ipsilateral sensorineural hearing loss, dizziness, imbalance and asymmetric tinnitus.[1] Large tumors may compress adjacent structures including cranial nerves (CN) V, VII, IX, X, XI, the brainstem, or cerebellum. Overall incidence rates are estimated to be 3 to 5 cases per 100,000 person-years.[2,3] Incidental diagnoses of vestibular schwannoma have increased in parallel with access to high-resolution imaging.[1,2] Correspondingly, the treatment paradigm has evolved to include the options of conservative observation, microsurgery and radiation therapy (RT)[4] based on tumor size, growth rate, hearing status, symptoms, patient age, comorbidities, and preferences.

RT is an effective treatment modality for vestibular schwannoma, especially for patients who decline surgery, are not surgical candidates due to comorbidity, or have surgically inaccessible or recurrent tumors. For appropriately selected cases, stereotactic radiosurgery (SRS) delivers high-dose conformal radiation to a limited target volume in a single fraction facilitated by high-precision localization in contrast to conventional regimens of 25 to 30 fractions.[5] Both conventional fractionated external-beam RT and SRS achieve high rates of tumor control (84% to 100% at 5 years).[5] Thus, treatment goals include minimizing long-term toxicities, including hearing loss, imbalance, and toxicity to other cranial nerves.

Feasibility of SRS depends on factors including tumor size and anatomical interface with the brainstem and cochlea if hearing is intact. SRS dose < 13 Gy are given to decrease risk of facial nerve dysfunction, trigeminal neuralgia and hearing loss.[6,7] SRS may be delivered via several modalities including Gamma Knife (Elekta) or CyberKnife (Accuray), linear accelerators (linac), and proton units. Proton beams are highly conformal, have sharp lateral penumbras, low scatter, and preferential dose deposition within the target without exit dose due to its finite path length. As noted in The Congress of Neurological Surgeons evidence-based guidelines on vestibular schwannoma treatment, regarding radiosurgery technology, no studies directly compare SRS modalities, thus recommendations on outcomes based on modality cannot be made.[4] Most studies of proton or photon SRS are single-institution experiences that do not directly compare these modalities but report similar tumor control efficacy.[8,9] Furthermore, data are inadequate to compare hearing, cranial nerve preservation, cognitive function, and secondary tumors with each modality.[8,9]

In the absence of rigorous comparisons of SRS technologies, physicians must rely on theoretical benefits of each modality, limited series, and clinical experience. As protons are not widely available, patients may incur additional health care system costs and treatment burdens associated with referral to a center capable of performing proton SRS (PSRS). Thus, understanding the practical strengths of each modality can inform shared decision-making between physicians and patients. Future direct PSRS vs photon SRS (XSRS) comparison clinical trials are unlikely. Dosimetric data from centers such as ours with extensive PSRS experience may elucidate potential benefits of PSRS and XSRS in representative clinical scenarios. In the present study, we plan and dosimetrically evaluate 9 representative cases of vestibular schwannoma using PSRS vs linac-based XSRS with 2 common multileaf collimator sizes.

Methods

Study Population

We identified a representative sample of patients with vestibular schwannomas among patients who received single-fraction PSRS between 2015 and 2018. The selected 9 cases varied in pertinent anatomic characteristics, including canal involvement, abutment/proximity to the brainstem as assessed per Koos grade (**Table 1, Figure 1**), and clinical characteristics (**Table 2**). The study was approved by our institutional review board.

Table 1. Koos Grading Scale

GRADE	DESCRIPTION
1	Intracanalicular tumor
2	Protruding into cerebellopontine angle
3	Reaching the brainstem surface
4	Deforming the brainstem surface

Simulation

Patients were immobilized with a modified Gill-Thomas-Cosman head frame (Integra-Radionics) and 1/16-inch diameter stainless steel fiducial markers were placed in the skull's outer table to facilitate target volume alignment to the isocenter of the radiosurgical system.[10,11] CT simulation with intravenous contrast was performed. Simulation images were obtained at 1.25-mm axial intervals and fused with diagnostic MRI to assist target delineation.

Treatment planning

PSRS plans were generated using the XiO planning system (Elekta Inc.). PSRS was delivered with a 3-D conformal, passive, single-scattering proton therapy unit via 3 equally or unequally weighted isocentric fields. Per department protocol, we defined case-specific lateral margins for penumbra and set-up uncertainty and a beam-specific, end-range margin with a 3.5% CT density correction plus 1 mm for range uncertainty.[12]

XSRS plans with volumetric-modulated arc therapy (VMAT) were generated using RayStation (RaySearch Laboratories) with 2.5-mm

Table 2. Patient and Tumor Characteristics

CASE	AGE	SEX	LATERALITY	KOOS CLASSIFICATION	PRESENTATION	PRIOR RESECTION	TARGET VOLUME (CC)
1	71	F	R	Grade 2	Hearing loss, Facial weakness	No	0.2
2	67	M	L	Grade 2	Disequilibrium	No	0.3
3	81	M	R	Grade 2	Hearing loss	No	0.3
4	59	M	R	Grade 3	Tinnitus, Disequilibrium	No	0.6
5	45	M	L	Grade 3	Tinnitus, Hearing loss, Vertigo	No	0.9
6	68	M	R	Grade 3	Hearing loss	No	1.0
7	54	M	R	Grade 3	Hearing loss	Yes	1.8
8	76	F	L	Grade 2	Hearing loss	No	0.5
9	72	M	L	Grade 2	Hearing loss	No	1.0

All tumors treated with prescription dose 12 Gy (RBE). Abbreviations: F, Female; M, Male; R, Right; L, Left; cc, cubic centimeter

(2.5 XSRS) and 5-mm (5 XSRS) multileaf collimators (MLC) on the Varian Edge and TrueBeam systems, respectively, with a 6-MV flattening filter-free beam. VMAT plans were optimized with up to 3 partial arcs and avoided direct irradiation or exit dose through the ocular globes.

All cases were prescribed 12 Gy relative biological effectiveness (RBE) with standard RBE of 1.1 for protons. The gross target volume (GTV) encompassed radiographically apparent gross tumor. The planning target volume (PTV) consisted of the GTV with a 0.5- to 1.0-mm isotropic expansion. Dose heterogeneity was limited by ensuring an effective normalization of approximately 90%, while ensuring 98.8% PTV prescription coverage. Organs at risk (OAR) including brainstem, chiasm, cochlea, vestibule, ocular globes, hypothalamus, optic nerves, temporal lobe and brain, were verified by a neuro-anatomist and

Figure 1. Axial images of gross target volume and critical structures including the cochlea, vestibule and brainstem for each case.

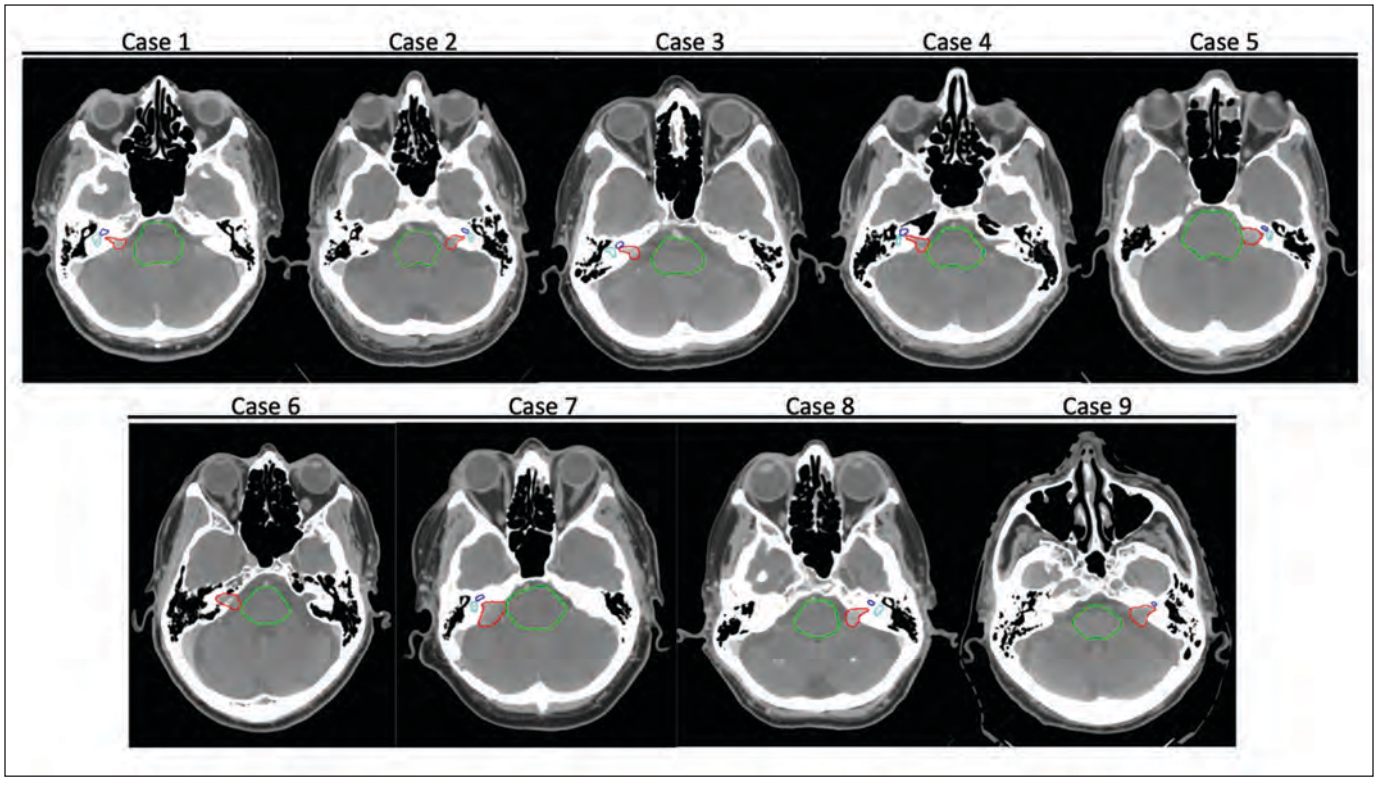
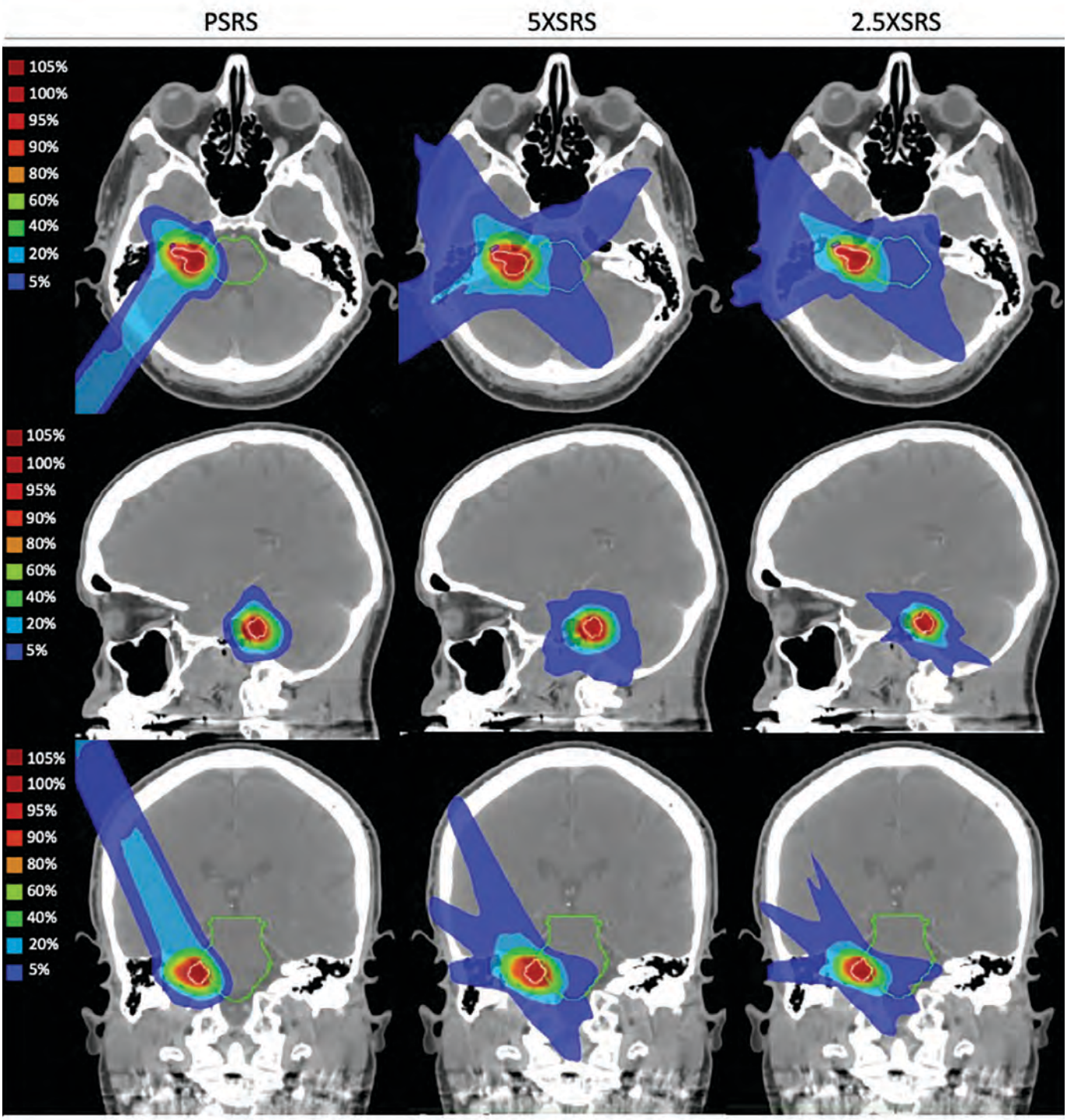


Figure 2. Representative cross-sectional (axial, sagittal, coronal) planning images for proton stereotactic radiosurgery (PSRS) and photon stereotactic radiosurgery delivered via volumetric-modulated arc therapy using 2.5- and 5-mm multileaf collimators (2.5 XSRS and 5 XSRS, respectively) for case 4 (Table 1) patient with vestibular schwannoma, 0.6 cc target, prescribed 12 Gy (RBE).



CNS-specialized radiation oncologist. For bilateral structures, the ipsilateral and contralateral volumes were delineated separately.

Plan Comparison

All plans were transferred to MIM software solutions for centralized, unbiased dosimetric comparison based on target volume dosimetry and estimated clinical toxicity.

Parameters assessed for target volume dosimetry included: 1) GTV coverage defined as the percent of the GTV receiving at least a given percentage of the prescription dose (V90%, V95% and V100%); 2) Dmax%, maximum percent dose to GTV defined as the highest percent of prescription dose to a 0.1 cc volume within the GTV; 3) homogeneity index, the maximum dose within the GTV divided by the prescription dose; 4) conformity index,[13,14] the reference isodose volume divided by PTV target volume; and 5) gradient index (GI),[15] defined as 50% of the prescription isodose volume divided by the prescription volume.

Clinical toxicity was estimated based on dose to OARs and excess risk of radiation-associated secondary intracranial tumor. The maximum dose to OARs (Dmax) was defined as the highest dose delivered to a 0.1 cc volume within the OAR with a 0.2 Gy buffer. To characterize inhomogeneous dose to each OAR, the equivalent uniform dose (EUD) was calculated. As first described by Niemierko, the EUD is the dose that when uniformly distributed over a given volume causes the same radiobiologic effect as the delivered nonuniform dose distribution.[16] The computation is as follows $EUD = [\frac{1}{N}\sum_{i=1}^{N} v_i (D_i)^a]$, where D_i is the dose and v_i is the partial volume of the i'th bin of the corresponding differential dose-volume histogram (DVH), and a is the model parameter specific to the OAR of interest.[16] Parameter a was set to the following values: whole brain, 10; brainstem, 12; temporal lobes, 10; cochlea, 20; vestibule, 20; optic chiasm/nerves/ocular globes, 10; and hypothalamus, 5.[17]

Excess risk of radiation-associated secondary intracranial tumor was modeled using the method proposed by Schneider based on organ equivalent dose, the dose that when uniformly distributed over a given volume causes the same radiation-induced tumor incidence as the delivered inhomogeneous dose.[18] In the present study, organ equivalent dose is calculated using the dose-volume histogram for whole brain as $OED = \frac{1}{N}\sum_{i=1}^{N} v_i D_i e^{-\alpha D_i}$, where the sum is taken over N bins of a differential DVH, v_i is the relative size of the i'th bin corresponding to dose D_i, and α is an organ-specific cell sterilization parameter. The excess risk of tumors ('I') is an organ-specific tumor incidence rate for a low radiation dose (I_0) multiplied by the OED, $I = I_0 OED$ with the assumption that secondary tumor incidence rate is proportional to the number of mutated cells relative to the number of stem cells prior to irradiation. For intracranial irradiation, we use model parameters estimated by Schneider based on data published by the United Nation Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) of I_0 of 29.7 cancer cases per 10,000 patients per year per Sv and α = 0.08.

Parameters for target volume dosimetry and estimated clinical toxicity were evaluated using the Wilcoxon matched-pairs signed-ranks test and paired t-test with *P* value ≤ 0.05 considered statistically significant.

Results

The selected 9 cases of vestibular schwannoma represent diverse patient characteristics, tumor volumes and anatomic characteristics (**Table 2**). One patient underwent prior resection. Four lesions were either adjacent to or abutting the brainstem (**Figure 1**). The average target volume was 0.71 cc (range, 0.2-1.8). All cases were treated to a dose of 12 Gy (RBE).

Treatment plans were compared based on target volume dosimetry and estimated clinical toxicity. **Figure 2** illustrates the differential dose distribution for each treatment modality with representative cross-sectional planning images for case 4, a patient with right-sided 0.6-cc vestibular schwannoma that abuts the brainstem. Summary target volume dosimetry metrics are shown in **Table 3** (mean for all 9 cases according to modality and corresponding statistical comparisons). There were no significant differences in V100%, homogeneity index or Dmax% between treatment modalities. However, 5 XSRS and 2.5 XSRS offered equal or superior V90% and V95% compared with PSRS for all 9 cases. The gradient index, driven by the clinical directive of 98.8% PTV coverage, was highest for 5 XSRS (PSRS, 4.87; 5 XSRS, 5.98; 2.5 XSRS, 4.78). The conformity index was lowest for 2.5 XSRS (1.44) vs PSRS (1.59, *P* = NS) and 5 XSRS (1.61, *P* = 0.003).

Table 4 shows the Dmax in Gy (RBE) to pertinent OAR receiving > 1Gy (RBE) averaged across the 9 cases according to modality and corresponding statistical comparisons. Dmax to the ocular globes (ipsilateral and contralateral), optic nerves (ipsilateral and contralateral), optic chiasm, contralateral cochlea, contralateral vestibule, contralateral temporal lobe and hypothalamus was < 1 Gy (RBE) for each modality. Dmax to the ipsilateral temporal lobe was significantly lower with 2.5 XSRS, 7.7 compared with PSRS, 9.5, *P* = 0.001 and 5 XSRS, 8.2, *P* = 0.03. Dmax to ipsilateral cochlea was also lowest for 2.5 XSRS, 9.6 vs PSRS, 10.9, *P* = < 0.001 and 5 XSRS, 10.6, *P* = 0.007. Similarly, Dmax to ipsilateral vestibule was lowest for 2.5 XSRS, 7.7 vs PSRS, 8.7, *P* = 0.02 and vs 5 XSRS, 8.5, *P* = 0.02. Dmax to brainstem was lowest with

Table 3: Target volume dosimetry including mean values for all 9 cases according to modality and corresponding statistical comparisons

PARAMETER	PSRS	5XSRS	2.5XSRS	PSRS VS 5XSRS *P*-VALUE	PSRS VS 2.5XSRS *P*-VALUE	5XSRS VS 2.5XSRS *P*-VALUE
V100%	100.0	100.0	100.0	0.37	0.19	0.17
V95%	99.8	100.0	100.0	0.16	0.16	1.00
V90%	98.9	99.3	99.6	0.35	0.35	1.00
Homogeneity Index	1.12	1.11	1.11	0.16	0.29	0.30
Gradient Index	4.87	5.98	4.78	0.05	0.73	0.02*
Dmax%	112.1	110.7	111.5	0.16	0.29	0.30
Conformity Index	1.59	1.61	1.44	0.910	0.29	0.003*

Abbreviations
*PSRS = Proton stereotactic radiosurgery; 2.5XSRS, 5XSRS = Photon stereotactic radiosurgery delivered via volumetric-modulated arc therapy using 2.5mm and 5mm multileaf collimators, respectively; VX (%) = Percentage of total gross target volume receiving X% of the prescribed dose; Homogeneity index = Maximum dose within gross target volume divided by prescription dose; Gradient index = 50% prescription isodose volume divided by prescription volume; Dmax (%) = Dose maximum to 0.1ml volume of gross target volume as a percentage of prescribed dose; Conformity index = Reference isodose volume divided by target volume; *p-value ≤ 0.05 on paired t-test considered significant*

Table 4: Maximum dose in Gy (RBE) to organs at risk including mean values for all 9 cases according to modality and corresponding statistical comparisons

ORGAN AT RISK	PSRS	5XSRS	2.5XSRS	PSRS VS 5XSRS *P*-VALUE	PSRS VS 2.5XSRS *P*-VALUE	5XSRS VS 2.5XSRS *P*-VALUE
Ipsilateral temporal lobe	9.5	8.2	7.7	0.016*	0.001*	0.03*
Ipsilateral vestibule	8.7	8.5	7.7	0.61	0.02*	0.02*
Ipsilateral cochlea	10.9	10.6	9.6	0.38	<0.001*	0.007*
Brainstem	8.6	9.2	8.8	0.04*	0.26	0.12

Abbreviations
*PSRS = Proton stereotactic radiosurgery; 2.5XSRS, 5XSRS = Photon stereotactic radiosurgery delivered via volumetric-modulated arc therapy using 2.5mm and 5mm multileaf collimators, respectively; Maximum dose to organs at risk = highest dose delivered to a 0.1cc volume within the structure; *p-value ≤ 0.05 considered significant*

PSRS, 8.6 vs 5 XSRS, 9.2, $P = 0.04$, and 2.5 XSRS, 8.8, P = NS.

The EUD to pertinent OAR in Gy (RBE) according to treatment modality for each case is shown in **Figure 3** and numerical values for EUD averaged over the 9 cases for all OARs are provided in **Supplementary Table 1** (online with article, www.appliedradiationoncology.com). The mean EUD to the ocular globes (ipsilateral and contralateral), optic nerves (ipsilateral and contralateral), chiasm, contralateral temporal lobe, hypothalamus, contralateral vestibule, and contralateral cochlea was < 1 Gy (RBE). OAR with significantly lower EUD in Gy (RBE) with 2.5 XSRS vs paired PSRS or 5 XSRS plans, respectively, included the ipsilateral cochlea (9.3, 10.3, 10.1), ipsilateral vestibule (7.7, 8.5, 8.4) and ipsilateral temporal lobe (3.8, 4.8, 4.2), $P < 0.05$ for 2.5 XSRS vs PSRS and 2.5 XSRS vs 5 XSRS. Mean EUD in Gy (RBE) to the brainstem was significantly lower with 2.5 XSRS, 4.7, and PSRS, 4.6, vs 5 XSRS, 5.0, $P = .021$ for both comparisons.

The projected excess risk of secondary tumor for each case according to treatment modality is graphically displayed in **Figure 4** and corresponding numerical values are shown in **Supplementary Table 2** (online with article, www.appliedradiationoncology.com). The estimated incidence of radiation-induced secondary tumors in cases per 10,000 patient-years was lowest for PSRS, 2.8, vs 5 XSRS, 6.6 and 2.5 XSRS, 5.5, ($P < 0.008$ for PSRS vs 2.5 XSRS, PSRS vs 5 XSRS and 5 XSRS vs 2.5 XSRS).

Discussion

In the present study, we rigorously compared the dosimetric advantages and limitations of PSRS, 5 XSRS and 2.5 XSRS by identifying 9 cases treated with PSRS representing various clinical characteristics and re-planning them with both 2.5 XSRS and 5 XSRS using the original treatment dose of 12 Gy (RBE) in 1 fraction. Our results demonstrate that metrics of target volume coverage and homogeneity are similar between modalities. The gradient and conformity indices were most optimal (closest to 1.0) for 2.5 XSRS. Regarding OAR, the mean

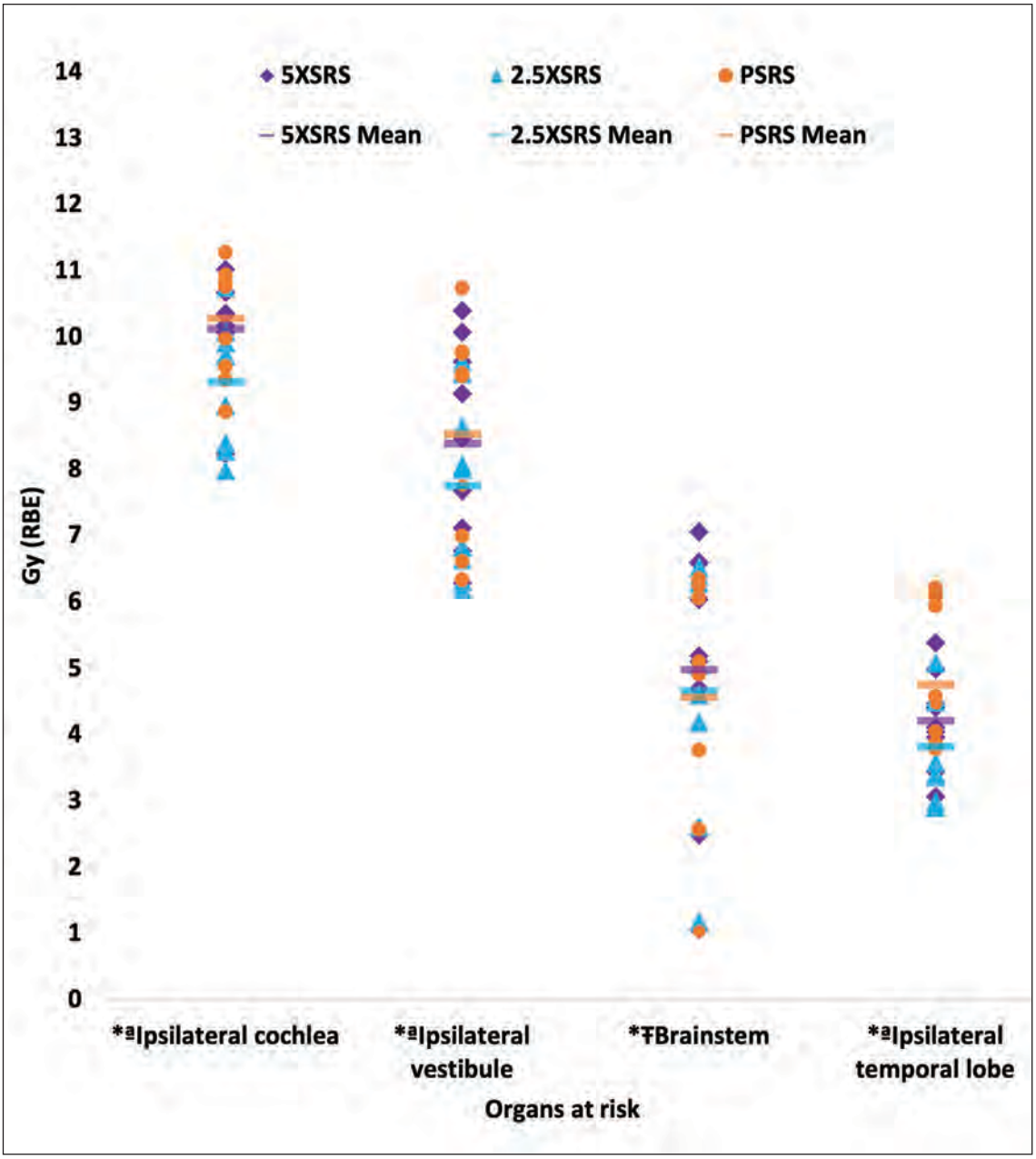


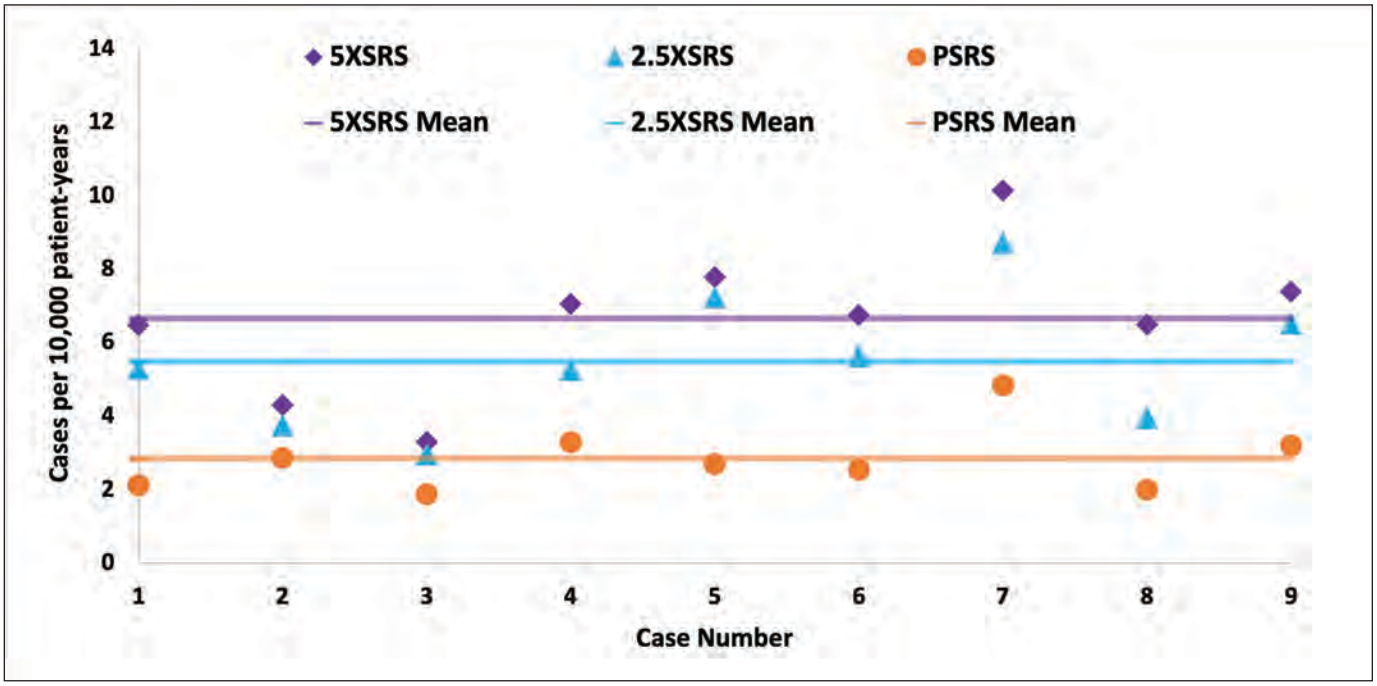
Figure 3. Equivalent uniform dose for organs at risk for all 9 cases according to stereotactic radiosurgery treatment modality.

*Abbreviations: PSRS, proton stereotactic radiosurgery; 2.5 XSRS and 5 XSRS, volumetric-modulated arc therapy SRS using 2.5- and 5-mm multileaf collimators, respectively; *P < 0.05 for 2.5 XSRS v-s 5 XSRS; ₸ P <0.05 for 5 XSRS vs PSRS; a P < 0.05 for 2.5 XSRS vs PSRS.*

Dmax and EUD to the ipsilateral temporal lobe, ipsilateral vestibule and ipsilateral cochlea were lowest with 2.5 XSRS. The relatively limited low-dose bath with PSRS was reflected in a projected excess risk of secondary tumor that was significantly different between treatment modalities — highest for 5 XSRS followed by 2.5 XSRS and nearly halved for PSRS.

Our results show that in treating vestibular schwannoma, dosimetric advantages are similar between PSRS and XSRS, but depending on clinical scenarios and acceptable tradeoffs, a given treatment modality might be favored. For many patients, select small statistically significant dosimetric advantages may not constitute a clinically relevant margin. Our formal dosimetric comparison to elucidate the subtleties of representative scenarios enables clinicians to decide when protons may be appropriate. These findings are important as dosimetric comparisons between PSRS and XSRS are limited[4] and a randomized controlled trial between PSRS and XSRS is unlikely considering the large number of participants

Figure 4. Projected risk of secondary tumors (expressed as cases of secondary tumors per 10,000 patient-years) for all 9 cases according to stereotactic radiosurgery treatment modality.



Abbreviations: PSRS, proton stereotactic radiosurgery; 2.5 XSRS and 5 XSRS, volumetric-modulated arc therapy SRS using 2.5- and 5-mm multileaf collimators, respectively.

and long follow-up required to detect differences in tumor control and treatment toxicity. Furthermore, an informed decision in this setting may lower the additional health care system costs and individual patient treatment burden associated with referral to a center capable of performing PSRS.

Tumor control rates for modern series of vestibular schwannoma treated with XSRS delivered via Gamma Knife, CyberKnife or linac with tumor margin doses of equivalent to 12 Gy (RBE) in 1 fraction are upwards of 90%.[19] A single institution series of 221 patients receiving proton radiation therapy (PSRS or fractionated), with approximately 62% of patients receiving PSRS using a passive scattering system, showed a 5-year tumor control rate of 96%.[20] In seminal studies, doses > 12.5 to 13 Gy (RBE) were associated with increased morbidity with regard to cranial nerve toxicity (CN V, CN VII) without substantial gains in tumor control, whereas dose < 10 Gy (RBE) trended towards lower tumor control supporting modern dose regimens that aim to mitigate treatment toxicity.[6,7,21]

The impact of SRS on hearing preservation is controversial as there are inherent patient selection biases and variable findings in the literature with some series reporting a long-term decline in hearing[22] and others reporting rates of hearing loss similar to observation.[23] To maintain < 25% risk of serviceable hearing loss defined as hearing that is useful with or without a hearing aid, Quantitative Analysis of Normal Tissue Effects in the Clinic (QUANTEC) recommends a single-fraction maximum dose to the cochlea < 12 to 14 Gy.[24,25] Our dosimetric analysis of dose to cochlea with PSRS and XSRS shows dose to ipsilateral cochlea is different between PSRS and 5 XSRS vs 2.5 XSRS with a small but potentially impactful difference applicable in situations where it is challenging to meet cochlear dose constraints.

Brainstem injury during SRS is typically due to treatment of adjacent lesions, especially vestibular schwannomas. Data in this setting are limited; however, in one of the largest vestibular schwannoma SRS series including 149 patients by Foote et al, significant risk factors for cranial neuropathy included tumor to brainstem distance, prior surgical resection and Dmax to brainstem with neuropathy rates of 2% vs 24% corresponding to dose < 12.5 vs > 12.5 Gy (RBE).[21] Based on analysis of this study and other series, a Dmax of 12.5 Gy (RBE) to the brainstem during single-fraction SRS is recommended to limit the risk of permanent cranial neuropathy (due to proximity of cranial nerves to the brainstem) or necrosis to < 5% for patients with acoustic tumors.[25,26] Our representative sample included tumors with varying distance from the brainstem. Although our small sample size may limit the ability to detect statistically significant differences, in these paired plans PSRS

offered a lower brainstem Dmax compared with 2.5 XSRS and 5 XSRS. This difference may be clinically relevant in situations where tumor is in proximity to the brainstem.

Temporal lobe and brain parenchymal toxicity are anticipated to be low with typical vestibular schwannoma dose prescriptions of approximately 12 Gy (RBE). The volume of brain receiving 12 Gy is significantly associated with development of symptomatic postradiosurgical imaging changes[27] and symptomatic radiation necrosis.[28] The QUANTEC analysis recommends limiting the V12 Gy to < 5 to10 cc corresponding to a < 20% risk of symptomatic necrosis in single-fraction SRS.[25] In our study, the prescription dose is 12 Gy (RBE) and the mean Dmax to ipsilateral temporal lobes was ≤ 9.5 Gy (RBE) across all modalities.

Reports of secondary tumors and malignant transformation are rare, as anticipated, given the low probability of these events and long latency period. In a retrospective series of 440 patients with vestibular schwannoma, median follow-up of 12.5 years, treated with Gamma Knife SRS between 1991 and 2000, 1 patient (0.03%) developed malignant transformation.[29] Pollock et al performed a retrospective review of 1837 patients receiving SRS between 1990 and 2009 for benign tumors or indications with median follow-up of 9 years; they reported no radiation-induced tumors in 11,264 patient-years of follow-up and a predicted 5-, 10-, and 15-year risk of malignant transformation of 0.5%, 0.8% and 2.4%, respectively.[30] Among the reported cases of malignant transformation in a vestibular schwannoma, 41% were in patients with neurofibromatosis, and reported histologies included malignant peripheral nerve sheath tumor, triton tumor, rhabdomyosarcoma and sarcoma.[31] Based on a literature review and analysis of 36 cases of SRS-induced neoplasms, Patel and Chiang estimate the overall risk of developing an SRS-induced neoplasm is approximately 0.04% at 15 years; notably more than half of the initially treated tumors in this analysis were vestibular schwannomas.[32] This is anticipated to be an underestimate as only a fraction of cases of secondary tumors are likely to be submitted as reports and accepted for publication. Furthermore, they note that the mean latency to development of an SRS-induced neoplasm is 7.9 years (range, 0.7-19 years),[32] a duration that is relatively shorter than those observed with fractionated radiation therapy (median latency 15.2 ± 8.7 years in the pituitary adenoma experience).[33] Historical series with long-term follow-up in the setting of fractionated radiation for pituitary adenoma report cumulative risk of second brain tumors of 2.0% at 10 years and 2.4% at 20 years without plateau,[34] underscoring that the risk of secondary tumors even with older techniques is low but still a tangible risk that should be mitigated through careful modality selection and treatment planning.

To our knowledge, the present study is the first dosimetric comparison of PSRS with modern linac-based XSRS techniques specifically for treatment of vestibular schwannoma. Our results differ from dosimetric studies published 20 years ago but are similar to contemporary studies for other skull base tumors. For example, in a dosimetric comparison study of proton (spot scanning or passive scattering) and photon (3D conformal, stereotactic arc therapy, intensity-modulated RT) for benign brain tumors including 5 acoustic neuromas in 2003, Bolsi et al concluded that proton techniques were shown to be superior to all photon approaches for the irradiation of small brain lesions with regard to target dose uniformity, conformity and sparing of OAR.[35] In contrast, our results show that neither modality has empirically superior dosimetry, which likely reflects technological progress in treatment planning, target localization and treatment delivery in recent decades leading to gains in photon dosimetry relative to proton dosimetry. Our results are consistent with the modern literature comparing proton and photon radiation for intracranial and skull base lesions, although there are no dedicated comparisons for vestibular schwannoma. In the setting of hypofractionated treatment (2-5 fractions) of intracranial tumors > 3 cm delivered via multiple modalities of SRS including protons (double-scattering proton therapy and intensity-modulated proton therapy) and photons (Gamma Knife, CyberKnife, and coplanar- and noncoplanar-arc VMAT), Cao et al showed that PSRS consistently offered the lowest integral dose to normal brain and most optimal homogeneity index, but each modality had dosimetric advantages and limitations on a case-by-case basis.[36] In the setting of pituitary adenoma, PSRS compared with XSRS offered similar target volume dosimetry and a lower risk of radiation-induced secondary tumors.[37] In the setting of conventional fractionation, Arvold et al[38] and Winkfield et al[39] report that for benign meningioma (mean target volume ~27 cc) and pituitary adenoma (target volume 2.4 cc), respectively, proton radiation compared with photon radiation decreased the risk of RT-associated secondary tumors and offered optimal OAR sparing. In our analysis, differences in OAR dose were modest, which may reflect similar small target volume dosimetry (mean target volume 0.71 cc) between photon and proton approaches. PSRS did offer a consistently lower risk of secondary tumors. In addition, 2.5 XSRS offered consistently equal target coverage and optimal OAR sparing relative to 5 XSRS, supporting use of this MLC size when available for linac-based SRS systems.

This study has several important limitations. The 9 cases were selected to be representative of common clinical scenarios applicable to vestibular schwannoma SRS – various anatomic characteristics, presentations, and prior resection and target volumes. However, this selection is not exhaustive. Many systems can deliver XSRS, including the linac, CyberKnife and Gamma Knife, among others. We focused our analysis on linac-based SRS, as this is a widely available modality in academic and community-based practices, and evaluated 2 common MLC sizes to address an important question in XSRS treatment planning. Our PSRS treatment planning is performed for a unique proton passive scattering system with optimized characteristics intended for small field delivery. Thus, our dosimetric assessments may not transfer to all other passive scattering systems and may not directly apply to pencil-beam scanning with or without aperture collimation. SRS plans can be modified based on planning priorities and resources. The plans presented in our study may differ from those generated at other institutions. As described in our methods, we used commercially available software and common planning criteria; thus, major variations from our data can occur but would be unlikely.

Conclusion

In conclusion, this study compared the dosimetric advantages and limitations of PSRS, 5 XSRS and 2.5 XSRS for vestibular schwannoma. We show similar target coverage and OAR sparing with XSRS and PSRS; 2.5 XSRS offers greater target conformality and lower dose to OAR than 5 XSRS, and PSRS offers significantly lower excess risk of secondary tumor than XSRS, although the absolute risk of secondary tumors is low across modalities.

References

1) Carlson ML, Link MJ. Vestibular schwannomas. Ingelfinger JR, ed. *N Engl J Med*. 2021;384(14):1335-1348. doi:10.1056/NEJMra2020394

2) Reznitsky M, Petersen MMBS, West N, Stangerup SE, Cayé-Thomasen P. Epidemiology of vestibular schwannomas – prospective 40-year data from an unselected national cohort. *Clin Epidemiol*. 2019;(11):981-986. doi:10.2147/CLEP.S218670

3) Marinelli JP, Lohse CM, Carlson ML. Incidence of vestibular schwannoma over the past half-century: a population-based study of Olmsted County, Minnesota. *Otolaryngol Neck Surg*. 2018;159(4):717-723. doi:10.1177/0194599818770629

4) Olson JJ, Kalkanis SN, Ryken TC. Congress of Neurological Surgeons systematic review and evidence-based guidelines on the treatment of adults with vestibular schwannomas: executive summary. *Neurosurgery*. 2018;82(2):129-134. doi:10.1093/neuros/nyx586

5) Murphy ES, Suh JH. Radiotherapy for vestibular schwannomas: a critical review. *Int J Radiat Oncol*. 2011;79(4):985-997. doi:10.1016/j.ijrobp.2010.10.010

6) Combs SE, Welzel T, Schulz-Ertner D, Huber PE, Debus J. Differences in clinical results after LINAC-based single-dose radiosurgery versus fractionated stereotactic radiotherapy for patients with vestibular schwannomas. *Int J Radiat Oncol Biol Phys*. 2010;76(1):193-200. doi:10.1016/j.ijrobp.2009.01.064

7) Mendenhall WM, Friedman WA, Buatti JM, Bova FJ. Preliminary results of linear accelerator radiosurgery for acoustic schwannomas. *J Neurosurg*. 1996;85(6):1013-1019. doi:10.3171/jns.1996.85.6.1013

8) Koetsier KS, Hensen EF, Wiggenraad R, et al. Clinical outcomes and toxicity of proton radiotherapy for vestibular schwannomas: a systematic review. *J Radiat Oncol*. 2019;8(4):357-368. doi:10.1007/s13566-019-00410-1

9) Persson O, Bartek J, Shalom NB, Wangerid T, Jakola AS, Förander P. Stereotactic radiosurgery vs. fractionated radiotherapy for tumor control in vestibular schwannoma patients: a systematic review. *Acta Neurochir (Wien)*. 2017;159(6):1013-1021. doi:10.1007/s00701-017-3164-6

10) Gall KP, Verhey LJ, Wagner M. Computer-assisted positioning of radiotherapy patients using implanted radiopaque fiducials. *Med Phys*. 1993;20(4):1153-1159. doi:10.1118/1.596969

11) Winey B, Daartz J, Dankers F, Bussière M. Immobilization precision of a modified GTC frame. *J Appl Clin Med Phys*. 2012;13(3):3690. doi:10.1120/jacmp.v13i3.3690

12) Paganetti H. Range uncertainties in proton therapy and the role of Monte Carlo simulations. *Phys Med Biol*. 2012;57(11):R99-R117. doi:10.1088/0031-9155/57/11/R99

13) Shaw E, Kline R, Gillin M, et al. Radiation therapy oncology group: radiosurgery quality assurance guidelines. *Int J Radiat Oncol*. 1993;27(5):1231-1239. doi:10.1016/0360-3016(93)90548-A

14) Feuvret L, Noël G, Mazeron JJ, Bey P. Conformity index: a review. *Int J Radiat Oncol*. 2006;64(2):333-342. doi:10.1016/j.ijrobp.2005.09.028

15) Paddick I, Lippitz B. A simple dose gradient measurement tool to complement the conformity index. *J Neurosurg*. 2006;105 Suppl:194-201. doi:10.3171/sup.2006.105.7.194

16) Niemierko A. Reporting and analyzing dose distributions: a concept of equivalent uniform dose. *Med Phys*. 1997;24(1):103-110. doi:10.1118/1.598063

17) Gay HA, Niemierko A. A free program for calculating EUD-based NTCP and TCP in external beam radiotherapy. *Phys Med*. 2007;23(3-4):115-125. doi:10.1016/j.ejmp.2007.07.001

18) Schneider U, Zwahlen D, Ross D, Kaser-Hotz B. Estimation of radiation-induced cancer from three-dimensional dose distributions: concept of organ equivalent dose. *Int J Radiat Oncol*. 2005;61(5):1510-1515. doi:10.1016/j.ijrobp.2004.12.040

19) Soltys SG, Milano MT, Xue J, et al. Stereotactic radiosurgery for vestibular schwannomas: tumor control probability analyses and recommended reporting standards. *Int J Radiat Oncol*. 2021;110(1):100-111. doi:10.1016/j.ijrobp.2020.11.019

20) Koetsier KS, Hensen EF, Niemierko A, et al. Outcome and toxicity of proton therapy for vestibular schwannoma: a cohort study. *Otol Neurotol Off Publ Am Otol Soc Am Neurotol Soc Eur Acad Otol Neurotol*. 2021;42(10):1560-1571. doi:10.1097/MAO.0000000000003313

21) Foote KD, Friedman WA, Buatti JM, Meeks SL, Bova FJ, Kubilis PS. Analysis of risk factors associated with radiosurgery for vestibular schwannoma. *J Neurosurg*. 2001;95(3):440-449. doi:10.3171/jns.2001.95.3.0440

22) Carlson ML, Jacob JT, Pollock BE, et al. Long-term hearing outcomes following stereotactic radiosurgery for vestibular schwannoma: patterns of hearing loss and variables influencing audiometric decline. *J Neurosurg*. 2013;118(3):579-587. doi:10.3171/2012.9.JNS12919

23) Breivik CN, Nilsen RM, Myrseth E, et al. Conservative management or gamma knife radiosurgery for vestibular schwannoma: tumor growth, symptoms, and quality of life. *Neurosurgery*. 2013;73(1):48-56; discussion 56-57. doi:10.1227/01.neu.0000429862.50018.b9

24) Bhandare N, Jackson A, Eisbruch A, et al. Radiation therapy and hearing loss. *Int J Radiat Oncol*. 2010;76(3):S50-S57. doi:10.1016/j.ijrobp.2009.04.096

25) Marks LB, Yorke ED, Jackson A, et al. Use of normal tissue complication probability models in the clinic. *Int J Radiat Oncol*. 2010;76(3):S10-S19. doi:10.1016/j.ijrobp.2009.07.1754

26) Mayo C, Yorke E, Merchant TE. Radiation associated brainstem injury. *Int J Radiat Oncol*. 2010;76(3):S36-S41. doi:10.1016/j.ijrobp.2009.08.078

27) Flickinger JC, Kondziolka D, Pollock BE, Maitz AH, Lunsford LD. Complications from arteriovenous malformation radiosurgery: multivariate analysis and risk modeling. *Int J Radiat Oncol Biol Phys*. 1997;38(3):485-490. doi:10.1016/s0360-3016(97)89481-3

28) Korytko T, Radivoyevitch T, Colussi V, et al. 12 Gy Gamma Knife radiosurgical volume is a predictor for radiation necrosis in non-AVM intracranial tumors. *Int J Radiat Oncol Biol Phys*. 2006;64(2):419-424. doi:10.1016/j.ijrobp.2005.07.980

29) Hasegawa T, Kida Y, Kato T, Iizuka H, Kuramitsu S, Yamamoto T. Long-term safety and efficacy of stereotactic radiosurgery for vestibular schwannomas: evaluation of 440 patients more than 10 years after treatment with Gamma Knife surgery. *J Neurosurg*. 2013;118(3):557-565. doi:10.3171/2012.10.JNS12523

30) Pollock BE, Link MJ, Stafford SL, Parney IF, Garces YI, Foote RL. The risk of radiation-induced tumors or malignant transformation after single-fraction intracranial radiosurgery: results based on a 25-year experience. *Int J Radiat Oncol*. 2017;97(5):919-923. doi:10.1016/j.ijrobp.2017.01.004

31) Seferis C, Torrens M, Paraskevopoulou C, Psichidis G. Malignant transformation in vestibular schwannoma: report of a single case, literature search, and debate: case report. *J Neurosurg*. 2014;121(Suppl_2):160-166. doi:10.3171/2014.7.GKS141311

32) Patel TR, Chiang VLS. Secondary neoplasms after stereotactic radiosurgery. *World Neurosurg*. 2014;81(3-4):594-599. doi:10.1016/j.wneu.2013.10.043

33) Yamanaka R, Abe E, Sato T, Hayano A, Takashima Y. Secondary intracranial tumors following radiotherapy for pituitary adenomas: a systematic review. *Cancers*. 2017;9(12):103. doi:10.3390/cancers9080103

34) Minniti G, Traish D, Ashley S, Gonsalves A, Brada M. Risk of second brain tumor after conservative surgery and radiotherapy for pituitary adenoma: update after an additional 10 years. *J Clin Endocrinol Metab*. 2005;90(2):800-804. doi:10.1210/jc.2004-1152

35) Bolsi A, Fogliata A, Cozzi L. Radiotherapy of small intracranial tumours with different advanced techniques using photon and proton beams: a treatment planning study. *Radiother Oncol J Eur Soc Ther Radiol Oncol*. 2003;68(1):1-14. doi:10.1016/s0167-8140(03)00117-8

36) Cao H, Xiao Z, Zhang Y, et al. Dosimetric comparisons of different hypofractionated stereotactic radiotherapy techniques in treating intracranial tumors > 3 cm in longest diameter. *J Neurosurg*. 2020;132(4):1024-1032. doi:10.3171/2018.12.JNS181578

37) Sud S, Botticello T, Niemierko A, Daly J, Bussiere M, Shih HA. Dosimetric comparison of proton versus photon radiosurgery for treatment of pituitary adenoma. *Adv Radiat Oncol*. 2021;6(6):100806. doi:10.1016/j.adro.2021.100806

38) Arvold ND, Niemierko A, Broussard GP, et al. Projected second tumor risk and dose to neurocognitive structures after proton versus photon radiotherapy for benign meningioma. *Int J Radiat Oncol*. 2012;83(4):e495-e500. doi:10.1016/j.ijrobp.2011.10.056

39) Winkfield KM, Niemierko A, Bussière MR, et al. Modeling intracranial second tumor risk and estimates of clinical toxicity with various radiation therapy techniques for patients with pituitary adenoma. *Technol Cancer Res Treat*. 2011;10(3):243-251. doi:10.7785/tcrt.2012.500199

Radiation Therapy in Cancer of Accessory Breast Tissue: Questions for Treatment Guidelines, Case Series, and Literature Review

Simran Polce, BS;[1] Collin Noldner, MD;[2] Sandeep Ailawadi, MS, CMD;[2] Samuel Ryu, MD;[2] Alexander Stessin, MD, PhD[2]*

Abstract

Background: The presence of accessory breast tissue (ABT) has been documented throughout medical literature and, like prepectoral breast tissue, is at risk of developing cancer. However, there is a clear lack of data and reported experience to guide clinicians in choosing the optimal treatment for ABT cancers. Specifically, there is limited information on the role of adjuvant radiation therapy (RT) and no clear consensus on guidelines.

Methods: We conducted a literature review of previously reported ABT cancers and their treatment. We also queried the database of breast cancer patients treated at our institution and identified 3 cases of ABT cancer for which adjuvant RT was offered.

Results: We present 3 cases of ABT cancer, treated at our institution, with 3 approaches to adjuvant RT. The first 2 were stage 1 ER/PR+ HER2- invasive ductal carcinomas in postmenopausal women. Of these, 1 received adjuvant endocrine therapy only without RT, while the other received hypofractionated RT, 26 Gy in 5 fractions. The third case was locally advanced ER/PR+ HER2+ invasive ductal carcinoma in a premenopausal female. She underwent adjuvant breast and nodal irradiation with a boost to the axillary tumor bed. In each of the cases, the rationale behind the recommendations, dose and treatment volume are discussed.

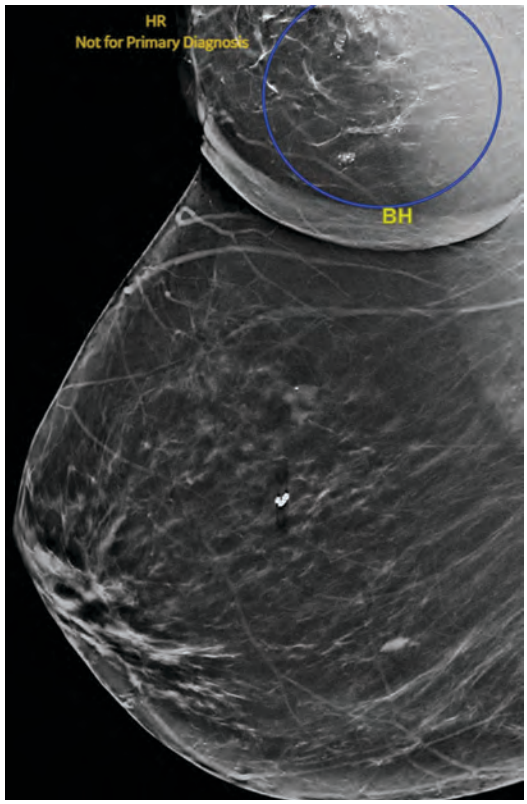
Conclusions: In formulating treatment recommendations for patients with ABT cancer, clinicians face several questions without answers from the existing data. Small case series and literature reviews such as this one can be used to provide the framework for considering treatment options in these challenging cases.

Keywords: accessory breast tissue, ectopic breast tissue, supernumerary breast tissue, axillary breast tissue, adjuvant radiation therapy

The presence of accessory breast tissue (ABT) has been well documented throughout medical literature. Most accessory breast tissue develops along the mammary ride (milk line), and the current classification of ABT is based on the system first developed by Kajava in 1915. In most cases, individuals develop polythelia (extra nipples) without functioning ductal tissue. However, there have been reports of fully functioning ABT, which includes the production of milk.[1] ABT, like regular breast tissue, is at risk of developing cancer, but literature regarding the incidence and treatment of cancer in ABT is limited. Specifically, there is little to no guidance on how to approach these cases from the standpoint of adjuvant radiation therapy (RT). Here we present 3 cases of resected carcinoma in the ABT treated at our institution, describe 3 radiotherapeutic approaches, summarize the current literature, and discuss the clinical considerations that may guide recommendations in this unusual scenario.

Affiliations: [1]Renaissance School, [2]Department of Radiation Medicine at Stony Brook University, NY
Corresponding author: *Alexander Stessin MD, PhD, Department of Radiation Medicine, Stony Brook University, 3 Edmund D. Pellegrino Rd, Stony Brook, NY, 11794. (Alexander.Stessin@Stonybrookmedicine.edu)
Disclosure/informed consent: The authors have no conflicts of interest to disclose. None of the authors received outside funding for the production of this original manuscript and no part of this article has been previously published elsewhere. The patient has provided informed consent for the publication of this case report.
Data availability statement: Research data are stored in an institutional repository and will be shared upon request to the corresponding author.

Figure 1. Right preoperative mediolateral oblique-craniocaudal view (MLO-CC).



Case Presentations

Case 1

The first case involves a G1P1 61-year-old postmenopausal woman with a documented history of bilateral axillary ABT for several years. She had previously undergone a biopsy for suspicious calcifications in her left breast with benign findings. In March 2021, the patient underwent a routine bilateral screening mammogram. She was asymptomatic and had no acute concerns. Her mammogram demonstrated 9 foci of calcifications in the right axillary ABT (**Figure 1**).

Subsequent stereotactic biopsy demonstrated moderately differentiated invasive ductal cancer, estrogen receptor (ER) and progesterone receptor (PR) positive, HER2 negative, Ki-67 8%. She was clinically staged as T1N0. She was then evaluated by the breast surgical oncology team in April 2021 and elected to undergo wide local excision of the ABT with wire localization and sentinel lymph node biopsy. Surgical pathology demonstrated invasive ductal carcinoma (IDC) 20 mm at its largest width and ductal carcinoma in situ (DCIS) 5 cm at its largest width. The posterior and lateral surgical margins were identified by direct visualization of the deep tissue below the pectoralis and lateral to the latissimus muscles, respectively.

All final margins were negative for carcinoma (IDC and DCIS are more than 1 cm away from all margins). Tissue testing demonstrated similar molecular profile to that of the biopsy, and Oncotype Dx Recurrence score was 1. In addition, her sentinel lymph node biopsy was negative (0/1). She was therefore staged as pT1cN0. Postoperatively, she required multiple seroma aspirations and developed palpable cording in her axilla. She was evaluated by a medical oncologist and started on letrozole with plans to continue endocrine therapy for 5 years.

She then presented to the radiation oncology department for consideration of adjuvant radiation. The patient was presented with 2 treatment options: 1) RT to the axillary area only, since there was felt to be no anatomic communication between the ABT and regular breast tissue; and 2) no RT, since all ectopic mammary tissue had been removed, and this could, in a sense, be considered a full mastectomy of the supernumerary breast. After extensive discussion, she opted to forgo the RT. At the time of writing this paper she had completed an 18-month imaging follow-up and a 15-month clinic follow-up. She was tolerating letrozole well with minimal side effects, and her bilateral mammogram was negative for disease recurrence.

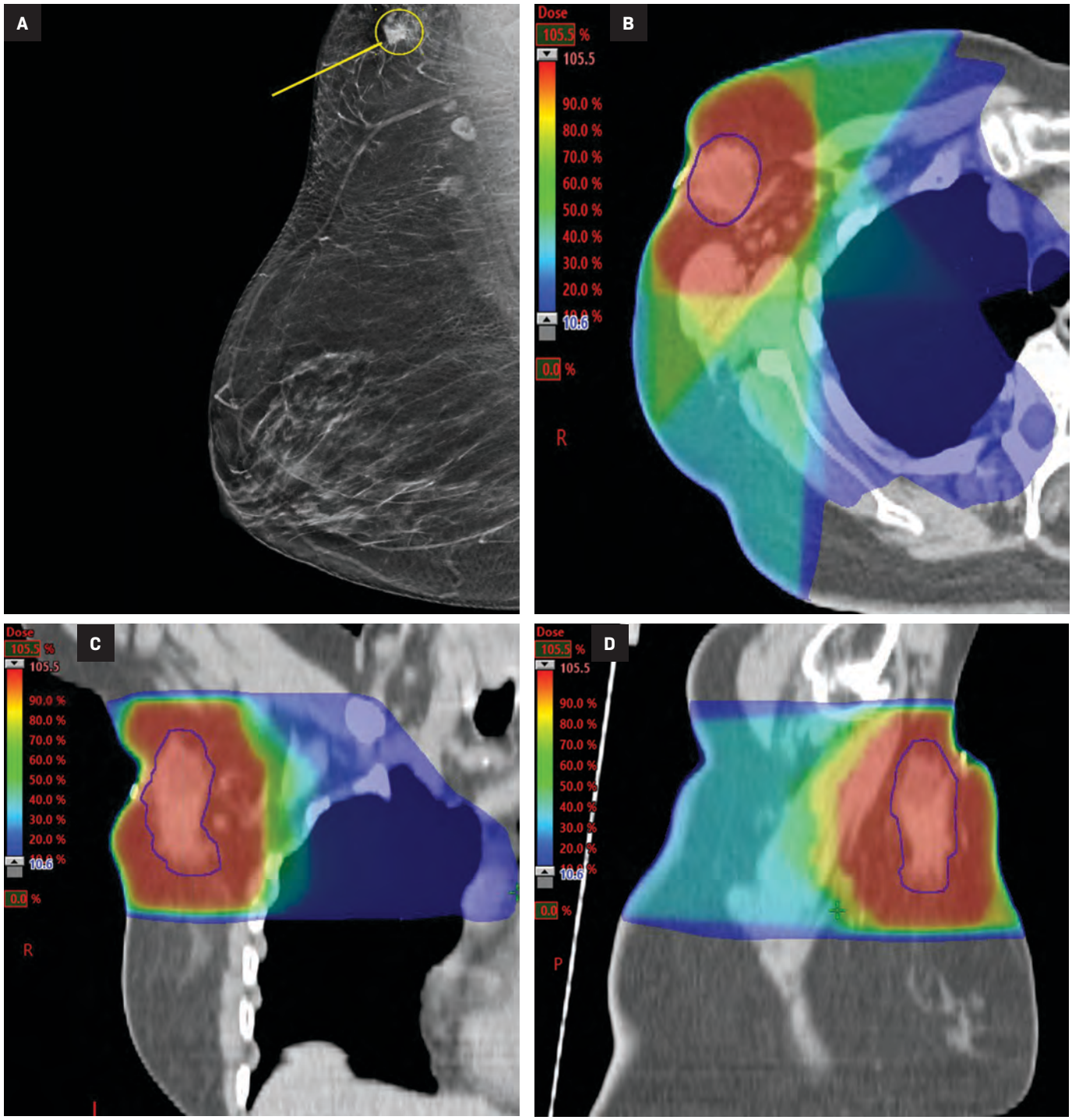
Case 2

The second case involves a G3P2 76-year-old postmenopausal woman who had never been diagnosed with ABT. Over the years, she had undergone 2 biopsies for suspicious findings on screening mammograms, but both were benign. In November 2021, she underwent a routine bilateral mammogram where a 1.2 cm site of asymmetry was identified in the right axilla (**Figure 2A**). A biopsy of the site demonstrated IDC that was well differentiated, ER/PR positive, Her-2 negative, and Ki-67 5%.

She was then evaluated by the breast surgical oncology team and underwent local resection aided by SAVI SCOUT (Merit Medical) with sentinel lymph node biopsy. Surgical pathology demonstrated that the mass excised was an accessory breast with a 1.8-cm single site of IDC. On the surgical specimen, invasive carcinoma was 0.2 mm from the inked anterior margin, < 1 mm from the posterior margin, and 1.5 mm from the inferior margin. Additional superior, inferior, lateral, medial, anterior, and posterior margins measuring at least 1.0 × 1.0 × 0.5 cm, only contained benign breast tissue or benign fibroadipose tissue. All final margins were negative, and her sentinel lymph node biopsy was negative (0/1). Tissue testing demonstrated similar molecular profile to that of the biopsy sample, and Oncotype Dx Recurrence score was 16.

She was diagnosed with pT1cN0 IDC of a right axillary accessory breast. She met with a medical oncologist and was started on anastrozole. She then presented to the radiation oncology department for evaluation of adjuvant radiation. Similar to the previous case, this patient was presented with the options of RT to the axillary area only vs no RT since all the ectopic mammary tissue had been removed. After extensive discussion, this patient opted to complete 2600 cGy in 5 fractions to the axillary area (**Figures 2B-C**). At the time of writing, she had completed a 9-month imaging follow-up

Figure 2. A) Right preoperative MLO-CC view with the lesion circled in yellow. The treatment plan with the planning target volume delineated in purple in the B) axial C) coronal, and D) sagittal view.

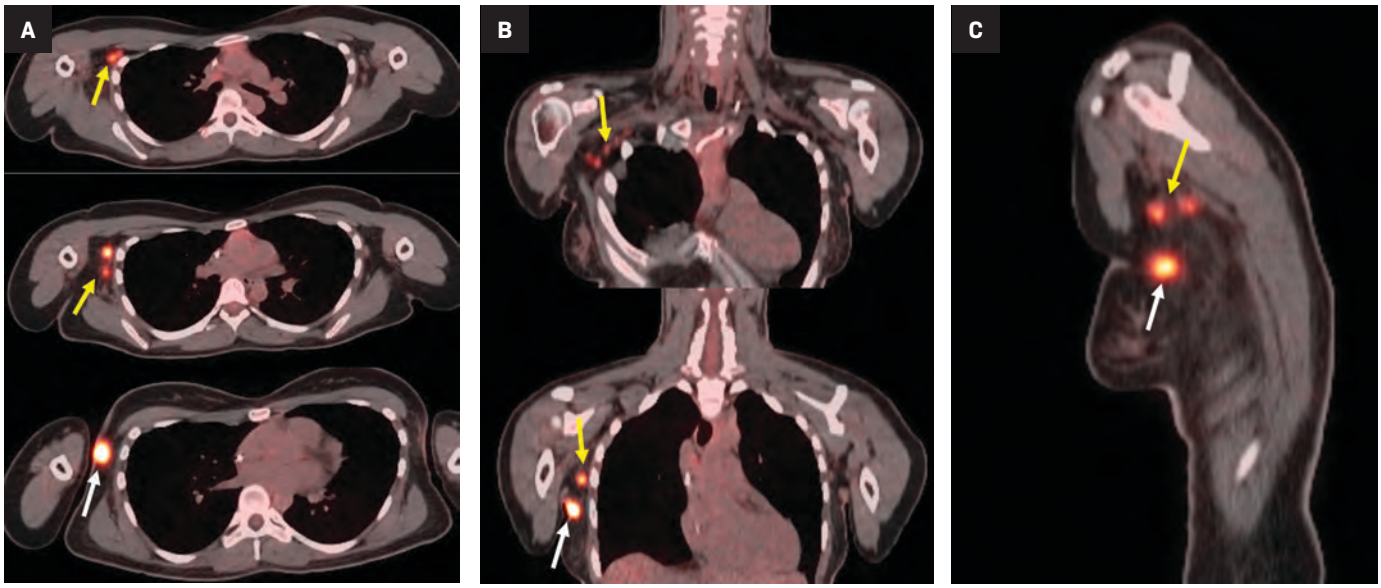


and a 10-month clinic follow-up. She was tolerating anastrozole well with minimal side effects, and her bilateral mammogram was negative for disease recurrence.

Case 3

The third case involves a G1P1 33-year-old premenopausal woman. The patient reported first feeling bilateral axillary fullness at the time of her pregnancy in 2019. She indicated she was able to express milk from tissue in her left axilla during nursing. The right-sided axillary fullness persisted after she stopped nursing

Figure 3. Positron emission tomography scan at diagnosis demonstrating the primary mass (white arrows) and multiple FDG-avid lymph nodes (yellow arrows) in the A) axial, B) coronal, and C) sagittal view.



and she had reported feeling a nodule in her right axilla. She underwent an ultrasound in August 2021, demonstrating a 1.2-cm hypoechoic nodule in what was initially believed to be the right axillary tail, and 2 likely reactive hypoechoic lymph nodes measuring 1.3 cm and 1.6 cm, respectively (BIRADS 3).

Repeat ultrasound and mammogram (**Figure 4A**) in November 2021 demonstrated a 1.7-cm irregular spiculated mass in the right axillary tail. A second irregular spiculated mass likely representing a 1.2-cm lymph node was noted in the right axilla. A biopsy of the right axillary tail mass demonstrated poorly differentiated IDC measuring 1.4 cm and was associated with calcifications, ER 82%, PR 35%, HER2 +3 positive, and Ki-67 43%. PET demonstrated a hypermetabolic right axillary lesion corresponding to her known malignancy as well as multiple hypermetabolic right axillary lymph nodes consistent with metastases **(Figure 3)**. She was therefore staged as cT1N2.

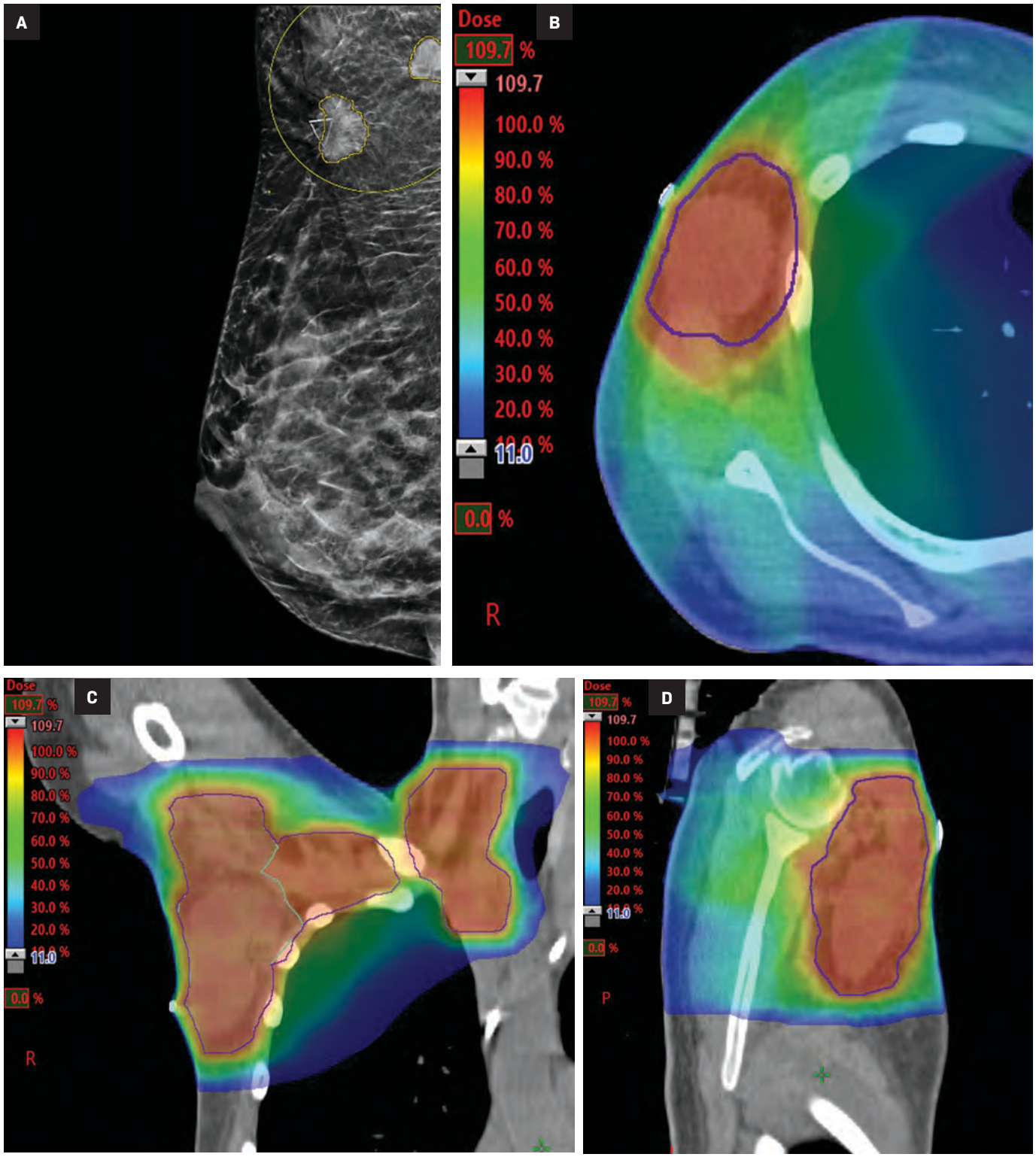
The patient completed 4 cycles of neoadjuvant doxorubicin/cyclophosphamide followed by 4 cycles of TCHP (Taxotere/Carboplatin/Herceptin/Perjeta). She was then evaluated by a breast surgeon in May 2022 and underwent local resection aided by SAVI SCOUT and sentinel lymph node biopsy. The surgical specimen measured 7.7 × 1.9 × 3.1 cm and pathology was negative for residual carcinoma. Sentinel lymph node biopsy did not show residual carcinoma (0/5), yet multiple lymph nodes exhibited treatment effect with evidence of fibrous scarring and focal calcifications.

Of note during the operation, the surgeon noted a distinct anatomical separation between the axillary tail of the breast and area containing the primary lesion. Thus, this was determined to be an ABT cancer rather than an axillary tail cancer, contiguous with the breast, as had been initially assumed. All final surgical margins (≥ 1 mm) were negative, and the patient was staged ypT0N0. She was re-evaluated by the medical oncologist after the surgery, and the recommendation was to start KADCYLA. She then presented to the radiation oncology department for discussion of adjuvant radiation. Given her young age and the locally advanced nature of her initial disease, the options presented to her were different from those discussed with the patients above. Specifically, the issues discussed were: 1) regional nodal irradiation to include the axillary and supraclavicular nodal stations but not internal mammary lymph nodes; 2) irradiation of the axillary tumor bed but not the entire right breast because, as in the other cases, there was felt to be an anatomic barrier between the ABT and regular breast tissue; 3) boosting the axillary tumor bed (which is normally given after a lumpectomy but not after a mastectomy).

After extensive discussion, the patient opted to undergo a hypofractionated course of 4256 cGy in 16 fractions to the right axilla and supraclavicular fossa, followed by a boost of 1000 cGy in 4 fractions to the axillary tumor bed (**Figures 4B-D**).

At the time of writing, the patient has completed the intended RT course with minimal toxicity and completed 16 cycles of KADCYLA. She has also completed a 3-month imaging follow-up PET/CT, which showed no F-18 fluorodeoxyglucose (FDG)-avid lesions in the right axilla and supraclavicular fossa, and a

Figure 4. A) Right MLO-CC view pretreatment with the lesion and lymph node outlined in yellow. The treatment plan with the planning target volume delineated in purple and boost volume in cyan in the B) axial, C) coronal, and D) sagittal view.



6-month clinic follow-up at which time her breast examination was negative for evidence of disease.

Discussion

ABT is an umbrella term encompassing both supernumerary and aberrant anatomy. Supernumerary breast tissue is found along the milk line — an embryologic landmark running bilaterally from the axilla to the inguinal region. By contrast, aberrant refers to breast tissue found close to the normal breast tissue and by definition lacks organized secretory systems.[2] In either case, the defined mass is an isolated fragment of glandular tissue without any connection to the native or "pectoral" breast. ABT is present in roughly 2% to 5% of the general population and incidence varies with ethnicity, sex, geographic region, and method used to determine its presence.

The presence of ABT was first described in detail in 1915, and first was classified into 8 types according to the existence of glandular tissue, nipple, areola, skin, and patch of hair.[1] This system is still widely used in the literature today. Class 1 (also termed polymastia) consists of a complete breast with a nipple, areola and glandular tissue. Class 2 refers to glandular tissue and a nipple but no areola. Class 3 consists of an areola and glandular tissue but no nipple. Class 4 is glandular tissue only. Class 5 (also called pseudomamma) tissue contains a nipple and areola. Class 6 is composed of a nipple only (also termed polythelia) and class 7 consists of an areola only. Lastly, class 8 refers to just a patch of hair. All of our cases are strictly fibroglandular tissue in the axilla, which represents class 4 according to this system.

Literature is divided on whether there is an increased risk of malignant transformation in ABT. Of note, cancer in ABT appears to arise at an earlier age than in developmentally normal pectoral tissue. One review of 82 cases found the mean age at diagnosis to be 53.3 years in patients with cancer of ABT, whereas the mean age for pectoral breast cancer according to the National Cancer Institute is 61 years.[3] Moreover, patients with ABT cancer tend to present with more advanced disease.[4] It is important to note that ABT is generally not included in routine breast cancer screening studies. This may, in part, explain why some patients present at a later stage than traditionally located breast cancer.

To date, the literature is limited to case reports of ABT cancer with no established treatment paradigms. A literature review was conducted utilizing key words and phrases such as *accessory breast tissue* and *ectopic breast tissue* in PubMed to identify reported cases and guidelines. Upon our review, most case reports present a combination of preoperative chemotherapy, surgical resection, postoperative chemotherapy, RT, and endocrine therapy. RT is still recommended for maximizing locoregional control. In a 2009 review of case reports by Madej B et al,[5] most radiation prescriptions were 5000 to 6600 cGy in 200 cGy per fraction. More recently in 2013, Hallam et al[6] proposed extrapolating from the UK START B trial where 4000 cGy was given over 15 fractions. Notably though, there was no consensus on treatment fields. Proposed plans ranged from treating the tumor bed alone to including the ipsilateral uninvolved pectoral breast, axilla, and supraclavicular fossa even in the absence of nodal metastases.

In evaluating the cases presented here, we were faced with several key questions to help guide treatment recommendations:

The first question is how to classify the extent of surgery. Does the fact that the ABT, from which the carcinoma arises, and is an independent structure from the pectoral breast, imply that the surgical resection is effectively a mastectomy? If so, one decision-making approach would be to extrapolate the indications for postmastectomy radiation therapy from the classic studies, ie, only offer it in the cases of nodal involvement, T3 or T4 disease, and positive margins. If, on the other hand, this is considered a lumpectomy rather than mastectomy, in a low-risk patient one may consider applying criteria from the Hughes et al trial (CALGB C9343)[7] for patients older than 70 or the PRIME II trial[8] to identify those in whom omitting postoperative RT is an option. If radiation is offered as part of breast conservation therapy in these cases, we must also consider the applicability of accelerated partial breast irradiation (APBI) regimens, such as 600c Gy × 5 fractions.[9,10] In a similar vein, if we are considering it whole-breast irradiation for the supernumerary breast tissue, the appropriateness of ultrahypofractionated regimens, such as 2600 cGy in 5 fractions as per the UK FAST FORWARD trial, should be assessed, particularly with respect to conferring a higher risk of lymphedema. In the first 2 cases, the patient stage was pT1cN0, the profile was consistent with luminal A molecular subtype, and the Oncotype Score was low. Considering these factors, as well as patient age and performance status, we presented several options, including: 1) hypofractionated RT to the axillary area of 4000-4256 cGy/15-16Fx +/- boost 1000-1600 cGy/5-8Fx; 2) Ultrahypofractionated RT 2600 cGy/5Fx as per UK FAST FORWARD trial (we felt this to be somewhat safer than the 600 cGy × 5 fractions APBI regimen from the standpoint of causing lymphedema); 3) endocrine therapy alone. The case for no RT can be made if one considers surgical resection of ABT as a mastectomy. One can also consider omitting RT based on relatively low recurrence rates in select low-risk

patients after BCT, as seen in the CALGB and PRIME II studies.

Another important question is the utility of Oncotype scores in guiding treatment recommendations for ABT cancers, in the fashion that is being explored in the ongoing MA-39[11] and DEBRA[12] trials. Of note, our first patient would have been a candidate for the DEBRA trial had her cancer been in the pectoral breast.

Finally, in a locally advanced case, such as the one presented above, what is the optimal target volume, which nodal areas need to be included, and is a tumor bed boost warranted? In our third case the patient was cT1cN2 with biopsy-proven nodal involvement, and abnormal PET-avid nodes identified in both level 3 of the axilla and the supraclavicular fossa. Despite having a complete response to neoadjuvant chemotherapy, she was deemed a high-risk patient and adjuvant RT was offered to both the tumor bed and regional lymphatics. As in the other cases, the pectoral breast was not included in the treatment field as there was no anatomic connection between it and the resected ABT. Similarly, internal mammary LNs were not included in the treatment field, because the risk of spread to that location from the ABT was considered exceedingly low. Despite concerns about increased risk of lymphedema and after extensive discussion with the patient, a boost was given to the tumor bed because of the initially high tumor grade and Ki-67.

Conclusion

In formulating treatment recommendations for these patients, we were faced with several questions without answers from existing data. Considering the rarity of such clinical scenarios, there is little chance that large-scale randomized clinical trials can be carried out to guide clinicians in the future. In the absence of these trials, our hope is that small case series and literature reviews, such as this one, can at least provide the framework for considering treatment options in these challenging cases. To our knowledge, this is the first report where several possible radiotherapeutic approaches to carcinoma of the ABT are delineated.

References

1) Kajava Y. The proportions of supernumerary nipples in the Finnish population. *Duodecim*. 1915;31:143-170. Accessed June 11, 2022. https://www.scienceopen.com/document?vid=0e2368fe-6e58-424f-9685-15b27c323485

2) Laor T, Collins MH, Emery KH, Donnelly LF, Bove KE, Ballard ET. MRI appearance ofbaccessory breast tissue: a diagnostic consideration for an axillary mass in a peripubertal or pubertal girl. *Am J Roentgenol*. 2004;183(6):1779-1781. doi:10.2214/ajr.183.6.01831779

3) Francone E, Nathan MJ, Murelli F, Bruno MS, Traverso E, Friedman D. Ectopic breast cancer: case report and review of the literature. *Aesthetic Plast Surg*. 37(4):746-749. doi:10.1007/s00266-013-0125-1

4) DeFilippis EM, Arleo EK. The ABCs of accessory breast tissue: basic information every radiologist should know. *Am J Roentgenol*. 2014;202(5):1157-1162. doi:10.2214/AJR.13.10930

5) Madej B, Balak B, Winkler I, Burdan F. Cancer of the accessory breast – a case report. *Adv Med Sci*. 2009;54(2):308-310. doi:10.2478/v10039-009-0031-6

6) Hallam S, Aggarwal A, Predolac D, Cunnick G, Ashford R. Primary ectopic breast carcinoma in a supernumerary breast arising in the anterior chest wall: a case report and review of the literature. *J Surg Case Rep*. 2013;2013(12):rjt107. doi:10.1093/jscr/rjt107

7) Hughes KS, Schnaper LA, Bellon JR, et al. Lumpectomy plus tamoxifen with or without irradiation in women age 70 years or older with early breast cancer: long-term follow-up of CALGB 9343. *J Clin Oncol*. 2013;31(19):2382-2387. doi:10.1200/JCO.2012.45.2615

8) Kunkler IH, Williams LJ, Jack WJ, Cameron DA, Dixon JM; PRIME II investigators. Breast-conserving surgery with or without irradiation in women aged 65 years or older with early breast cancer (PRIME II): a randomised controlled trial (published correction appears in *Lancet Oncol*. 2015;16(3):e105). *Lancet Oncol*. 2015;16(3):266-273. doi:10.1016/S1470-2045(14)71221-5

9) Livi L, Meattini I, Marrazzo L, et al. Accelerated partial breast irradiation using intensity-modulated radiotherapy versus whole breast irradiation: 5-year survival analysis of a phase 3 randomised controlled trial. *Eur J Cancer*. 2015;51(4):451-463. doi:10.1016/j.ejca.2014.12.013

10) Formenti SC, Gidea-Addeo D, Goldberg JD, et al. Phase I-II trial of prone accelerated intensity modulated radiation therapy to the breast to optimally spare normal tissue. *J Clin Oncol*. 2007;25(16):2236-2242. doi:10.1200/JCO.2006.09.1041

11) Parulekar WR, Berrang T, Kong I, et al. Cctg Ma.39 tailor RT: a randomized trial of regional radiotherapy in biomarker low-risk node-positive breast cancer (NCT03488693). *J Clin Oncol*. 2019;37(15_suppl). doi:10.1200/jco.2019.37.15_suppl.tps602

12) White JR, Anderson SJ, Harris EE, et al. NRG-BR007: a phase III trial evaluating de-escalation of breast radiation (DEBRA) following breast-conserving surgery (BCS) of stage 1, hormone receptor+, HER2-, rs ≤18 breast cancer. *J Clin Oncol*. 2022;40(16_suppl). doi:10.1200/jco.2022.40.16_suppl.tps613

Role of Boswellia Serrata in Management of CNS Radiation Necrosis After Radiosurgery for Brain Metastases

Rituraj Upadhyay, MD;[1] Haley Perlow, MD;[1] Evan Thomas, MD;[1] Sasha Beyer, MD;[1] Raju Raval, MD;[1] John Grecula, MD;[1] Dukagjin Blakaj, MD;[1] Arnab Chakravarti, MD;[1] Wayne H. Slone, MD;[2] Pierre Giglio, MD;[3] James B. Elder, MD;[4] Joshua D. Palmer, MD[1]*

Abstract

Radiation necrosis (RN) is a concerning late toxicity after radiation therapy for brain metastases. The management of RN primarily depends on the extent of edema on imaging and presence of symptoms. Oral corticosteroids are the mainstay of management; however, they are not optimal for long-term management because of multiple side effects and drug interactions. Boswellia serrata is an extract derived from Indian frankincense, which is available as an over-the-counter supplement, and has been traditionally used in the treatment of asthma, arthritis and colitis due to its anti-inflammatory properties. Recent data have reported the benefits of Boswellia on reducing cerebral edema. We discuss a case report involving a patient with brain metastases treated with stereotactic radiosurgery who developed early RN and had a good response with resolution of postradiation edema with the use of Boswellia.

Keywords: Radiation necrosis, Boswellia, steroid, brain metastases, stereotactic radiosurgery

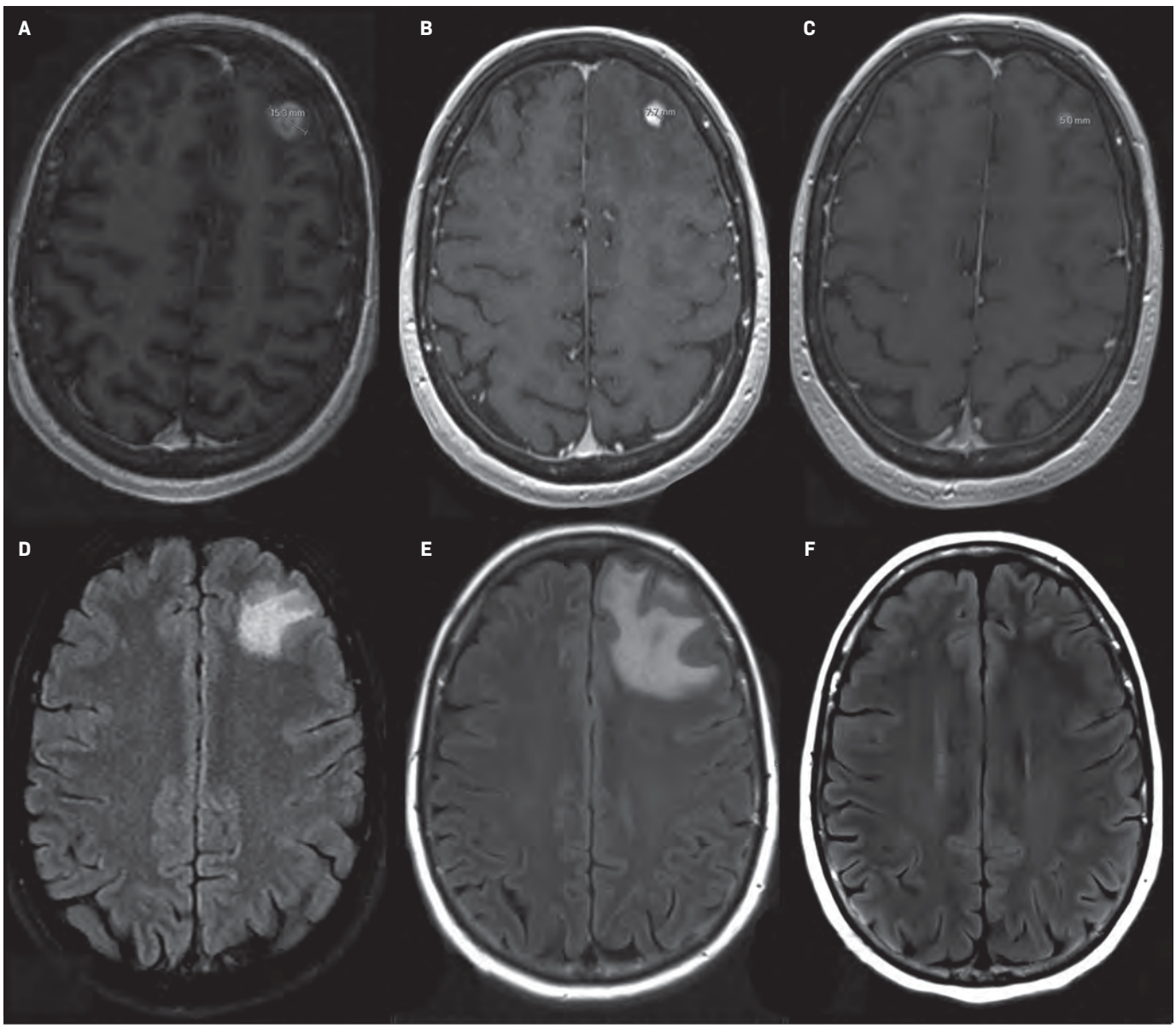
Case Summary

A 59-year-old woman with no significant past medical history presented with abdominal discomfort and elevated liver function tests. She was incidentally found to have a left upper quadrant abdominal mass. She underwent left robotic nephrectomy with pathology suggestive of multifocal clear-cell renal cell carcinoma, with a 9-cm and a 3.5-cm tumor, negative margins and 0/6 lymph nodes involved (pT3 pN0). Systemic staging scans revealed right-sided, pleural-based enhancing nodules and pleural effusion. She had an F-18 fluorodeoxyglucose (FDG) PET/CT scan, which demonstrated hypermetabolic activity in the right pleural surface in the mid to lower hemithorax (SUV max 3.0), with no other distant metastases. She underwent video-assisted thoracoscopic surgery (VATS) biopsy of parietal pleural nodules, which confirmed metastatic renal cell carcinoma. Baseline contrast-enhanced MRI of brain was negative for intracranial metastases. She was started on first-line systemic therapy with pembrolizumab and axitinib. Restaging scans revealed good response with improvement in small pulmonary nodules with minimal residual pleural thickening in the right lung base.

About 6 months after initial diagnosis, the patient presented with headaches and left-sided neck pain. A brain MRI with and without contrast revealed interval development of a 1.5 × 1.4-cm enhancing nodule in the left frontal lobe with mild to moderate surrounding vasogenic edema and mass effect. She also had an MRI of the cervical spine, which demonstrated multilevel degenerative changes but no metastatic disease. She was started on a short course of tapering

Affiliations: [1]Department of Radiation Oncology; [2]Division of Diagnostic Radiology; [3]Division of Neuro Oncology; [4]Division of Neurosurgery; all at Ohio State University Comprehensive Cancer Center and Richard J. Solove Research Institute, Arthur G. James Cancer Hospital, Columbus, OH.
Corresponding author: *Joshua D. Palmer, MD, The James Cancer Hospital and Solove Research Institute, 460 W 10th Ave, Columbus, OH 43210. (Joshua.Palmer@osumc.edu)
Disclosure/informed consent: The authors have no conflicts of interest to disclose. None of the authors received outside funding for the production of this original manuscript and no part of this article has been previously published elsewhere. The patient has provided informed consent for the publication of this case report.

Figure 1. Serial MRI imaging, with T1 postcontrast axial images (A-C) and T2 FLAIR images (D-F) demonstrate good tumor response (B, C), while there was increase in surrounding edema 2 months after fractionated stereotactic radiosurgery (E), which subsided after initiating Boswellia (F).



dexamethasone. She had no significant findings on her neurological examination and had an excellent performance status with a Karnofsky performance score of 90. Her baseline cognitive objective Patient-Reported Outcome Measurement Information System (PROMIS) score was 39/40. She completed fractionated stereotactic radiosurgery (fSRS) to her left frontal lesion to a dose of 24 Gy in 3 fractions using 4 volumetric-modulated arc therapy (VMAT) arcs of 6 MV flattening filter-free photons. A planning target volume (PTV) was created using a 2-mm margin around the gross tumor volume (GTV). The conformity index was 0.95 and the GTV received a mean dose of 27 Gy. She tolerated the treatment well with no acute side effects and continued pembrolizumab every 3 weeks and axitinib 5 mg twice a day.

She continued to have occasional headaches immediately after treatment and completed 2 short-term tapering doses of dexamethasone after her radiation treatment, with resolution of her headaches. Her follow-up brain MRI 2 months after treatment revealed a decrease in the left frontal enhancing lesion, but increased surrounding edema, consistent with grade 1 radiation injury, according to Common Terminology Criteria for Adverse Events (CTCAE) v5.0. She was instructed to begin over-the-counter Boswellia

Table 1. Treatment Options for Cerebral Radiation Necrosis

MODALITY	MECHANISM OF ACTION	ADEQUATE FOR	SIDE EFFECTS / DISADVANTAGES
Oral corticosteroids	Anti-inflammatory by suppressing migration of leukocytes, Repress NF-ΚB regulated inflammatory genes	Grade 2-3, symptomatic patients	Myopathy, iatrogenic Cushing's syndrome, gastric ulcers, fluid retention, neuropsychiatric effects
Bevacizumab	VEGF inhibition	Steroid-refractory patients	Hemorrhage, thrombosis and impaired wound healing
Laser interstitial thermal therapy (LITT)	Ablates both tumor tissue and VEGF-producing reactive glial cells	Steroid-refractory patients	Operative morbidity, transient and permanent weakness, hemorrhage, seizures, and hyponatremia
Hyperbaric oxygen therapy	Increased central oxygen levels promote perfusion and healing	Steroid-refractory patients	Expensive, requires specialized facilities and significant time commitment
Oral pentoxifylline and vitamin E	Improved perfusion	Grade 1-2, asymptomatic patients	Poor response rates
Boswellia serrata	**Herbal over-the-counter supplement with anti-inflammatory properties**	**Grade 1-3, asymptomatic and mildly symptomatic patients**	**Minimal, occasional gastrointestinal intolerance**
Surgical resection	Removes necrotic tissue	Symptomatic patients with mass effect on imaging, unclear local failure vs necrosis	Operative morbidity

serrata 4.2 to 4.5 gms daily in divided doses. She was taking Boswellia 3 × 1200 mg capsules (TNV vitamin brand) and 2 × 450 mg capsules (GNC brand) daily equaling a total dose of 4.5 gms daily in 3 divided doses. She tolerated the drug well with mild fatigue. She did not have any nausea, vomiting, gastrointestinal intolerance or any other side effects. She had a follow-up brain MRI at 5 months and 8 months post-treatment, which was consistent with interval improvement of FLAIR enhancement and edema around the prior treated left frontal lesion. No other new enhancing lesions were noted. Her serial PROMIS scores were 40, 40 and 39 at 2, 5 and 8 months of follow-up, respectively. At the last follow-up, 8.5 months after fSRS, she had remained free of headaches or any new neurological symptoms or signs.

Imaging Findings

A baseline, pretreatment brain MRI revealed a 14 × 15-mm post-contrast enhancing lesion in the left frontal lobe (**Figure 1A**) with minimal surrounding edema (**Figure 1D).** Post-treatment scans 2 months after completing fSRS revealed a decrease in the left frontal lobe enhancing lesion, measuring 8 × 7 mm (**Figure 1B**). There was extensive increase in surrounding T2 FLAIR signal abnormality compatible with edema, measuring 5.6 × 3.6 cm in perpendicular diameters (**Figure 1E**). Further follow-up brain MRI at 5 months after treatment showed continued decrease of the enhancing lesion in the left frontal lobe (**Figure 1C**). There was significant decrease in surrounding T2 FLAIR edema, which was now 1.4 × 0.8 cm (**Figure 1F**). This corresponded to a > 90% response per updated Response Assessment in Neuro-Oncology (RANO) criteria with measurement of sum of product of perpendicular diameters (SPPDs).[1] The irregular enhancing lesion within the left frontal lobe and surrounding edema continued to decrease, as shown in a brain MRI at an 8-month follow-up. No increase in perfusion around the treated metastases was noted on follow-up imaging at 5 and 8 months, and there was no evidence of new enhancing lesions in the brain parenchyma.

Diagnosis

CTCAE v5.0 Grade 1 radiation injury after fSRS for brain metastases

Discussion

Radiation necrosis (RN) is a dose-limiting late toxicity after radiation therapy for brain metastases. With advancements in radiation techniques and systemic therapies, patients with brain metastases tend to live longer, making late toxicities such as RN more relevant. Within the context of brain metastases, the true incidence of RN is hard to estimate and probably lies between 5% and 20%.[2,3] Using primarily imaging-based diagnosis, Minniti et al reported a 24% incidence of RN (14% symptomatic, 10% asymptomatic).[4] Although the pathophysiology of RN is multifactorial, vascular injury and glial cell damage are attributed. Management of RN primarily depends on symptoms and the extent of edema on imaging. **Table 1** summarizes various treatment options for managing cerebral radiation necrosis. Oral corticosteroids (such as dexamethasone) are the preferred first line of management

for symptomatic patients. However, corticosteroids often fail to control RN and are not optimal for long-term management because of multiple side effects and drug interactions. Many patients may require steroids for a long duration and are at risk for chronic steroid toxicity such as myopathy, iatrogenic Cushing's syndrome, gastric ulcers, etc.

Multiple other treatment modalities have been tried with limited success. Bevacizumab (humanized monoclonal antibody against VEGF) is used to treat steroid-refractory RN. A pooled analysis involving 71 patients showed that bevacizumab had a radiographic response rate of 97% and clinical improvement rate of 79% with a mean decrease in dexamethasone dose of 6 mg.[5] As such, bevacizumab appears to be a promising agent; however, the durability of response and toxicities associated with bevacizumab, such as hemorrhage, thrombosis and impaired wound healing, must be considered.[3,6] Multiple other treatment modalities have been tried with limited success, including hyperbaric oxygen therapy, oral pentoxifylline and vitamin E, and laser interstitial thermal therapy (LITT), and their use is not well established.[7] Surgical resection when feasible can provide control, relieve the mass effect, and provide pathological confirmation, but is associated with postoperative complications. In this context, evaluation of newer agents effective in preventing and managing cerebral edema after radiation therapy is warranted.

Easily available as an over-the-counter supplement, Boswellia serrata is an extract derived from Indian frankincense. It has been traditionally used in treatment of asthma, arthritis and colitis, given its anti-inflammatory properties. Recent data have reported the beneficial effects of Boswellia on reducing cerebral edema.[8] Kirste et al conducted the first randomized clinical trial to study the efficacy of Boswellia in reducing cerebral edema in brain tumor patients treated with radiation, and observed that 60% of patients receiving Boswellia reached a > 75% decrease in edema compared to only 26% in the placebo group.[8] The Boswellia preparation has reported no adverse effects. No studies have reported differential response rates based on Boswellia dose and preparation used so far. In another study, a Boswellic acid abstract given to 20 glioblastoma patients after surgery and chemoradiation led to considerable decrease in cerebral edema with maintained quality of life.[9]

In our patient, we were able to achieve a significant response with Boswellia with near complete resolution of edema, and our patient was able to avoid long-term steroid use. In this context, Boswellia can be used in various settings including decreasing existing cerebral edema, prophylactic risk reduction of symptomatic necrosis, and in management of RN, especially since it has no adverse effects. Drug interactions with steroid use become a particular concern in the modern era given the emergence of immunotherapy for several cancers. Boswellia can potentially decrease steroid dependence in these patients, thus reducing the risk of several side effects. Further prospective studies to evaluate the response rate with the use of Boswellia in patients who develop significant edema after fSRS for brain metastases is warranted.

Conclusion

Radiation necrosis is a dose-limiting late toxicity after stereotactic radiosurgery for brain metastases. Boswellia serrata is a promising treatment option for early radiation injury with no added side effects seen in our patient. It may be a suitable alternative to long-term steroid use. Further prospective studies evaluating the response rates with Boswellia for radiation necrosis are warranted.

References

1) Wen PY, Macdonald DR, Reardon DA, et al. Updated response assessment criteria for high-grade gliomas: response assessment in neuro-oncology working group. *J Clin Oncol*. 2010;28(11):1963-1972. doi:10.1200/JCO.2009.26.3541

2) Milano MT, Grimm J, Niemierko A, et al. Single- and multifraction stereotactic radiosurgery dose/volume tolerances of the brain. *Int J Radiat Oncol Biol Phys*. 2021;110(1):68-86. doi:10.1016/j.ijrobp.2020.08.013

3) Alnahhas I, Rayi A, Palmer JD, et al. The role of VEGF receptor inhibitors in preventing cerebral radiation necrosis: a retrospective cohort study. *Neurooncol Pract*. 2021;8(1):75-80. doi:10.1093/nop/npaa067

4) Minniti G, Clarke E, Lanzetta G, et al. Stereotactic radiosurgery for brain metastases: analysis of outcome and risk of brain radionecrosis. *Radiat Oncol*. 2011;6:48. doi:10.1186/1748-717X-6-48

5) Vellayappan B, Tan CL, Yong C, et al. Diagnosis and management of radiation necrosis in patients with brain metastases. *Front Oncol*. 2018;8:395. doi:10.3389/fonc.2018.00395

6) Tye K, Engelhard HH, Slavin KV, et al. An analysis of radiation necrosis of the central nervous system treated with bevacizumab. *J Neurooncol*. 2014;117(2):321-327. doi:10.1007/s11060-014-1391-8

7) Ohguri T, Imada H, Kohshi K, et al. Effect of prophylactic hyperbaric oxygen treatment for radiation-induced brain injury after stereotactic radiosurgery of brain metastases. *Int J Radiat Oncol Biol Phys*. 2007;67(1):248-255. doi:10.1016/j.ijrobp.2006.08.009

8) Kirste S, Treier M, Wehrle SJ, et al. Boswellia serrata acts on cerebral edema in patients irradiated for brain tumors: a prospective, randomized, placebo-controlled, double-blind pilot trial. *Cancer*. 2011;117(16):3788-3795. doi:10.1002/cncr.25945

9) Di Pierro F, Simonetti G, Petruzzi A, et al. A novel lecithin-based delivery form of Boswellic acids as complementary treatment of radiochemotherapy-induced cerebral edema in patients with glioblastoma multiforme: a longitudinal pilot experience. *J Neurosurg Sci*. 2019;63(3):286-291. doi:10.23736/S0390-5616.19.04662-9

Navigating Radiation Oncology Emergencies: Are We Maximizing Inpatient Call for Residents?

Rituraj Upadhyay, MD;* Benjin D. Facer, MD

Dr. Upadhyay is a PGY3 resident physician, Department of Radiation Oncology, The Ohio State University Wexner Medical Center.

Dr. Facer is a PGY3 resident physician, Department of Radiation Oncology, The Ohio State University Wexner Medical Center.

Oncological emergencies are defined as "conditions arising from a reversible threat to an organ function, requiring treatment within hours of diagnosis."[1] For inpatient radiation, common emergency indications include spinal cord compression, superior vena cava syndrome, and vaginal bleeding.[2] As cancer therapies improve and more people live with metastatic disease, demand for inpatient radiation will likely increase. This raises 2 important questions:

1. What is the optimal format for an inpatient call system?
2. How can resident education be maximized during inpatient call?

The format for inpatient call varies based on department size and inpatient volume. In an attending-led format, the attending is notified of the consult and is expected to evaluate/treat as needed, only involving the resident as they see fit. In a resident-led format, the resident is expected to independently evaluate the patient and discuss the management plan with the attending. The attending may be a subspecialist (thoracic, central nervous system, etc.), a designated on-call attending from an inpatient service, or an attending on a daily/weekly schedule with clinic duties. Depending on format, resident responsibilities may extend from care coordination to treatment consent and contouring.

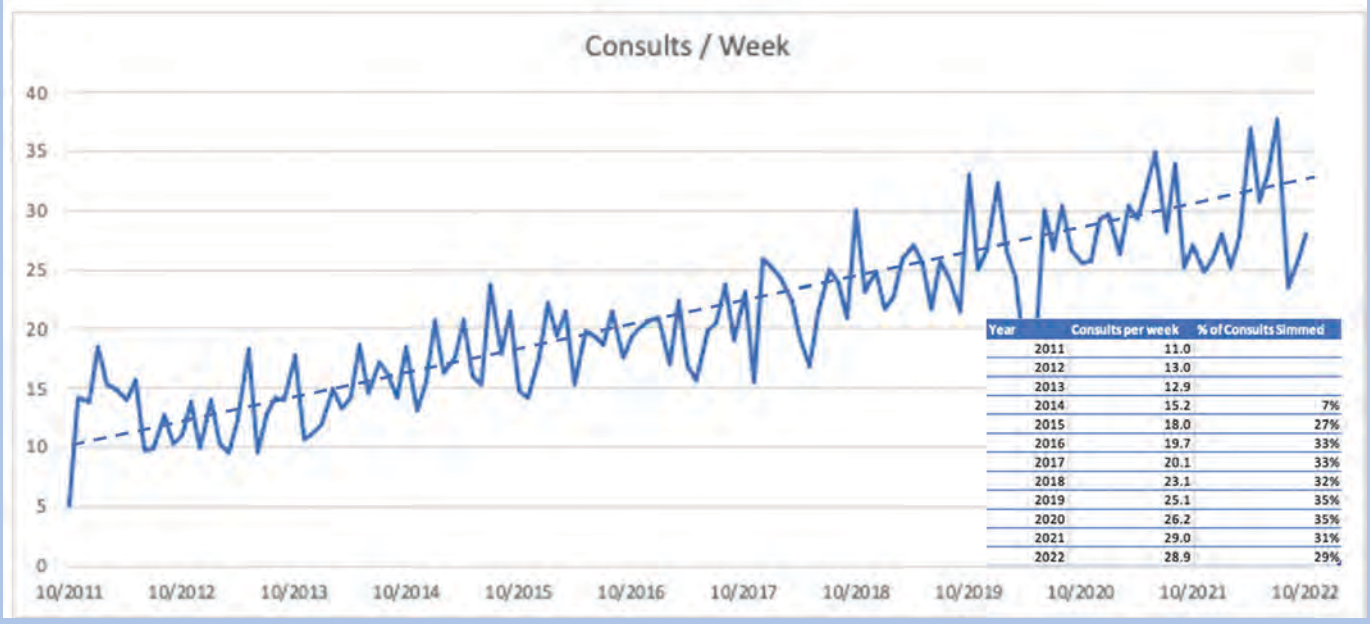
In our program, the on-call residents are primarily responsible for seeing all inpatient consults and after-hour patient calls for 1 week. This includes communicating with the primary teams, obtaining patient consents, and contouring treatment volumes. We also recently transitioned to a system in which the on-call resident has no primary service-related clinical responsibilities during this week, although the attendings with whom they staff cases continue to remain in clinic.

The tasks associated with inpatient call vary across institutions. These opportunities can be highly educational as residents learn about radiation toxicities, logistics of urgent radiation therapy, and workup of new cancer diagnoses. The educational value of inpatient call depends on the inpatient volume and the amount of added administrative work (consents, coordination emails, etc.). However, the educational value decreases if consults per week increase or administrative burden is high.

At our hospital, call volumes have risen more than 50% over the last 5 years (**Figure 1**), with highs approaching more than 40 consults per week in 2022. As the demand for inpatient radiation therapy grows, so will its place in residency training experience. Per the Accreditation Council for Graduate Medical Education (ACGME),

Disclosure: The authors have no conflicts of interest to disclose. None of the authors received outside funding for the production of this original manuscript and no part of this article has been previously published elsewhere.
Corresponding author: *Rituraj Upadhyay, MD, Arthur G. James Cancer Hospital, D259, 460 W 10th Avenue, Columbus, OH 43210 (rituraj.upadhyay@osumc.edu)

Figure 1. Line graph depicting a 10-year trend for the number of inpatient consults received per week by our department of radiation oncology, and percentage of consults simulated for urgent inpatient radiation treatment.



Year	Consults per week	% of Consults Simmed
2011	11.0	
2012	13.0	
2013	12.9	
2014	15.2	7%
2015	18.0	27%
2016	19.7	33%
2017	20.1	33%
2018	23.1	32%
2019	25.1	35%
2020	26.2	35%
2021	29.0	31%
2022	28.9	29%

duration of on-call weeks is not a prerequisite to meet graduate medical education (GME) requirements in radiation oncology. Although on-call hours are counted toward the 80-hour weekly limit, on-call experiences do not necessarily count toward the 36-month minimum clinical radiation oncology experience, as they are not considered "comprehensive management of patients in treatment."[3] Hence, important considerations are how much the residents should remain involved in inpatient care and whether additional training/lectures are warranted.

Our call system has several advantages overall. As a resident, we gain independence in the patient management thought process. Increased exposure to various palliative scenarios and extensive repetition within those domains boost our confidence in independently evaluating patients, as noted by recent graduates. We also learn to deal with several nuances, especially in a resource-limited setting.

Take-Home Points

A one-size-fits-all approach to inpatient call is not likely, and radiation oncology programs should regularly evaluate their inpatient format to ensure the hospital's inpatient radiation requirements maximize a resident's educational experience. In a high-volume center, adjustments may be needed, including excusing residents from normal clinical duties, creating inpatient-specific didactics, forming an inpatient radiation oncology service, or integrating midlevel providers. A nuanced solution to enhance learning and take the experience to the next level may be having PGY5s complete more low-risk palliative cases independently from contours through plan review, all the way to alignment at the machines, with only minimal guidance from attendings. We encourage residency programs to experiment with and share ideas for successful call systems. In doing so, we will be better prepared to expand inpatient radiation services to maximize resident education and effective patient care.

References

1) Donato V, Bonfili P, Bulzonetti N, et al. Radiation therapy for oncological emergencies. *Anticancer Res.* 2001;21(3C):2219-2224.

2) Narang M, Mohindra P, Mishra M, Regine W, Kwok Y. Radiation oncology emergencies. *Hematol Oncol Clin North Am.* 2020;34(1):279-292. doi:10.1016/j.hoc.2019.09.004

3) Radiation Oncology Program Requirements and FAQs. Accessed January 19, 2023. https://www.acgme.org/specialties/radiation-oncology/program-requirements-and-faqs-and-applications/

Locoregional Chemoradiation for a Patient with BRCA1 Stage IV Pancreatic Adenocarcinoma

Pranit Singh, BS;[1] Jacob Adams, BS;[1] Sylvia Choo, BA;[1] Matthew Adams, BS;[2] Jordan McDonald MD;[3] Laura Barton, MS;[4] Richard Levine, MD;[5] Dae Won Kim, MD;[6] Russell Palm, MD;[7] Jessica Frakes, MD;[7] Sarah Hoffe, MD[7]

Abstract

Although the highest lifetime cancer risk in the setting of a BRCA 1 mutation is the development of a breast and ovarian malignancy, there is also a < 5% lifetime risk of pancreatic cancer.[1] Recent recommendations suggest annual contrast-enhanced pancreatic MR imaging or endoscopic ultrasound for pancreatic cancer screening for these patients.[2] In this case report, a patient undergoing MRI breast surveillance was incidentally found to have metastatic pancreatic cancer in the liver. The patient was treated with leucovorin, 5-fluorouracil, irinotecan, and oxaliplatin (FOLFIRINOX) alone and was rendered disease-free. Five years later, she developed an isolated nodal recurrence for which she received systemic gemcitabine and cisplatin chemotherapy with a partial response followed by consolidation chemoradiation to 50.4 Gy with intensity-modulated radiation therapy and concurrent capecitabine, with a complete response. This case highlights the potential for long disease-free intervals in the setting of BRCA1-metastatic pancreatic cancer and suggests an individualized role for locoregional radiation.

Keywords: BRCA1, ATM, pancreatic adenocarcinoma

Case Summary

A 70-year-old White woman with no personal history of radiation therapy, but with a prior history of breast cancer following postbilateral mastectomy with transverse rectus abdominis muscle (TRAM) reconstructions, presented for her annual MRI in 2015. She was a heavy smoker with additional oncological history of stage III ovarian cancer 22 years prior and a family history of breast/colon cancer. Multiple bilobar liver lesions were incidentally found on breast MRI and confirmed on triple-phase computed tomography (CT) and positron emission tomography (PET) scans, which also identified a hypermetabolic mass in the body of the pancreas with CA 19-9 > 400. Ultrasound-guided fine-needle aspiration (FNA) of a liver lesion confirmed the diagnosis of T2N0M1, stage IV pancreatic adenocarcinoma. She received 16 cycles of FOLFIRINOX (5-FU at 1800 gm, oxaliplatin at 65 mg/m2, and irinotecan at 100 mg/m2 every 3 weeks) followed by no evidence of disease until 2021, when FNA confirmed a celiac nodal recurrence. Germline testing confirmed BRCA1 and ATM mutations. Chemotherapy with gemcitabine and cisplatin achieved a partial radiographic response. Capecitabine chemoradiation with 50.4 Gy of intensity-modulated radiation therapy (IMRT) achieved a complete response. She did not experience any known early or late toxicity related to her radiation treatment.

Affiliations: [1]University of South Florida Health Morsani College of Medicine, Tampa. [2]Lake Erie College of Osteopathic Medicine, Bradenton, FL. [3]Department of Radiation Oncology, University of Texas Health Science Center, Houston. Departments of [4]Personalized Medicine, [5]Medical Oncology, [6]Gastrointestinal Oncology, and [7]Radiation Oncology, H. Lee Moffitt Cancer Center, Tampa, FL
Corresponding author: *Sarah Hoffe, MD, Department of Radiation Oncology, Moffitt Cancer Center, 12902 Magnolia Dr, Tampa, FL 33612. (sarah.hoffe@moffitt.org)
Disclosure/informed consent: Matthew Adams is a member of the *Applied Radiation Oncology* (ARO) Future Content Medical Student Committee. Dr. Hoffe is an editorial board member for ARO and faculty advisor for ARO's medical student committees. Dr. Frakes is a co-head of ARO's gastrointestinal section. No other authors have conflicts of interest to disclose. None of the authors received outside funding for the production of this original manuscript and no part of this article has been previously published elsewhere. The patient has provided informed consent for the publication of this case report.

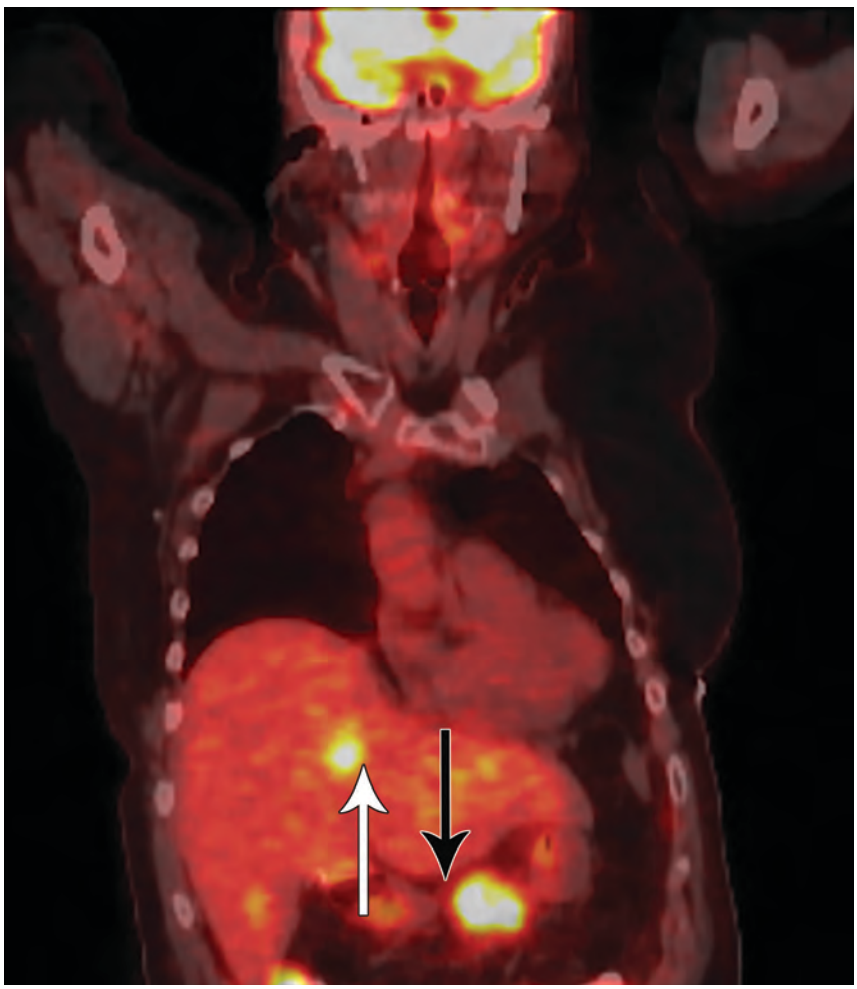


Figure 1. Positron emission tomography / computed tomography (PET/CT) image shows hypermetabolic lesions in the liver and pancreatic body. White arrow shows liver lesion; black arrow points to the pancreas primary tumor.

Diagnosis

In this patient's case, the workup confirmed she had developed a pancreatic body primary adenocarcinoma (**Figure 1**), which metastasized to multiple sites in the liver (**Figure 2**). There were no obvious involved abdominal lymph nodes on imaging at the time of initial diagnosis in 2015. The FNA of one of the liver lesions showed the cells were positive for *CK7, CK19, CA125, CA19-9,* pancytokeratin (*AE1/AE3 CAM5.2*), beta catenin, and *GATA3*.

At the time of recurrence (**Figure 3)** in 2021, FNA of the celiac node was interpreted as poorly differentiated carcinoma consistent with the history of prior pancreatic cancer. After systemic chemotherapy with 3 months of gemcitabine and cisplatin every 21 days, the patient received chemoradiation with capecitabine and an IMRT plan to a dose of 45 Gy in 25 fractions to the clinical target volume followed by a boost of 5.4 Gy in 3 fractions (**Figure 4**) to the gross disease.

Discussion

Despite recent advances in cancer therapy, pancreatic cancer continues to have one of the lowest 5-year overall survival rates (11%).[3] The majority of cases are sporadic but genomic evidence now suggests there is a heterogeneous landscape of molecular subtypes.[4] Several genetic syndromes are associated with pancreatic cancer including mutations in DNA mismatch repair (Lynch syndrome), BRCA1 and BRCA2.[5] The *BRCA* tumor suppressor genes are responsible for numerous functions regarding DNA-damage-dependent cellular checkpoints, DNA repair, and cell death.[6] Mutations that alter the functions of these proteins may lead to targetable treatment. Given the rarity of BRCA-mutated pancreatic cancer (BMPC), it is unclear how much the prognosis differs from wildtype. However, there is agreement regarding the improved sensitivity of BMPC to platinum-based chemotherapies and poly (ADP-ribose) polymerase inhibitors, such as olaparib.[7] The role of radiation therapy in BMPC is not clear, with some laboratory studies showing enhanced radiosensitivity, but clinical studies failing to show clearly improved outcomes.[8]

In addition to BRCA1, our patient had an ATM mutation, which is

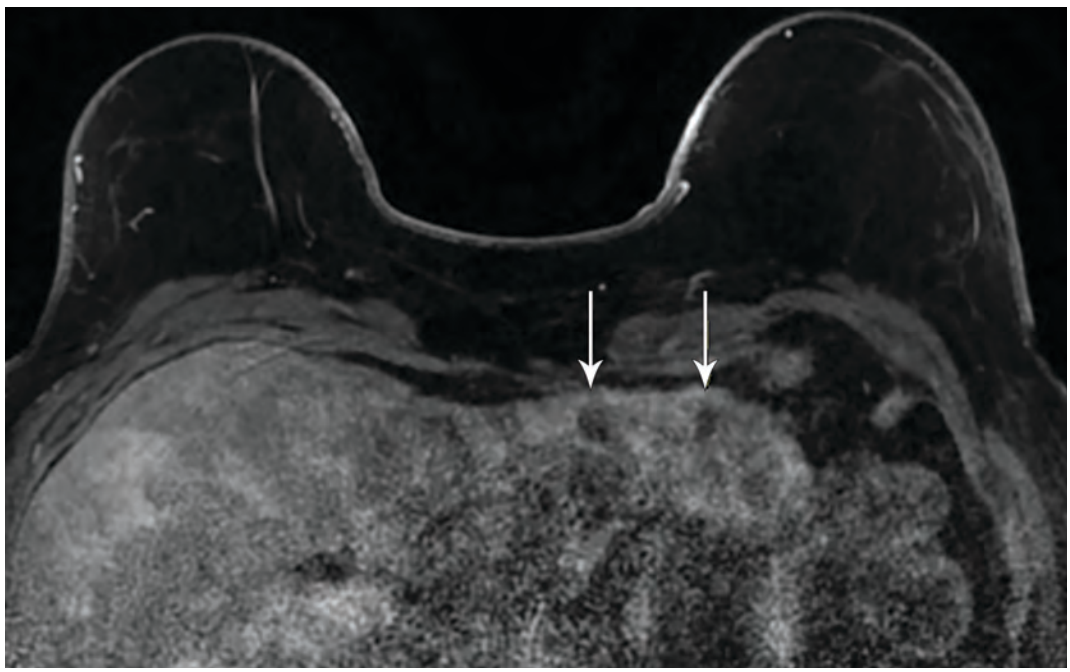


Figure 2. A surveillance MRI scan of the breast shows occult liver lesions (white arrows).

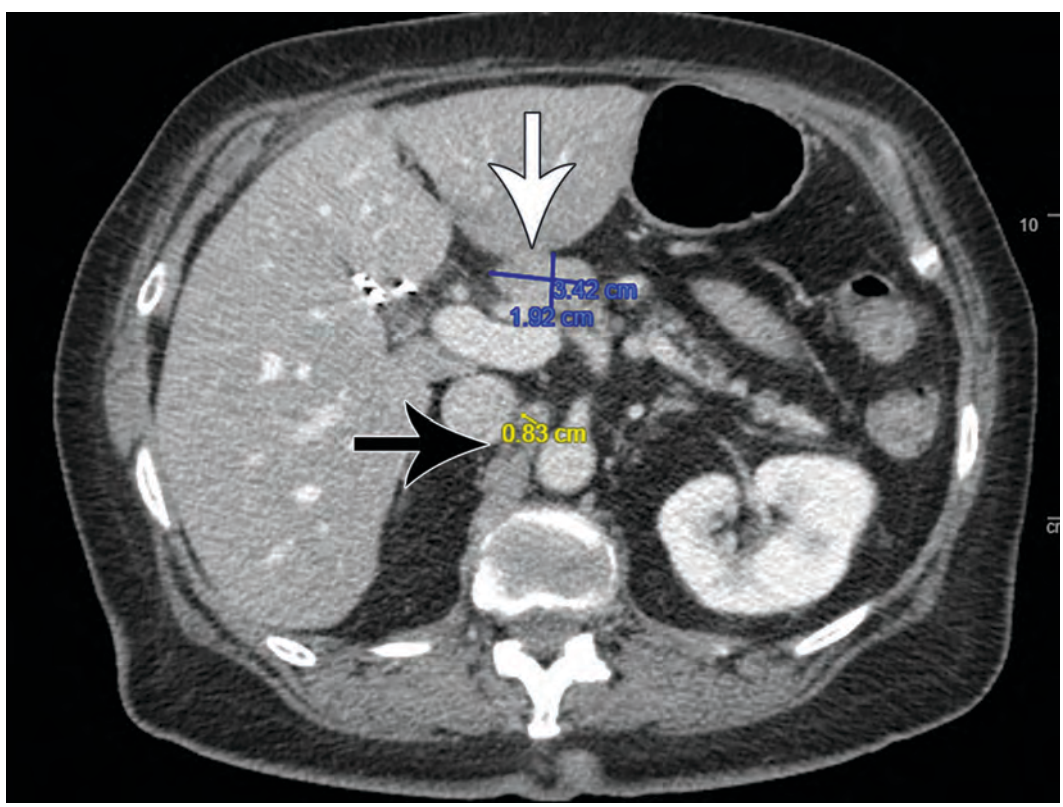
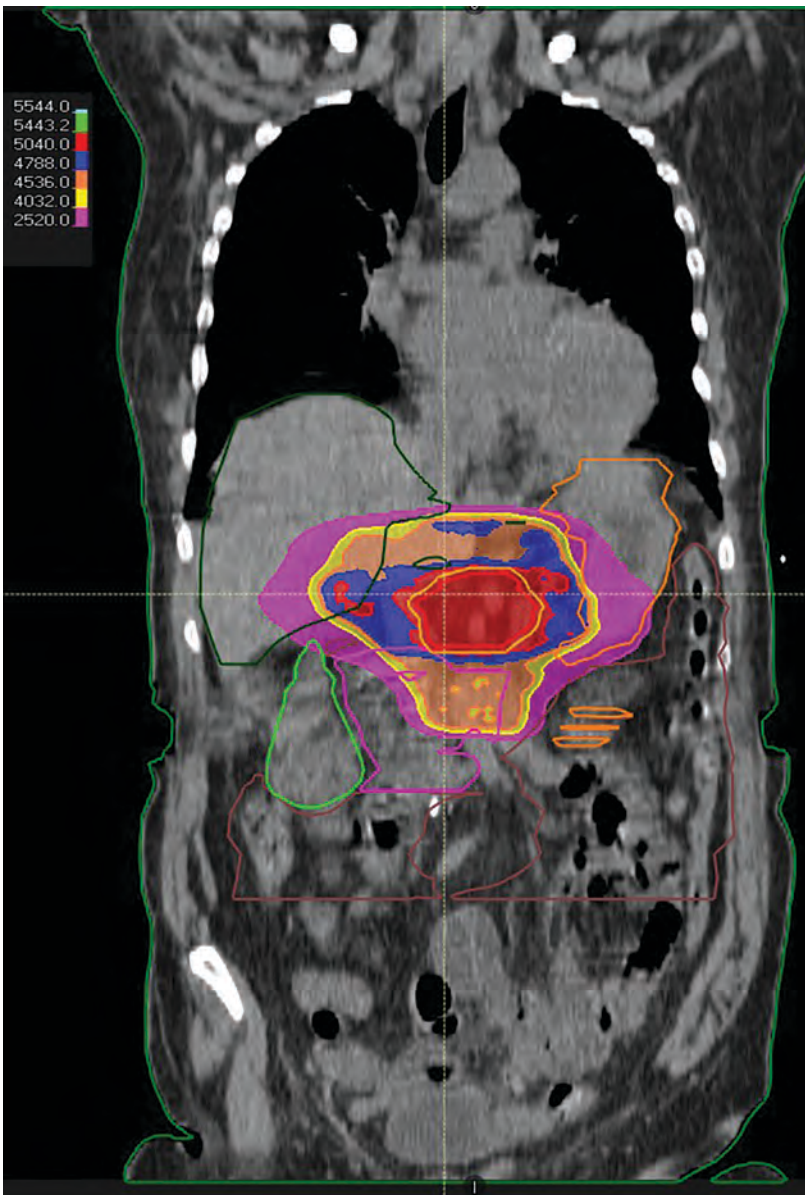


Figure 3. Axial contrast-enhanced scan showing nodal recurrence in the celiac and aortocaval regions. Celiac nodes shown at the white arrow; aortocaval node shown at the black arrow.

associated with ataxia telangiectasia and has been characterized by extreme radiosensitivity.[9] Recent studies have shown that both heterozygous and homozygous ATM inactivation are associated with increased radiosensitivity[10] and that patients with cancer and both BRCA and ATM mutations may have significantly increased radiosensitivity and an enhanced response to radiation therapies.[11] ATM mutations have been of concern due to the potential of excessive radiation-associated toxicity particularly in breast cancer. Recent evidence indicates, however, that overall there is no excess in clinically significant acute toxicity, although caution is warranted as subvariants such as c5557G>A may have a higher risk of late toxicity

Figure 4. Axial contrast-enhanced scan showing nodal recurrence in the celiac and aortocaval regions. Coronal dose distribution of the composite plan: 45 Gy in 25 fractions to the clinical target volume, followed by 5.4 Gy in 3 fractions to the gross tumor volume, for a total dose of 50.4 Gy with intensity-modulated radiation therapy.



or radiation-induced contralateral breast cancer.[12,13]

The clinical implications of germline genetic mutations illustrate the importance for genetic testing of all patients diagnosed with pancreatic cancer. Our patient declined *BRCA* testing after her first breast cancer diagnosis in her 30s, believing it was no longer important since she underwent bilateral mastectomy, only to be diagnosed with ovarian and pancreatic cancer over the next 40 years. Early genetic testing would have also revealed her ATM H231fs mutation earlier, which is significant given the associated increased cancer predisposition to malignancies of the lung, thyroid, pancreas and other areas, which could have led to more frequent screening intervals. In addition, the ATM mutation has relevance to her sensitivity to platinum chemotherapy agents since this mutation can be associated with increased response rates.[14] The current standard of care is to offer genetic testing to all patients diagnosed with pancreatic cancer.[15]

In our case, the patient had a clinical complete response of her pancreatic primary and metastatic liver disease to FOLFIRINOX. Our patient has vastly exceeded the average prognosis of her condition with over 6 years of survival to date and 5 years of remission prior to recurrence.[16] Interestingly, our patient relapsed in the celiac and adjacent nodes only without any recurrence in the pancreas primary site or liver. This was confirmed with an MRI scan of the abdomen before treatment initiation. After 3 months of gemcitabine and cisplatin chemotherapy, the MRI showed a persistent nodal viable tumor. Since multidisciplinary tumor board evaluation centered around her current age of 76 and her comorbidities, focusing on treatments to maintain her quality of life were preferred, leading to the decision to proceed with consolidation to all sites of nodal activity with chemoradiation (CRT).

For gastrointestinal tumor sites with adenocarcinoma histology, there is a paucity of literature supporting radiation therapy for stage IV disease. In metastatic cancers of the esophagus, there is a potential survival benefit associated with CRT, suggesting that patients with chemotherapy intervals of 3 months or longer have improved outcomes, approaching 20% at 5 years for gastroesophageal junction tumors.[17] In colorectal cancer patients, after immune checkpoint blockade, oligoprogression can be a frequent pattern of failure and local therapy strategies that include radiation may improve clinical outcomes.[18] In pancreatic cancer, there is as yet no literature to support the role of consolidation to nodal targets post-chemotherapy for stage IV disease.

For our patient, the decision to offer her consolidation CRT was made

after extrapolation from esophageal adenocarcinoma outcomes, recognizing that her radiosensitivity was likely increased secondary to her underlying BRCA1 and ATM mutational status. IMRT was incorporated to maximize her normal tissue sparing since the potential to enhance organ at risk (OAR) sensitization was unknown. The patient tolerated her CRT well and did not have any high-grade toxicities. At nearly 1 year post-therapy, her CA 19-9 and imaging have not shown evidence of recurrence. The multidisciplinary tumor board has discussed the possibility of olaparib as maintenance therapy. Due to the results of the recent POLO trial,[19] the patient prefers to consider this if she recurs and not as maintenance therapy, given the lack of a survival benefit.

Conclusion

This case highlights the potential for long disease-free survival in BRCA-mutated metastatic pancreatic cancer. Although enhanced radiosensitivity of BRCA-mutated tumors has been described in the laboratory, correlative clinical outcomes are lacking. The resolution of primary and metastatic disease on systemic FOLFIRINOX therapy for 5 years postdiagnosis supports the efficacy of platinum-based chemotherapy in this patient population. After regional nodal recurrence, salvage CRT was delivered to the abdomen, and nearly 1 year post-treatment, the patient remains radiographically and biochemically without evidence of disease. As expert consensus opinions recommend all patients with pancreatic cancer obtain genetic testing, more patients may be identified with BMPC, and a personalized strategy that includes radiation may be warranted for patients that respond to systemic therapy.

References

1) Thompson D, Easton DF, Breast Cancer Linkage Consortium. Cancer incidence in BRCA1 mutation carriers. *J Nat Cancer Inst*. 2002;94(18):1358-1365. doi:10.1093/jnci/94.18.1358

2) Roch AM, Schneider J, Carr RA, et al. Are BRCA1 and BRCA2 gene mutation patients underscreened for pancreatic adenocarcinoma? *J Surgl Oncol*. 2019;119(6):777-783. doi:10.1002/jso.25376

3) Siegel, RL, Miller, KD, Fuchs, HE, Jemal, A. Cancer statistics, 2022. *CA Cancer J Clin*. 2022. https://doi.org/10.3322/caac.21708

4) Lomberk G, Dusetti N, Iovanna J, Urrutia R. Emerging epigenomic landscapes of pancreatic cancer in the era of precision medicine. *Nat Commun*. 2019;10(1):3875. doi:10.1038/s41467-019-11812-7

5) Goral V. Pancreatic cancer: pathogenesis and diagnosis. *Asian Pac J Cancer Prev*. 2015;16(14):5619-5624. doi:10.7314/APJCP.2015.16.14.5619

6) Wu J, Lu LY, Yu X. The role of BRCA1 in DNA damage response. *Protein & Cell*. 2010;1(2):117-123. doi:10.1007/s13238-010-0010-5

7) Leung K, Saif MW. BRCA-associated pancreatic cancer: the evolving management. *J Pancreas*. 2013;14(2):149-151. doi:10.6092/1590-8577/1462

8) Bernier J, Poortmans P. Clinical relevance of normal and tumour cell radiosensitivity in BRCA1/BRCA2 mutation carriers: a review. *Breast*. 2015;24(2):100-106. doi:10.1016/j.breast.2014.12.003

9) Ayars M, Eshleman J, Goggins M. Susceptibility of ATM-deficient pancreatic cancer cells to radiation. *Cell Cycle*. 2017;16(10):991-998. doi:10.1080/15384101.2017.1312236

10) Aghamohammadi A, Akrami SM, Yaghmaie M, et al. Individual radiosensitivity assessment of the families of *ataxia-telangiectasia* patients by g2-checkpoint abrogation. *Sultan Qaboos Univ Med J*. 2018;18(4):e440-e446. doi:10.18295/squmj.2018.18.04.003

11) Kim KH, Kim HS, Kim SS, et al. Increased radiosensitivity of solid tumors harboring ATM and BRCA1/2 mutations. *Cancer Res Treat*. 2022;54(1):54-64. doi:10.4143/crt.2020.1247

12) Modlin LA, Flynn J, Zhang Z, et al. Tolerability of breast radiotherapy among carriers of ATM germline variants. *JCO Precis Oncol*. 2021;5:PO.20.00334. doi:10.1200/PO.20.00334

13) McDuff SGR, Bellon JR, Shannon KM, et al. ATM variants in breast cancer: implications for breast radiation therapy treatment recommendations. *Int J Radiat Oncol Biol Phys*. 2021;110(5):1373-1382. doi:10.1016/j.ijrobp.2021.01.045

14) Choi M, Kipps T, Kurzrock R. ATM mutations in cancer: therapeutic implications. *Mol Cancer Ther*. 2016;15(8):1781-1791. doi:10.1158/1535-7163.MCT-15-0945

15) Mohindroo C, De Jesus-Acosta A, Yurgelun MB, Maitra A, Mork M, McAllister F. The evolving paradigm of germline testing in pancreatic ductal adenocarcinoma and implications for clinical practice. *Surg Pathol Clin*. 2022;15(3):491-502. doi:10.1016/j.path.2022.05.004

16) Azar I, Virk G, Esfandiarifard S, Wazir A, Mehdi S. Treatment and survival rates of stage IV pancreatic cancer at VA hospitals: a nation-wide study. *J Gastrointest Oncol*. 2019;10(4):703-711. doi:10.21037/jgo.2018.07.08

17) Mizrak Kaya D, Wang X, Harada K, et al. 101 Long-term survivors who had metastatic gastroesophageal cancer and received local consolidative therapy. *Oncology*. 2017;93(4):243-248. doi:10.1159/000475550

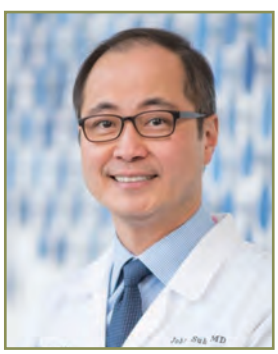
18) Marmorino F, Boccaccino A, Germani MM, Falcone A, Cremolini C. Immune checkpoint inhibitors in pMMR metastatic colorectal cancer: a tough challenge. *Cancers*. 2020;12(8):2317. doi:10.3390/cancers12082317

19) Golan T, Hammel P, Reni M, et al. Overall survival from the phase 3 POLO trial: maintenance olaparib for germline BRCA-mutated metastatic pancreatic cancer. *J Clin Oncol*. 2021;39(3_suppl):378. doi:10.1200/JCO.2021.39.3_suppl.378

CALL FOR PAPERS

Applied Radiation Oncology

A key resource for practical clinical information and SA-CME credits



John Suh, MD, FASTRO, FACR

Dear Colleagues:

We are pleased to let you know that our journal and community of registered radiation oncologists have continued to expand over the last several years. We appreciate your support and, as part of our mission to foster a community where peers share practical solutions in the clinical setting, *Applied Radiation Oncology* is issuing a call for clinical cases, review articles and research articles.

We are looking for authors to write and submit on topics that include (but are not limited to): imaging, contouring, target delineation, treatment planning, patient immobilization, organ tracking, safety and quality, and other timely topics essential to the discipline. Important to note is that review articles accepted for publication may be accredited for Continuing Medical Education (CME). Submissions will undergo a double-blind peer review process through our external peer review panel.

If you or your colleagues have an interesting case, review article or research paper for publication consideration in *Applied Radiation Oncology*, please read our Submission Guidelines. As a reference for the types of articles published in *Applied Radiation Oncology*, visit appliedradiationoncology.com and browse our archives.

This is a wonderful opportunity to impart your knowledge to your peers and we look forward to your submissions.

Sincerely,

John Suh, MD, FASTRO, FACR
Editor-in-Chief, Applied Radiation Oncology

Dr. Suh is the editor-in-chief of *Applied Radiation Oncology,* and professor and chairman, Department of Radiation Oncology at the Taussig Cancer Institute, Rose Ella Burkhardt Brain Tumor and Neuro-oncology Center, Cleveland Clinic, Cleveland, OH.

AppliedRadiationOncology

www.appliedradiationoncology.com