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ASTRO news

The Scope of Practice of Radiation Oncology

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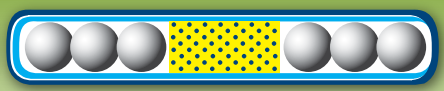

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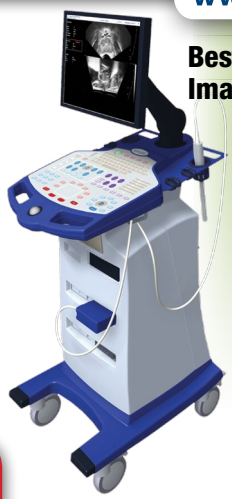

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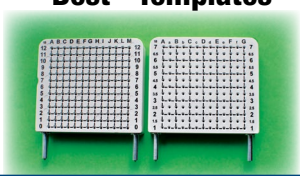

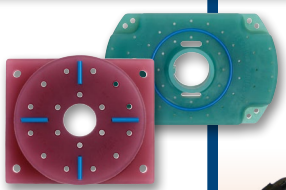

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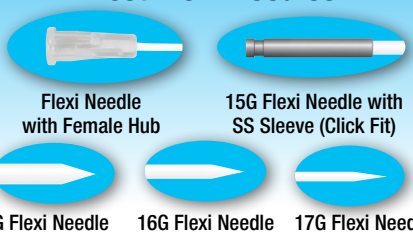


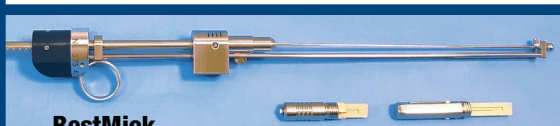
Flexi Needle with Female Hub

15G Flexi Needle with SS Sleeve (Click Fit)

15G Flexi Needle

16G Flexi Needle

17G Flexi Needle



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VOLUME 23 • NUMBER 4

ASTRO news

AMERICAN SOCIETY FOR RADIATION ONCOLOGY

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EDITOR'S*notes*

BY NAJEEB MOHIDEEN, MD, FASTRO
SENIOR EDITOR, *ASTRONEWS*

THE BRINK OF **HOPE**

QUEEN ELIZABETH II referred to 1992 as "annus horribilis" — a horrible year. Three royal marriages collapsed, a fire destroyed part of Windsor Castle and scandal rocked the monarchy. 2020 certainly deserves that appellation — bitter political divisions, social unrest and an unrelenting pandemic. COVID-19 has consumed and depleted health care systems. Under such extreme circumstances, you might think there would be added protections to preserve access to vital services such as cancer care. If radiation oncology practices in the U.S. were hoping to catch a break, they got just the opposite — deep cuts in the Medicare Physician Fee Schedule and the Radiation Oncology Model. Thanks to valiant advocacy by ASTRO and the broader radiation oncology stakeholder community, Congress delayed the RO Model until January 1, 2022, and ameliorated the 5% anticipated overall reduction that would have taken effect this New Year's Day.

That brings us to the theme for this issue of *ASTROnews*: The Scope of Practice of Radiation Oncology. While this loosely defines permitted functions by education, experience, certification and demonstrated competency, it is also a reflection of the role we play in patient care, and the say we have in that. What is our core skill set and how are we perceived by our patients and fellow professionals? In a recently published ASTRO survey, all respondents agreed that "radiation oncologists should be leaders in oncologic care." However, practice rarely matched aspiration. Why is there such a mismatch? That's something this issue examines, going into various aspects of our scope of practice. It also offers a fascinating look at how the scope of practice and roles vary across the world.

The challenge for us, in an ever-changing world, is this: We must imagine what the radiation oncologist of the future will do. There is no doubt there will be substantially more automation, augmented by artificial intelligence and robotic support in our process of care. We may play a decreasing role in target delineation, treatment planning steps, image guidance, online adaptations and supervision. Perhaps the scope of radiation therapists and dosimetrists will expand in these roles aided by automated tools, but every one of these changes could be contentious unless they are proven to not sacrifice quality patient care, are disconnected from whatever will be the reimbursement system of the future and not seen as threatening future job prospects. This could still generate heated disagreement. For instance, a recent JACR article said radiology extenders who read chest X-rays save attending radiologists more time during the day than radiology residents. The manuscript was withdrawn by the authors subsequent to publication.

Our training must evolve with the times to reflect education and knowledge in current and emerging areas of oncology for a more comprehensive picture of anticancer treatment options. The virtual ASTRO Annual Meeting featured discussions beyond the typical topics, such as cannabis in cancer care, radiopharmaceutical therapy (see page 33) and an engrossing session that included prescribing, managing and handling the side effects of the different second generation anti-androgens currently used in prostate cancer, which I found really useful. I am sure this type of exposure and training can help us expand the scope of services we offer, which won't be without the attendant political hurdles and turf battles. Our roles, in addition to being experts in radiation, brachytherapy and radiopharmaceuticals therapy, could expand to wider multidisciplinary decision making, intensive counseling of patients before, during and after treatment and move us closer to our goal of becoming leaders in oncology care.

The end of the year brings hope on many fronts. John Dryden wrote the poem "Annus Mirabilis" or Year of Miracles to mark 1667, in truth a time of misery that saw the Great Fire of London among other tragedies. Dryden was trying to say that things could have been worse. If 2020 was horrible, can 2021 bring recovery, rejuvenation and healing? Yes, it can. Not just thanks to the wonder of science but also by people believing in themselves, thinking as a community and bridging their differences as we embark on a brand new year.

The *ASTROnews* editorial board joins me in wishing you all a happier 2021.

CHAIR'S*update*

BY THOMAS J. EICHLER, MD, FASTRO

> "The American, by nature, is optimistic. He is experimental, an inventor and a builder who builds best when called upon to build greatly."
>
> *John F. Kennedy, upon announcing his candidacy for president, January 2, 1960*

AS YOU READ THESE WORDS, it is likely that some of you, and perhaps your staff, will have already been vaccinated, that maybe there is finally light at the end of this long tunnel. The genetic sequencing, creation, testing and approval of multiple vaccines in the space of a year is unprecedented. The words of JFK echo across decades and speak more broadly to the entire human family: optimistic, creative, building greatly. A new phase has begun.

The theme of this issue of *ASTROnews* is the scope of practice. There are several thoughtful and elegantly written articles within that address the current state of affairs while casting an eye to the future. What lies ahead? Where are we going as a discipline? As a specialty society?

I spoke in some detail about these questions in my Presidential Address at the Annual Meeting in October and will not rehash those comments but rather expand on their meaning and try to add some context. Spoiler alert! I cannot foretell the future, but I can offer some observations based on the available data, my discussions with some of you and my own experience of being a radiation oncologist for nearly 30 years.

The practice of radiation oncology is different today than it was 30 years ago, but in some respects it hasn't changed as much as we might think. We still see patients in consultation, develop therapy plans and follow our patients during and after treatment, but technology and the results of clinical trials have dramatically impacted the process of care. Like it or not, hypofractionation is a data-driven reality that will likely expand in the future. Yes, we all acknowledge that fewer fractions has negative economic ramifications for providers, but if you became a doctor simply to make money, you chose unwisely.

A thought: perhaps the radiation oncologist of the future needs to be more of a *clinical* oncologist than a *radiation* oncologist. Perhaps we need to take a more holistic approach to patient care rather than abnegating responsibility for overall patient management by deferring to our medical and surgical oncology colleagues. This would require a collective re-thinking of how radiation oncologists are trained and a gradual re-wiring of how we think and act. None of this will happen overnight, but the discussion has already begun and will continue until a clear path forward is identified and agreed upon. The times, they are a changin'.

There has been considerable hand-wringing re: workforce supply, often, unfortunately, in the unfiltered echo chamber of cyberspace. Although of little consolation, the specialty has been down this road before, on more than one occasion, and adjusted accordingly. We're still here. ASTRO does not and cannot, as has been stated *ad nauseam*, control the number of training programs and residency positions. The Society has issued a carefully worded statement that urges training programs to be mindful of the potential future oversupply of radiation oncologists, without crossing the legal red line that suggests an attempt to control the marketplace. We also continue to engage SCAROP and ADROP to gauge their efforts on this critical issue.

All of this must be done with a conscious sensitivity for diversity, equity and inclusion as the Society and the specialty strive to improve the richness of our social fabric and improve health outcomes for *all* of our patients. Likewise, this process has already begun and will continue unabated.

Finally, ASTRO continues unceasing efforts to rectify the broken RO Model. Despite pushing the start date to January 1, 2022, the reality is that the model is fatally flawed and deserves a fresh look by the new administration and, perhaps, going back to the drawing board. If there was ever a time when your participation in ASTRO's advocacy efforts was broadly needed, this is it!

There's so much more to say. Please reach out to me directly (ndmd1974@gmail.com) with your questions and concerns. I serve you!

SPECIAL*report*

BY LAURA I. THEVENOT,
ASTRO CHIEF EXECUTIVE OFFICER

ASTRO'S 2020 **YEAR IN REVIEW**

2020. WHAT A YEAR. Who could have imagined one year ago what our new normal would look like today? Despite the hurdles 2020 threw at all of us, I am so proud of the work the Society accomplished over the past year. Responding to the COVID-19 pandemic, with then-ASTRO President Thomas Eichler at the lead, ASTRO quickly produced many valuable resources for members who were, and still are, facing this public health emergency on the frontlines. From extensive FAQs, clinical guidance and webinars to expedited journal article publication and expert commentaries from those working directly with COVID patients, ASTRO utilized the expertise and experiences of our members around the world to quickly create and disseminate COVID-19 resources that remain available under the Daily Practice section of astro.org. In addition, we collaborated with a PPE supplier to make critical equipment available to members twice during the year. As the pandemic evolves, and hopefully soon dissipates, we will continue to provide resources, recommendations and guidance to support our members.

COVID-19 did not distract from ASTRO's mission to advance the field of radiation oncology. Over the past few years, concern around the job market and size of residency programs has emerged. While ASTRO cannot control the number of training programs or applications accepted, ASTRO has been in active communication with SCAROP, ADROP and ARRO regarding the data needed to inform the discussion. In addition, the Board of Directors recently issued a statement on this topic. I am pleased to report that in a recent ARRO Graduating Resident Survey, which received a 94% response rate from the 2020 graduating class, 89% of respondents reported high satisfaction with their job offers. On average, graduating residents had a median of five interviews and received two job offers. And when asked how well their training prepared them for independent practice, 90% responded they were satisfied. ASTRO continues to work side-by-side with ARRO to ensure residents' concerns are heard.

A large part of advancing the field is taking a hard look within to better understand how to improve recruitment and retention of Black and historically underrepresented minorities in candidates to residency programs. ASTRO is working to ensure that committees and councils provide opportunities for full engagement with all members, including those underrepresented in the field. As part of this effort, the Board approved the elevation of the Committee for Health Equity, Diversity and Inclusion (CHEDI) into a full ASTRO Council and with it, the associated two positions on the ASTRO Board. Ratification of this amendment to the ASTRO Bylaws will require a vote by membership later this year. The elevation of CHEDI to a full Council further demonstrates ASTRO's commitment to health equity for our patients, a stronger culture of inclusive excellence in our field, and supports our vision for a radiation oncology workforce that better reflects our diverse patient population.

In August, the long-awaited RO Model was released, largely ignoring many ASTRO recommendations. However, with indomitable persistence, ASTRO successfully convinced CMS to delay implementation to January 2022. We continue

to push for changes to the RO Model to make value-based care work best for our members. ASTRO continues to fight burdensome prior authorization practices and is building bipartisan support in Congress to reform prior authorization practices.

And finally, I cannot reflect on 2020 without mentioning the Annual Meeting. This was my 18th meeting, and so far we've had a hurricane, superstorm Sandy and blazing fires outside Los Angeles. I was thinking locusts would be next; for some reason pandemic was never on my list! Transitioning from the in-person to an all-virtual Annual Meeting was an incredible undertaking. In a virtual environment, ASTRO was able to offer educational content and the latest science, providing members with more than 200 CME credit opportunities. We were able to retain 110 exhibitors, who offered impressive virtual booths and product demonstrations. While we were able to maintain much of what you expect from the ASTRO Annual Meeting's science and content, we all missed the face-to-face networking and chance to catch up with friends from around the world. We hope to see everyone in Chicago in October and are working to make it a safe event for all.

Thank you for continuing to support ASTRO. This is a time when, with the many challenges we are all facing personally and professionally, you really take stock in what is important. I feel honored and blessed to lead ASTRO. I am so grateful to our leaders and Board who dedicate a great deal of time and energy to the Society and to you, our members, who volunteer countless hours to support the Society, all while treating patients. Thank you and best wishes for 2021!

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A unique year! ASTRO members share their insights in the 2020 Membership Survey

BY TIM SANDERS, ASTRO SENIOR RESEARCH ANALYST

THE ASTRO MEMBERSHIP SURVEY IS AN ANNUAL LOOK INTO HOW MEMBERS FEEL about their membership and the Society's initiatives, programs and direction. We truly appreciate the engagement of our ASTRO members. 2020 was a different year due to the challenges of facing a pandemic, and the 2020 survey included several questions about how the COVID-19 pandemic affected members. This survey was fielded from May 26 to July 21, 2020, pushed back a few weeks from our normal timeframe to capture as much information about the pandemic as possible. The web-based survey was completed by 1,376 ASTRO members for a response rate of 16.1%. Many reasons (including the pandemic) can be attributed to the slight decrease (<2%) in response when compared to the 2019 Membership Survey.

Who responded?

Of the 1,376 members who completed the 2020 Membership Survey, 76% are located in the United States. Of all members who completed the survey, 70% are radiation oncologists. Engagement from members, both from the United States and radiation oncologists, increased 5% from the 2019 survey. Medical physicists (15%) and radiation oncology (RO) residents (9%) are the second and third most reported profession (Figure 1).

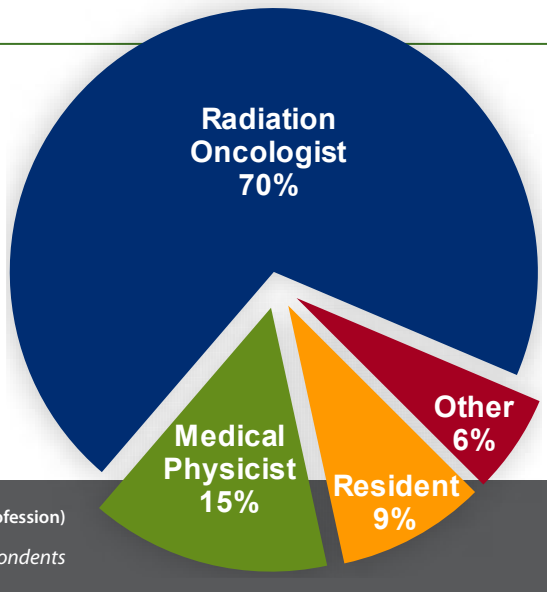


Figure 1: Respondent Demographics (Profession)

Profession breakdown of the 2020 Membership Survey respondents

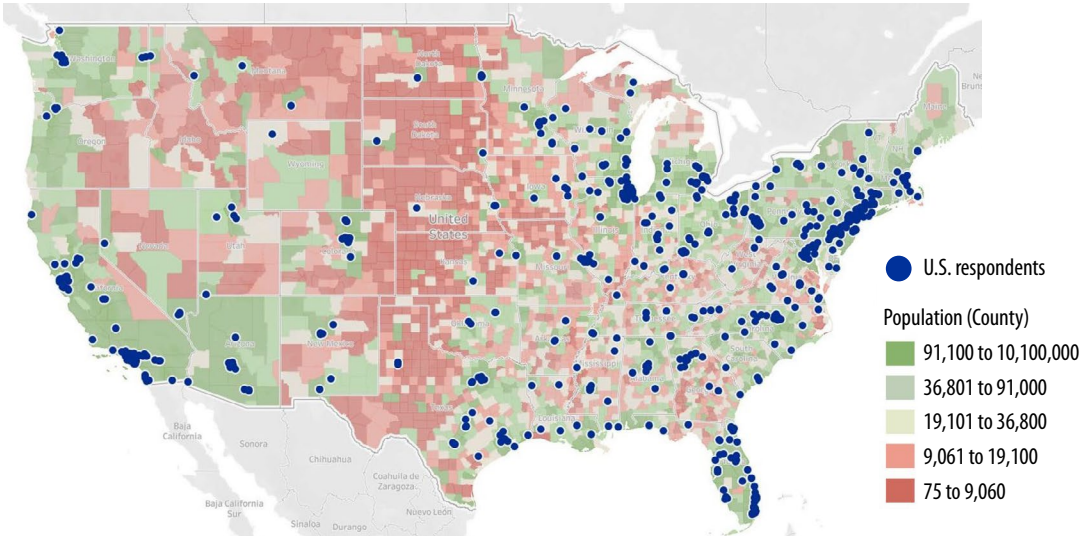
When we look across both our domestic and international respondents, half of all respondents practice at an academic setting, whereas only 39% practice in a private/community setting. When we look specifically at U.S. radiation oncologists, the academic/private practice split narrows, with 46% practicing at a private/community setting and 47% practicing in an academic setting. Across both domestic and international locations, the vast majority of respondents are hospital-based (88% international; 79% domestic).

Other demographic features of our respondents include:

- Slightly more than two-thirds of respondents are male.
- Respondents are experienced, averaging 17.8 years out of residency, spanning from less than one to 57 years.
- Domestically, respondents' engagement is greater in more populated areas, yet all states, including the District of Columbia, are represented in 2020 (Figure 2).
- 95% of respondents practice in metro areas, with only 5% practicing in non-metro/rural areas, mirroring the ASTRO membership as a whole (96% to 4%).

SOCIETY NEWS

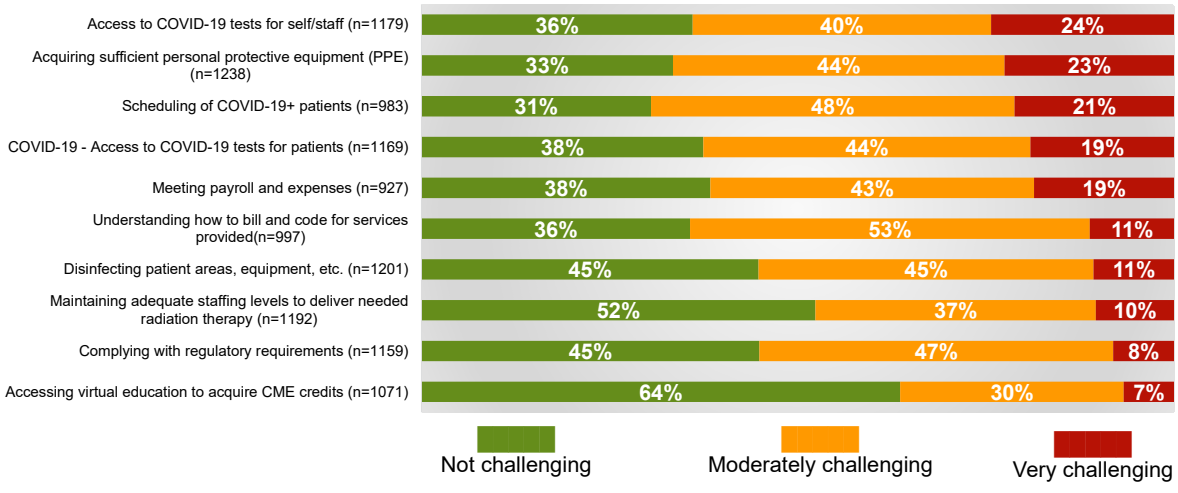
Figure 2: Geographical Distribution of the 2020 Membership Survey Respondents



U.S. respondents to the 2020 Membership Survey are located in more populated areas, mirroring the ASTRO membership database

Importantly, the respondents to the 2020 ASTRO Membership Survey represent our membership database on many attributes, including profession, gender, race/ethnicity, age, primary employer, practice location and geographic region, in addition to rurality. This representativeness gives us confidence that the survey results are reliable for ASTRO to use as we make decisions about future initiatives, programs and direction.

Figure 3: Challenges Faced by Respondents Regarding COVID-19



More than half of all respondents found all but one of these aspects at least moderately challenging due to the pandemic. Sorted by "Very Challenging"

COVID-19 and ASTRO members

The COVID-19 pandemic has affected many aspects within the field of radiation oncology. ASTRO included questions in the survey about the challenges, as well as specific ASTRO services provided, during the first few months of the pandemic. The top three challenges RO departments faced were: (Figure 3).

Continued on the following page

1. Scheduling COVID-19 positive patients.
2. Acquiring sufficient personal protective equipment (PPE).
3. Access to COVID-19 tests for self and staff.

ASTRO produced numerous resources as the pandemic hit that respondents found helpful. Respondents found ASTRO's clinical guidance most helpful during the first few months of the pandemic. Other resources respondents found helpful were ASTRO's COVID-19 information page on the ASTRO website, our advocacy, expedited journal article publication and our weekly ASTROgrams. The 2021 Membership Survey will take a deeper look at the far-reaching effects of the COVID-19 pandemic.

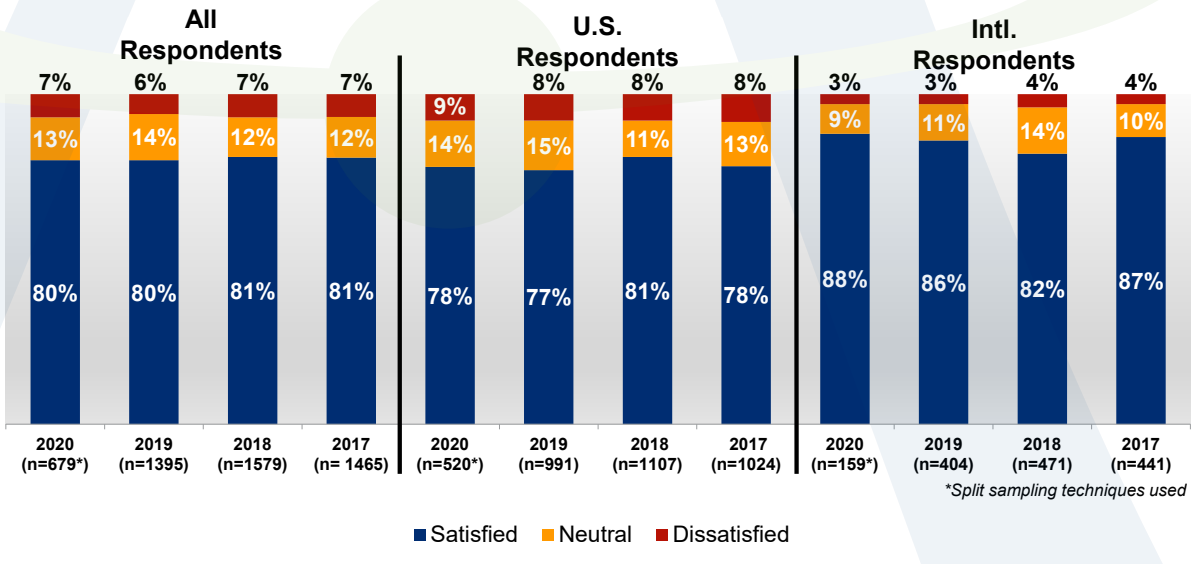
ASTRO also conducted a COVID-19 Practice Response Survey to understand and evaluate how radiation oncology practices were handling the pandemic. For more information, please see ASTRO's COVID-19 Practice Response Survey (ASTRO Impact Survey) media resources at www.astro.org.

Feelings about ASTRO

Satisfaction among all respondents has remained steady and high over the last four years (Figure 4). Radiation oncology residents report the lowest rates of satisfaction with ASTRO membership.

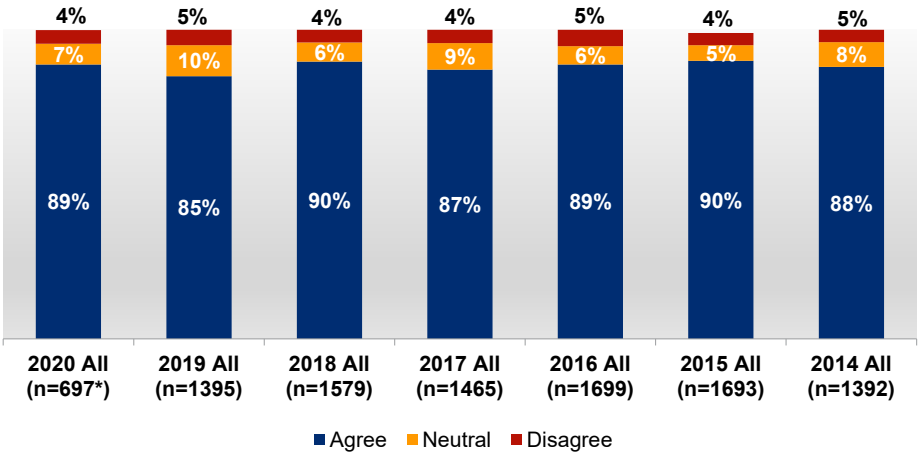
Each year, we ask ASTRO members if they find participation in ASTRO a good use of their time. Over the last seven years, this number has ranged 85-90% (Figure 5). In 2020, 89% of our members reported that they thought participation in ASTRO was a good use of their time, up 4% from 2019. This high level of volunteer engagement allows ASTRO to build initiatives and programs for all our members. Residents reporting dissatisfaction with ASTRO still rated participation in ASTRO as a good use of time.

Figure 4: Satisfaction with ASTRO Membership



Satisfaction with membership continues to stay high and consistent for all members with slight upticks for U.S. respondents

Figure 5: ASTRO Membership: A Good Use of Time?



Almost 9 in 10 respondents think that participation in ASTRO is a good use of their time
**Split sampling techniques used*

Importance of the functions ASTRO provides

Knowing what members find important in their ASTRO membership is crucial to understanding the wants and needs of our members. Every other year, we ask our members to rate the importance of ASTRO's core functions. These functions range from our advocacy, education and meetings to our journals, research and other programs. The most important function in 2020 among all respondents, both domestic and international, is to continue to publish scientific and practice journals, i.e., the Red Journal, *PRO* and *Advances*. U.S. radiation oncologists rate advocacy as the most important function, specifically, advocating on behalf of members for appropriate reimbursement.

Respondents' primary reason for being a member of ASTRO

When members were asked about their primary reason for being a member of ASTRO, several common themes emerged. The most common theme was ASTRO's education. This was followed by our journals, access and networking. Keeping up to date with field-related information and attending the Annual Meeting were also mentioned frequently (Figure 6). This, coupled with the functions mentioned earlier, give ASTRO a plethora of member services and benefits to build on moving forward.

Summary

ASTRO continues to use this feedback to inform and improve your membership experience and better the Society for the future. Thank you to everyone who took the time to complete the 2020 Membership Survey. The survey is sent out every summer, so don't miss it in 2021! Your input is essential to making ASTRO work best for you.

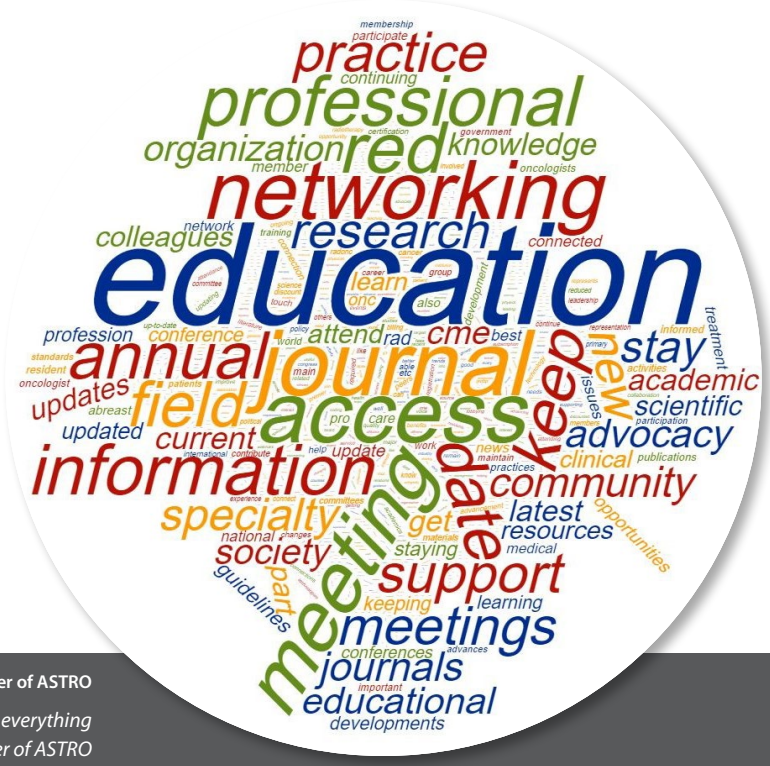


Figure 6: Primary reason for being a member of ASTRO

Respondents report "education," "journals" and "access" to everything radiation oncology as the primary reasons for being a member of ASTRO

Roundup of key abstracts from the 2020 ASTRO Annual Meeting

BY ANDREW KELLER, MD, AND SUSHIL BERIWAL, MD, MBA, FASTRO

NOW THAT THE 2020 ASTRO ANNUAL MEETING HAS CONCLUDED, it's time to reflect on some of the most exciting and noteworthy studies.

The CCTG SC.24/TROG 17.06 trial, a phase II/III trial that randomized patients with painful spinal metastases to 24 Gy in 2 fraction SBRT versus 20 Gy in 5 fraction CRT, demonstrated significant improvement in complete pain response favoring SBRT over CRT at three and six months. These findings are particularly noteworthy following RTOG 0631, which did not demonstrate improved pain response with single fraction SBRT to 16 or 18 Gy compared to single fraction EBRT to 8 Gy. As pain control is the primary objective of palliative radiation in this setting, the findings from SC.24 demonstrate that appropriately selected patients would likely benefit from 24 Gy in 2 fraction SBRT over CRT.

The most notable study presented from the gynecologic world was likely the PARCER trial, a phase III trial evaluating 3-D vs. IMRT for adjuvant radiation therapy for cervical cancer. This study demonstrated four-year grade 2+ late bowel toxicity of 19.2% in the IG-IMRT arm vs. 36.2% in the 3-D CRT arm (p=0.005). Complementing findings from the previously published TIME-C trial, which showed patient-reported significant improvements in acute GI morbidities, this study suggests a strong clinically meaningful benefit improvement in late GI effects with IG-IMRT in the post-operative gynecologic setting, making it a potential standard of care in this patient population.

The prostate cancer realm had several impactful studies as well. The FLAME trial was a multi-institutional phase III study, including 571 patients with intermediate- and high-risk prostate cancer, randomized to standard EBRT of 77 Gy in 35 fractions of 2.2 Gy to the whole prostate gland with or without simultaneous integrated boost (SIB) up to 95 Gy to visible tumor on multiparametric MRI. OAR constraints were prioritized over SIB dose. At a median follow-up of 71 months in a patient cohort that was 84% high-risk, five-year bDFS was 93% in the SIB arm vs. 86% in the standard EBRT arm. Late grade 3+ GI and GU toxicity was similar in both arms. Given the impressive five-year bDFS with dose escalation in a predominantly high-risk cohort, SIB to gross intraprostatic tumor with some type of functional imaging may eventually represent an effective option.

A combined analysis of the prostate-only arms of RTOG 9413 and a similarly designed Canadian trial from Malone et al., which randomized patients to neoadjuvant/concurrent or concurrent/adjuvant ADT, challenged ideas regarding sequencing of ADT. With median follow up of 14.9 years and inclusion of 1,065 patients, adjuvant ADT was shown to be superior to neoadjuvant ADT in terms of BF (15-yr 33% vs. 43%, p=0.002), DM (15-yr: 12% vs. 18%, p=0.04), and PFS (15-yr: 36% vs. 29%, p=0.01), with similar overall survival and no increase in late GI or GU toxicity. This analysis may change sequencing of ADT with radiation therapy with higher use of adjuvant ADT in comparison to neoadjuvant approach.

Finally, additional supporting data for use of advanced imaging for prostate cancer emerged, with the EMPIRE-1 trial being the most significant. In this phase II/III trial, patients with biochemically recurrent prostate cancer were randomized to salvage RT with conventional imaging alone vs. fluciclovine (^{18}F) PET/CT-guided XRT. The 165 patients enrolled had a median PSA of 0.34 ng/mL. Use of fluciclovine (^{18}F) PET prior to salvage XRT resulted in 35.4% rate of decision changes. Use of conventional imaging alone resulted in significantly worse biochemical control (HR 2.04, 95% CI 1.06-3.93, p=0.033). This trial was the first of its kind to demonstrate improvement in treatment outcomes with addition of fluciclovine (^{18}F) PET scan in prostate cancer prior to salvage XRT. Future studies are being done with more sensitive PSMA scan to see if PSMA can detect disease at an even lower PSA threshold.

Andrew Keller, MD, is a PGY-4 radiation oncology resident at UPMC Hillman Cancer Center in Pittsburgh.

Sushil Beriwal, MD, MBA, FASTRO, is a professor of radiation oncology at the University of Pittsburgh School of Medicine and residency program director at UPMC Hillman Cancer Center in Pittsburgh.

Five companies elected to ASTRO's Corporate Advisory Council

ASTRO'S CORPORATE MEMBERSHIP has elected the following companies to serve on the 2021 Corporate Advisory Council: GE Healthcare and Siemens Healthineers, both newly elected, and Standard Imaging and ViewRay, re-elected for another term. We are also pleased to announce that AstraZeneca will serve a second term. Having a pharmaceutical company on the Council is important, as it provides their unique industry perspective and contribution to the work of the Council.

The Council is a representative group of the Corporate Membership at-large, with a proportional mix of large and small companies from the Corporate Membership base. Seats on the Council are held by high-level decision makers within the corporations and represent a broad cross section of the industry.

The Council allows for collaboration between ASTRO and its corporate members by focusing on issues and initiatives of mutual concern in radiation oncology. Priorities include increasing awareness of radiation therapy and advancing the science and practice of cancer treatment and patient care. In cooperation with ASTRO leadership, the Council convenes several times a year via conference call and meets in-person at ASTRO's Annual Meeting.

All corporate members can nominate their company to serve on the Council. Nominations are accepted every fall with elections conducted during the winter. For more information about the Council and/or Corporate Membership, please contact Joanne DiCesare at joanne.dicesare@astro.org or 703-839-7398.

COMPANY	REPRESENTATIVE
AstraZeneca	Susan Galbraith, PhD
Blue Earth Diagnostics	Terri Wilson
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Lap Laser	Trent van Arkel
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Varian	Chris Toth
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Sun Nuclear	Jeff Simon
Xstrahl	Adrian Treverton
GE Healthcare	Sam Kandala
Standard Imaging	Eric DeWerd
Siemens Healthineers	Martin Tasler
ViewRay	Shar Matin

In Memoriam

ASTRO has learned that the following members have passed away. Our thoughts go out to their family and friends.

Alistair Baillie, PhD, Kelowna BC, Canada

Alan J. Stark, MD, Barrington, Rhode Island

The Radiation Oncology Institute (ROI) graciously accepts gifts in memory of or in tribute to individuals. For more information, visit www.roinstitute.org.

Shapers of Our Future: (Re)Defining the Radiation Oncologist

BY CLAIRE Y. FUNG, MD, MS, AND RONALD D. ENNIS, MD, FASTRO

IN THIS AGE OF RAPIDLY GROWING MEDICAL KNOWLEDGE and technological capability, radiation oncologists (ROs) are critical drivers of scientific advances and high quality patient-centered cancer care. To help assess ROs' perspective on their desired scope of practice to best meet the needs of today's patients, ASTRO conducted a survey on U.S. ROs' views on the ideal role of the RO, scope of practice and interest in service expansion.[1]

The online survey was distributed to 3,822 U.S. RO members of ASTRO during spring 2019. It generated 984 complete responses (26% response rate) for analysis.

Most respondents agreed that "ROs should be leaders in oncologic care," with only 4% disagreeing. Regarding the ideal approach to patient care, the majority (82.5%) indicated that their ideal was "to provide an independent opinion on radiation therapy and other treatment options (ideal = comprehensive opinion)," while for 16.1% it was "to provide an independent opinion on radiation therapy but not outside of it (ideal = RT-only opinion)" and for 1.4% it was "to provide radiation therapy at the request of referring physicians (ideal = RT on request)."

Not surprisingly, few (18.2%) reported their actual practice matched their ideal approach *completely*. The vast majority of respondents reported that their individual actual practices were a mix of the three approaches: providing, on average, a "comprehensive opinion" (39.0%) of the time, a "RT-only opinion" (37.0%) of the time and "RT on request" (24.0%) of the time. Respondents most commonly practiced according to the approach they had identified as their ideal, but, on average, provided radiation on request (the least favored ideal scenario) a quarter of the time.

The top reasons for a mismatch between actual practice and ideal approach were concern that a potential disagreement with the referring physician about treatment would cause alienation and change in referral patterns (26.6%) and concern that the referring physician would not be receptive to an independent opinion (14.8%). These very real concerns that asserting independence would adversely affect the relationship with the referring physician reflect a common power dynamic in radiation oncology practice.

Power, as such, relates to who controls the patient flow. In the U.S., a new cancer patient's first point of entry to the oncologic care path is often the surgeon, since surgery historically has been the first, and sometimes perceived to be the only, effective step in cancer treatment, in addition to the surgeon's common role in performing a diagnostic biopsy. With dramatic shifts in treatment paradigms across many diseases, multimodality therapy is often the norm, with modality sequencing a discussion point rather than a foregone conclusion. Nonetheless, the cancer patient's first encounter is still commonly the surgeon, sometimes the medical oncologist and, less commonly, the RO. The RO, being downstream, therefore holds a weaker political position.[2] In addition, cultural patterns of behavior may also undermine the RO's influence.[3] Surgeons, at the top of this hierarchy tend to speak confidently, while the status-disadvantaged may feel pressured, consciously or subconsciously, to acquiesce, even if they disagree, in order to avoid confrontation. To be sure, medicine has made huge strides in teamwork and professionalism, and such hierarchies are crumbling. Nonetheless, broader awareness of these potential undercurrents will benefit all stakeholders.

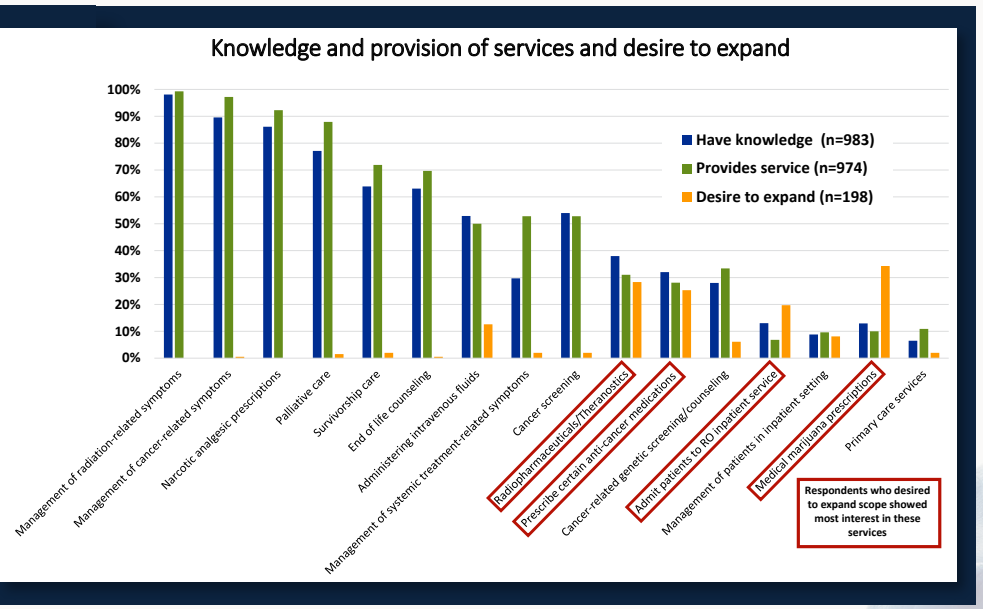
How can ROs improve their situation? One solution is to be the first point of oncology contact for the patient after a cancer diagnosis. In prostate cancer and head and neck cancer, for example, this would be entirely logical. Additionally, leadership in multidisciplinary clinics and conferences can also promote a strong, confident radiation oncology voice.

But ultimately the goal is not competition but collaboration among the specialties. A culture of mutual respect and partnership among medical, radiation and surgical oncologists would allow all disciplines to serve as co-leaders in cancer care and encourage ROs to practice with greater alignment with their ideal. Development of the social skills needed to navigate the interdisciplinary relationships is paramount. To this end, ASTRO presented the well-received "Leadership and Emotionally Intelligent Communication" masterclass at the 2020 Annual Meeting.

On the topic of practice scope, a majority of ROs provided management of radiation-related symptoms (99.3%), management of cancer-related symptoms (97.2%), narcotic analgesic prescriptions (92.3%), palliative care (87.9%), survivorship care (71.9%), end-of-life counseling (69.7%), administration of intravenous fluids (50%), management of systemic

treatment-related symptoms (52.8%) and cancer screening (52.8%). Between one-quarter to one-third of respondents provided cancer-related genetic counseling (33.4%), administered radiopharmaceuticals/theranostics (31.0%) or prescribed certain anti-cancer medications, hormonal or targeted systemic therapy (28.1%), for example. One in ten provided primary care services (10.9%) or medical marijuana prescriptions (10.0%).

Respondents with an interest in expanding practice scope (21.4%) were, on average, earlier in their career (average years in practice 13.3) than those who indicated no interest (average years in practice 17.2, p<0.001). The areas that held the most interest for expansion were medical marijuana prescribing, radiopharmaceuticals administration, and prescribing of certain anti-cancer medications. Coincidentally, <40% of all participants felt that they had the knowledge to provide these particular services. Participants believed that the top challenges to expanding services included: political infeasibility (49.0%), insufficient training (39.0%) or time to acquire expertise in that area (28.6%), and lack of support from leadership (19.5%). Among the respondents reporting no interest in expanding the scope of services, their reasons were insufficient time (59.4%), belief that this was not within a RO's role (28.8%), insufficient training (27.9%), and lack of interest (27.2%).



It is of interest that the services with the largest appeal for expansion represent emerging and evolving areas in which respondents admitted to lacking knowledge. The stronger interest among early-career respondents to expand services might suggest an eagerness for a means to boost radiation oncology utilization amid angst regarding workforce oversupply, which is more frequent among early-career ROs than late-career physicians.[4] In support of these interests, ASTRO held master classes on medical marijuana and radiopharmaceuticals at the 2020 Annual Meeting. Overall, these results provide insight into U.S. ROs' scope of practice and views on the ideal role of the RO. For most ROs, the ideal approach would be to provide an independent opinion on treatment options, but barriers such as concern of alienating referring physicians prevented many from fully living up to that ideal. Actual practice commonly comprised a mixed approach, including delivering radiation at the referring physician's request — the least favored scenario — one-quarter of the time, highlighting the influence of interspecialty politics on practice behavior. ROs need to advocate for greater institutional policies supporting professionalism and teamwork. In addition, ROs must become more adept at managing the complex interspecialty political dynamics and recognizing the advantages of early contact with the patient.

The study also identified interest, particularly among early-career ROs, in broadening services into radiopharmaceuticals administration and medical marijuana and anti-cancer medications prescribing. These nontraditional domains present opportunities to address unmet needs in the cancer patient's journey and elevate radiation oncology within the increasingly value-based U.S. health care system.

Dr. Fung is a radiation oncologist at Beth Israel Deaconess Medical Center and immediate past chair of the ASTRO Workforce subcommittee. Dr. Ennis is vice chair for Network Integration and Quality Radiation Oncology at the Rutgers Cancer Institute of New Jersey.

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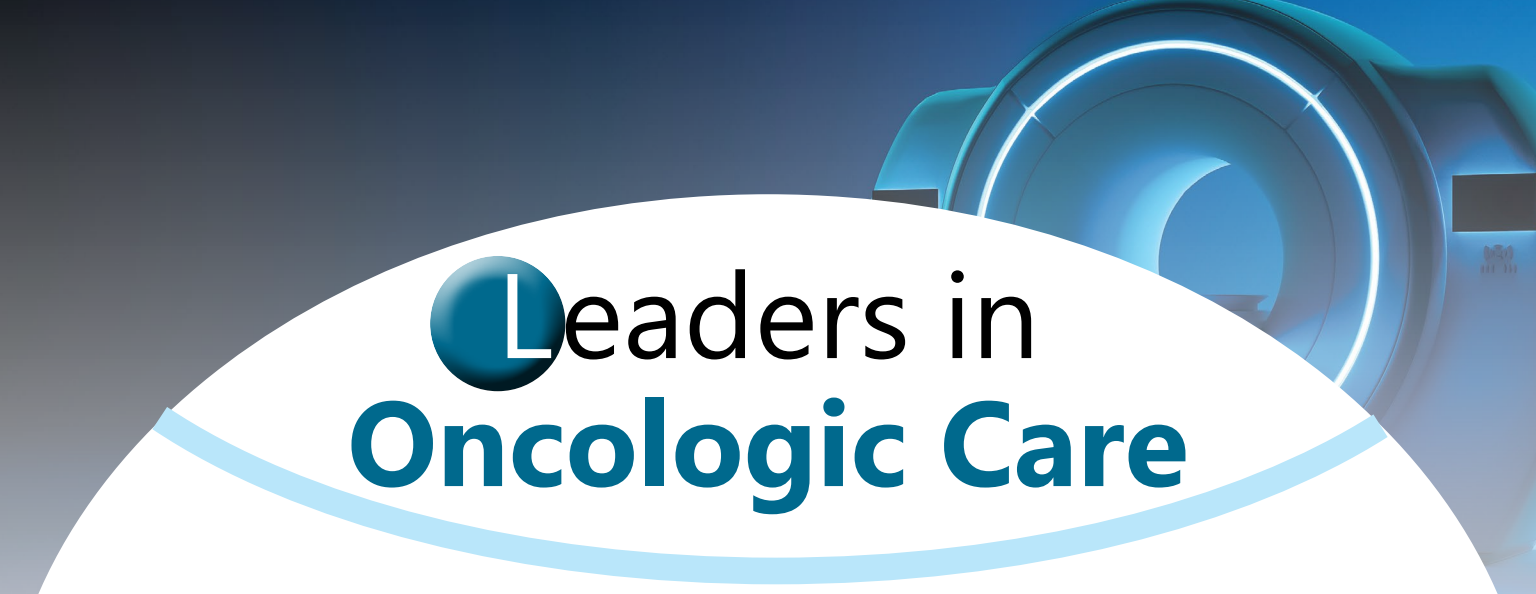

Leaders in Oncologic Care

Bottom Feeders or Fearless Leaders? Clinical Radiation Oncology in the Modern Era

BY TREVOR J. ROYCE MD, MS, MPH, AND LAWRENCE B. MARKS MD, FASTRO

THE FORCES MOLDING CONTEMPORARY CANCER CARE ARE FORMIDABLE. Disruptive examples include the shift towards value-based care (e.g., CMS's mandatory RO Model), therapeutic parsimony (e.g., observation in select patients with breast and prostate cancer; shorter fractionation schemes across disease sites) and telehealth catalyzed by COVID-19. Further, unprecedented advances in radiation dose-delivery precision (e.g., via SBRT, VMAT, IGRT, adaptive planning) for local/metastatic disease, integrating radiation with novel systemic/biologic agents[1] and in the fields of imaging, genomics, machine learning and artificial intelligence, all expand the frontiers of our specialty. These forces bring the apprehension of change and optimism of opportunity.

Such an environment logically stimulates existential dialogue. Fung and colleagues recently surveyed ASTRO's U.S. physicians on both what it means to be a radiation oncologist and what our role is in patient care.[2] Their results reveal the current conceptions of our radiation oncology world and hint at its future.

A primary finding by Fung and colleagues is that while 83% of respondents feel the ideal approach to patient care is to provide "an independent opinion on radiation and other treatment options" (i.e., practicing holistic oncology), their actual practice fully matched this ideal in only 18.2% of respondents. For the rest, their actual practice did not always match the ideal, and 37% of the time they provided a clinical opinion only on the role of radiation therapy (i.e., practicing niche oncology), and 24% of the time they provided radiation "on request" (i.e., practicing as a technician). These findings raise two critical questions: Why is there a chasm between the majority's ideal practice and actual practice? And how can we bridge the gap?

The first question is addressed in part by the survey results, with the most commonly stated reasons being concern that differences of clinical opinions would alienate the upstream physician and presumably result in fewer downstream patient referrals, the lifeblood of the specialist. To borrow from Edward Halperin, MD, in retelling a surgical chair's characterization of radiation oncologists, these results portray us as "clinical catfish: the bottom-feeding garbage-eater at the end of the clinical referral chain."[3]

The second question strikes at our existential core and forces us to re-examine the role of radiation oncologists. We believe that bridging the gap between ideal and actual clinical practice requires a return to the foundational aspects of clinical medicine (as has been noted by others and for many years, including the late Morton Kligerman, MD).[4] This is illustrated by the maxim often attributed to Samuel Hellman, MD, FASTRO: Be a good person, then a good doctor, then a good oncologist, then a good radiation oncologist, in that order.

Specifically, being considered integral members of the oncology care team requires dependable hard work and holistic care. One approach to actualizing this is with inpatient care. Our lack of an admitting inpatient service distinguishes U.S. radiation oncologists from many referring physicians. Whether we should desire admitting privileges is beyond the scope of this article, but fewer than 20% of radiation oncologists surveyed manage, or desire to manage, inpatients. At a minimum, it is essential that we be engaged participants with inpatient care to be considered an integral care team member. This includes seeing in-house consultations, and rounding on one's admitted patients, in their

Continued on the following page

inpatient rooms rather than "insisting that the inpatient be brought to the radiation oncology clinic."[3]

A second related example is adapting a perspective that there is no such thing as an "inappropriate consult." Rather, all consults represent a request for us to contribute to a patient's oncologic management, including but not limited to issues related to radiation. Opinions on oncologic management and the role of radiation are not mutually exclusive, and both fall under the purview of a competent radiation oncologist, who has had at minimum four years of oncology-specific graduate medical education. In many ways, our training, which encompasses all disease sites, provides us with unique inter-disease perspectives that can provide meaningful, integrated management decisions.

A third example is in our approach to multidisciplinary tumor boards. We should be active participants (i.e., visible in the front row and speaking our data-based opinions) who regularly attend not only when there are cases that "need radiation input." Our imaging-based practice provides us with a skillset for oncologic interpretations of diagnostic imaging, and our input can complement that of our diagnostic radiology colleagues. For example, radiation-induced normal tissue injury (e.g., manifesting as symptoms or imaging changes) can be misinterpreted as recurrent tumor. Often, we alone know where our beams have gone.

A fourth example is how we choose to approach supportive and palliative care. Following all patients, palliative and curative alike, can facilitate advance care planning, and ensures the opportunity to care for (and appreciate) the acute and chronic toxicities of our modality. Indeed, with short palliative courses, the acute effects often peak *after* radiation is completed. Being available to address these potential toxicities (e.g., via obtaining labs, giving intravenous fluids, prescriptions, or coordinating the necessary supportive services) sends an important message to our oncology colleagues. This is opposed to simply turfing them to the nearest emergency department at the first sign of distress. Of note, >50% of radiation oncologists surveyed reported providing these sorts of services.

Beyond the immediate effect of establishing oneself as an integral member of the care team, an inevitable consequence of these approaches is that radiation oncologists will be perceived as leaders in cancer care. Is this consequence desirable? The answer is a resounding yes: nearly all respondents (96%) felt that "radiation oncologists should be leaders in oncologic care." It is thus plausible that working toward this can help close the gap between the ideal and actual clinical practice.

The definition of "leader" in this context is vague and personal: leadership roles exist on a spectrum from within the multidisciplinary care team to beyond the cancer center. Regardless, leadership training resources are increasingly available to the membership. Examples include the 2020 ASTRO Annual Meeting Master Class in Leadership and ASCO's annual Leadership Development Program (in which many radiation oncologists have participated). The Cleveland Clinic Department of Radiation Oncology has integrated components into their standard curriculum.[5] While there are relatively few radiation oncologists in the upper leadership echelons of academia, there are several, and thus there is ample precedent. The sky is the limit! Many radiation oncologists have shed the shackles of our name and taken on extraordinary roles beyond the cozy confines of the basement department.[6,7] Perhaps the most visible contemporary examples are the two radiation oncologists currently serving as commissioner and deputy commissioner of the Food and Drug Administration, leading the regulatory side of the nation's vaccine development and deployment during a once-in-a-century global pandemic.[8]

Ultimately, how we respond to the formidable forces shaping contemporary cancer care is in our hands — whether we go the path of the bottom-feeder or of the fearless leader — and a return to the foundational aspects of clinical medicine may help show us the way.

Trevor Royce, MD, MS, MPH is an assistant professor in the Department of Radiation Oncology; Lawrence Marks, MD, FASTRO, is chair of the Department of Radiation Oncology, both at the University of North Carolina at Chapel Hill.

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BY DANIEL E. SPRATT, MD

Radiation Oncology as the Multidisciplinary Team Leader

MULTIDISCIPLINARY CARE RESULTS IN SUPERIOR OUTCOMES when compared to single provider sequential care. The reason is multi-factorial due to improved patient convenience by seeing multiple specialists at once, which can also reduce financial toxicity of taking multiple days off from work or finding care for family members; accelerating treatment decisions from reducing sequential visits, patients are seen by all relevant specialties; it builds a respect between radiation oncology and the other specialists and keeps the focus centered on the patient. I believe that in an optimal care delivery system it would be patient and disease-type centered, rather than department centered.

Radiation oncology can and should serve as a key driver of multidisciplinary care. I was fortunate enough to have trained under Josh Yamada, MD, Brett Cox, MD, and Mark Bilsky, MD, at Memorial Sloan Kettering (MSKCC). Drs. Yamada and Cox are radiation oncologists and Dr. Bilsky is a neurosurgeon, and together they started a multidisciplinary clinic in spine oncology. During my faculty orientation at the University of Michigan, I was in line to get my ID badge, and right behind me was Nick Szerlip, MD, a neurosurgeon who serendipitously did his spine oncology fellowship at MSKCC. After a few months, we both realized there was not a true multidisciplinary spine oncology program at U-M (yet). Like 99% of centers in the United States, care delivery was segregated within the departments of radiation oncology and neurosurgery. We decided we needed to change this, and despite many naysayers that said it wouldn't work, we set out to prove them wrong.

In December 2015, we started the official University of Michigan Spine Oncology Program. It heavily leveraged radiation physics (Kelly Paradis, PhD, and Martha Matuszak, PhD), dosimetry (Paul Archer), advanced practice providers (Amyre Mitchell, NP), interventional radiology, and physical medicine and rehabilitation (PM&R). Our team established comprehensive workflows and triage for the multitude of complex spine cases and built a consensus framework for managing these patients (Spratt DE et al., Lancet Onc 2017). We were both very clear in our goal: to give the best patient care. That is how we would grow the program and grow each of our respective clinical services. It was not a turf war in any way, and from day one we committed to focusing on the patient. If the program succeeds, we succeed, and, more importantly, the patient wins. For this reason, our motto has always been that surgery for spine metastasis and cord compression is not oncologic. Almost 100% of the time, even after major spine surgeries, the cancer will recur. Surgery has real potential side effects that should be recognized. The goal of surgery, therefore, is to allow optimal high doses of radiotherapy delivered as SBRT to eradicate the disease, to stabilize the spine or provide rapid decompression. However, and very importantly, I also fully recognize what radiation can't do: it can't stabilize the spine, reduce mechanical pain, heal a fracture, rapidly relieve cord compression or give sufficiently high doses to tumors abutting the spinal cord without damaging the cord. We heavily rely on PM&R and interventional radiology for vertebroplasty, and these specialties are likely used more than either surgery or radiation to help our patients. We are patient centered, not department centered.

Is it possible for radiation oncology to have a driver's seat in oncology? Absolutely. However, this takes work, time and leadership. Our spine multidisciplinary clinic began during one of my protected research days until it grew big enough to be a full-fledged program. My advice is to always focus on the patient and not on giving radiation therapy. They often may be one in the same, but at times they won't be. If referring providers know you will use your best judgement and avoid RT when appropriate, they will also listen to you when you recommend RT. Rather than trying to convince people with data, let them be part of the team and show them your results. Nothing is more powerful than a patient's voice.

Daniel Spratt, MD, is a professor of radiation oncology, a Laurie Snow Endowed Professor and associate chair of clinical research at the University of Michigan.

BY WILLIAM SMALL JR., MD, FASTRO

Radiation Oncology Leading the Cancer Center

RADIATION ONCOLOGISTS (ROS) ARE UNIQUE in the multidisciplinary field of oncology. We are highly trained clinicians, and, in many disease sites, we provide the primary treatment modality leading to long-term cures. We have the honor and privilege of taking care of people at a time in their lives that often can be extremely difficult for not only the patient but their entire family.

Our field has led improvements in survival in multiple malignancies, and with the advent of aggressive treatment of oligometastatic disease and the emergence of radiopharmaceuticals, we now are expanding our role in oncology.

My own expanded role in leading a cancer center began when after nearly three decades at Northwestern, I made the difficult decision to move to Loyola to become the chair of radiation oncology. The last seven years as chair have been the most exciting and fulfilling time in my career. I realize that if you recruit and retain talented faculty and give them mentorship and opportunity, growth of the department is inevitable. We have been able to find niches that have made our department unique, including advanced brachytherapy treatments, imaging research in physics, unique combinations of cytotoxic therapies and radiation, MRI-guided therapy, intraoperative radiation and the treatment of oligometastatic disease.

The Department of Radiation Oncology at Loyola is an integral part of Loyola's Cardinal Bernardin Cancer Center (CBCC). The CBCC has a long history of innovation and research paving the way for new therapies in hematological malignancies, solid tumors and a culture of clinical research. The CBCC has also developed its own CAR-T program and explored dendritic cell vaccines in ovarian cancer among many other achievements. In 2018, Dr. Patrick Stiff, a remarkable individual and leader in the field of hematological malignancies and bone marrow transplantation, made the decision to step back from administration. I was approached for this role with a mandate to continue Patrick's work and make CBCC even more competitive for an NCI Comprehensive Cancer Center grant.

When I reflected on this opportunity, I thought about the role of an RO in a cancer center that includes basic, translational and clinical researchers. ROs have markedly expanded our role in oncology; we interact with all manner of clinicians and scientists and as a specialty have a strong culture of innovation and research. Expanding our role to acting as cancer center directors is a natural evolution for our profession and, I believe, a benefit for oncology in general.

When I am asked to reflect on what skills I have acquired along the way that may have led to being asked to take on this wonderful opportunity, I think of various leadership positions I have held. These opportunities helped to develop the skills necessary to run a complex matrix of departments, clinicians and researchers. In particular, being the chair of the Gynecological Cancer Intergroup (GCIG) necessitated leading a large and diverse organization to advance gynecological research worldwide. Leading by consensus, getting leaders in a position for success and enacting strategic planning are all necessary skills for a cancer center director.

The last two years in the dual role of department chair and cancer center director have been personally challenging in terms of time management and priorities, as I have continued to carry a significant clinical load. Furthermore, my perspective has changed. As a department chair, I advocated primarily for the field of radiotherapy. As a cancer center director, I now have a duty to advocate for every aspect of oncology, with a focus on innovating along the entire spectrum of cancer control, research and treatment.

I would encourage young faculty interested in cancer center leadership to establish relationships with all levels of personnel involved in administration and research to develop an understanding of the whole spectrum of cancer. Most importantly, you must think big, understand our ultimate goal is to reduce or eliminate the burden of cancer and believe that you can be the difference.

It is incredibly fulfilling and exciting to be involved in every aspect of cancer care, with the ultimate goal of reducing, if not eliminating, the human burden of this terrible disease. My mother died of rectal cancer and I promised her I would do whatever I could to cure cancer. I think about that promise every day and, as a cancer center director, I can accomplish even more to try to make that promise a reality.

William Small Jr., MD, FASTRO is director of the Cardinal Bernardin Cancer Center and chair of radiation oncology at Loyola University Medical Center.

BY STEPHEN S. NIGH, MD

Relationships are Everything: Maximizing the Scope of Practice by Serving Others

Trust • Respect • Collaboration • Teamwork

IN A RECENT SURVEY ON THE SCOPE OF PRACTICE OF U.S. RADIATION ONCOLOGISTS, nearly everyone agreed that "ROs should be leaders in oncologic care," but only 18.2% felt actual practice matched this ideal.

As I reflected upon this and other questions, the concept of "How can I do this better?" came to mind. Is your scope of practice where you would like it to be? What can you do to change it?

As a practicing radiation oncologist in a community hospital setting, I believe our practice is an exception. We have striven and succeeded to be leaders in oncology care at our center. We all have our mentors. I have been fortunate enough to learn from stalwarts such as Eli Glatstein, Allen Lichter, Patricia Eifel, Herman Suit, Richard Evans, Carl Mansfield, Gilbert Fletcher and Jay Harris, to name a few — who helped shape my view of leadership in oncology. Our colleagues in medical and surgical oncology frequently look to us for co-managing patients, thanks not only to their great respect for our clinical acumen, knowledge and trust in our abilities, but also because of our excellent relationship with them.

We actively lead and participate in weekly tumor boards and multidisciplinary clinics. We hold positions of leadership in the Cancer Committee and lead the hospital's Oncology Service-line. By sub-specializing in the care of prostate and head and neck cancer patients, our colleagues in urology and ENT, respectively, are more willing to refer patients to us, knowing that exceptional care close to home is in their patients' best interest. It's similar in breast, lung and gynecologic patients. Through expertise, teamwork and collaboration, we elevate the care of patients as we raise the scope of our practice to reach more people, who in turn benefit from this multidisciplinary care.

Here are some of the ways we have achieved this level of engagement:

Clinical leadership: In addition to active involvement in multidisciplinary tumor boards and clinics, get involved in your center's cancer committee and site-specific program leadership committee. Offer to co-lead or serve on your hospital's palliative care team.

Patient access and visibility: Having nurse navigators can help patients see all the specialists involved and ensure multidisciplinary participation, in addition to timely care and a better patient experience. Eliminate barriers to care, allow easier access to care for patients and referring physicians. Organize physician-led community outreach events, educational functions and disease-specific support groups. Look for unmet needs in the patient's journey.

Communication: Improve rapid communication and availability among physicians, nurses and other key staff via secure texting and shared contacts. This includes primary care physicians who reach out directly with referrals.

Continuous Quality Improvement (CQI): The cornerstone of the practice has to be quality of care and constantly asking yourselves: How can we do this better?

Initiate innovative programs: This can be oncology specific – the precision medicine tumor board – or more general ones like the Schwartz Center Rounds.

Last, but not least, celebrate your department staff often.

I have been blessed to practice medicine in a culture where patients always come first. I am humbled daily by the trust of patients and referring physicians alike and challenged to do my part to preserve the unique culture of respect and caring that exists at my institution. Relationships are everything. If we are to elevate our specialty within the increasingly value-based U.S. health care system to touch more patients' lives, we have to continually find answers to the question: How can we do this better?

Stephen S. Nigh, MD, is the medical director of the Oncology Service-line, at Radiation Oncology Associates, Northwest Community Hospital, Arlington Heights, Illinois.

STAGE III NSCLC

4 YEARS MEDIAN OVERALL SURVIVAL IN UNRESECTABLE STAGE 3 NSCLC

4 IN 3

Indication

IMFINZI is indicated for the treatment of adult patients with unresectable Stage III non-small cell lung cancer (NSCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy.

Select Safety Information

There are no contraindications for IMFINZI® (durvalumab).

Immune-Mediated Adverse Reactions

Important immune-mediated adverse reactions listed under Warnings and Precautions may not include all possible severe and fatal immune-mediated reactions. Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue. Immune-mediated adverse reactions can occur at any time after starting treatment or after discontinuation. Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions.

In a post-hoc analysis

IMFINZI® (durvalumab):

UNPRECEDENTED 4 YEARS MEDIAN OVERALL SURVIVAL

in unresectable Stage 3 NSCLC following chemoradiotherapy[1]*

47.5 MONTHS
WITH IMFINZI (95% CI, 38.4-52.6)[1]

VS

29.1 MONTHS
WITH PLACEBO (95% CI, 22.1-35.1)[1]

Primary analysis at 2 years: Median OS not reached vs 28.7 months for placebo (HR=0.68; *P*=0.0025)[2†]

Safety and tolerability

- Serious, potentially fatal risks were seen with IMFINZI; serious adverse reactions occurred in 29% of patients receiving IMFINZI and 23% receiving placebo[3]
- The most frequent serious adverse reactions (≥2%) with IMFINZI were pneumonitis or radiation pneumonitis (7%) and pneumonia (6%). Fatal pneumonitis was <2% and was similar across arms[2]
- The most common adverse reactions (≥20%) with IMFINZI were cough, fatigue, pneumonitis or radiation pneumonitis, upper respiratory tract infections, dyspnea, and rash[2]
- Discontinuation rates due to adverse events (regardless of causality) were 15% in patients receiving IMFINZI and 10% in patients receiving placebo[3]

Learn more at IMFINZIhcp.com/pacific

NSCLC=non-small cell lung cancer; CI=confidence interval; OS=overall survival; HR=hazard ratio; CRT=chemoradiotherapy; WHO=World Health Organization; PFS=progression-free survival; RECIST=Response Evaluation Criteria in Solid Tumors; BICR=blinded independent central review; NR=not reached.

Study Design: The PACIFIC study was a large, Phase III, randomized, double-blind, placebo-controlled, international study of 713 patients with unresectable Stage III NSCLC who had not progressed following concurrent, platinum-based CRT. Patients had completed at least 2 cycles of concurrent CRT within 42 days prior to initiation of the study drug and had a WHO performance status of 0 or 1. Randomization at enrollment was stratified according to age, sex, and smoking history. Patients were randomized 2:1 to receive 10 mg/kg IMFINZI or placebo every 2 weeks for up to 26 doses (12 months) or until unacceptable toxicity or confirmed disease progression. Coprimary endpoints were PFS (measured based on RECIST v1.1 criteria by BICR) and OS.[2,3]

*The post-hoc 4-year OS analysis was conducted at ~4 years after last patient was randomized and was not powered to show statistical significance. Reduction in the risk of death vs placebo was 29% (HR=0.71; 95% CI, 0.57-0.88). OS rates with IMFINZI vs placebo were: 83% (95% CI, 79.4-86.2) vs 75% (95% CI, 68.5-79.7) at 12 months, 66% (95% CI, 61.8-70.4) vs 55% (95% CI, 48.6-61.4) at 24 months, 57% (95% CI, 52.3-61.4) vs 44% (95% CI, 37.0-49.9) at 36 months, and 50% vs 36% at 48 months.[1,4]

†The primary 2-year OS analysis was conducted after 299 deaths for 42% maturity (61% of targeted events) with a median follow-up of 25.2 months. Reduction in the risk of death vs placebo was 32% (95% CI, 0.53-0.87). Median OS was NR with IMFINZI (95% CI, 34.7-NR) vs 28.7 months with placebo (95% CI, 22.9-NR).[1,5]

Please see additional Select Safety Information and Brief Summary of complete Prescribing Information on adjacent pages.

IMFINZI®
durvalumab
Injection for Intravenous Use 50 mg/mL

Select Safety Information (continued)

Immune-Mediated Adverse Reactions (continued)

Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate. Withhold or permanently discontinue IMFINZI depending on severity. See Dosing and Administration for specific details. In general, if IMFINZI requires interruption or discontinuation, administer systemic corticosteroid therapy (1 mg to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroid therapy.

Immune-Mediated Pneumonitis

IMFINZI can cause immune-mediated pneumonitis. The incidence of pneumonitis is higher in patients who have received prior thoracic radiation. In patients who did not receive recent prior radiation, the incidence of immune-mediated pneumonitis was 2.0% (28/1414), including fatal (<0.1%), and Grade 3-4 (0.4%) adverse reactions. In patients who received recent prior radiation, the incidence of pneumonitis (including radiation pneumonitis) in patients with unresectable Stage III NSCLC following definitive chemoradiation within 42 days prior to initiation of IMFINZI in PACIFIC was 16.6% (79/475) in patients receiving IMFINZI and 13.2% (31/234) in patients receiving placebo. Of the 79 patients who received IMFINZI, 1.1% were fatal and 2.5% were Grade 3-4 adverse reactions. The frequency and severity of immune-mediated pneumonitis in patients who did not receive definitive chemoradiation prior to IMFINZI were similar in patients who received IMFINZI as a single agent or with ES-SCLC when in combination with chemotherapy.

Immune-Mediated Colitis

IMFINZI can cause immune-mediated colitis that is frequently associated with diarrhea. Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies. Immune-mediated colitis occurred in 1.6% (31/1889) of patients receiving IMFINZI, including Grade 4 (0.1%) and Grade 3 (0.3%) adverse reactions.

Immune-Mediated Hepatitis

IMFINZI can cause immune-mediated hepatitis. Immune-mediated hepatitis occurred in 1.0% (19/1889) of patients receiving IMFINZI, including fatal (<0.1%) and Grade 3 (0.6%) adverse reactions.

Immune-Mediated Endocrinopathies

- ***Adrenal Insufficiency:*** IMFINZI can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Immune-mediated adrenal insufficiency occurred in 0.4% (7/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.
- ***Hypophysitis:*** IMFINZI can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field cuts. Hypophysitis can cause hypopituitarism. Initiate symptomatic treatment including hormone replacement as clinically indicated. Grade 3 hypophysitis/hypopituitarism occurred in <0.1% (1/1889) of patients who received IMFINZI.
- ***Thyroid Disorders:*** IMFINZI can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement therapy for hypothyroidism or institute medical management of hyperthyroidism as clinically indicated.
- ***Thyroiditis:*** Immune-mediated thyroiditis occurred in 0.4% (7/1889) of patients receiving IMFINZI.
- ***Hyperthyroidism:*** Immune-mediated hyperthyroidism occurred in 1.4% (27/1889) of patients receiving IMFINZI.
- ***Hypothyroidism:*** Immune-mediated hypothyroidism occurred in 7.3% (137/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.
- ***Type 1 Diabetes Mellitus, which can present with diabetic ketoacidosis:*** Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Grade 3 immune-mediated type 1 diabetes mellitus occurred in <0.1% (1/1889) of patients receiving IMFINZI.

Immune-Mediated Nephritis with Renal Dysfunction

IMFINZI can cause immune-mediated nephritis. Immune-mediated nephritis occurred in 0.3% (5/1889) of patients receiving IMFINZI, including Grade 3 (0.1%) adverse reactions.

Immune-Mediated Dermatology Reactions

IMFINZI can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens Johnson Syndrome (SJS), drug rash with eosinophilia and systemic symptoms (DRESS), and toxic epidermal necrolysis (TEN), have occurred with PD-1/L-1 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Immune-mediated rash or dermatitis occurred in 1.6% (30/1889) of patients receiving IMFINZI, including Grade 3 (0.4%) adverse reactions.

Other Immune-Mediated Adverse Reactions

The following clinically significant, immune-mediated adverse reactions occurred at an incidence of less than 1% each in patients who received IMFINZI or were reported with the use of other PD-1/PD-L1 blocking antibodies.

- ***Cardiac/vascular:*** Myocarditis, pericarditis, vasculitis.
- ***Nervous system:*** Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, autoimmune neuropathy.
- ***Ocular:*** Uveitis, iritis, and other ocular inflammatory toxicities can occur. Some cases can be associated with retinal detachment. Various grades of visual impairment to include blindness can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada-like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss.

Select Safety Information (continued)

- ***Gastrointestinal:*** Pancreatitis including increases in serum amylase and lipase levels, gastritis, duodenitis.
- ***Musculoskeletal and connective tissue disorders:*** Myositis/polymyositis, rhabdomyolysis and associated sequelae including renal failure, arthritis, polymyalgia rheumatic.
- ***Endocrine:*** Hypoparathyroidism
- ***Other (hematologic/immune):*** Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenia, solid organ transplant rejection.

Infusion-Related Reactions

IMFINZI can cause severe or life-threatening infusion-related reactions. Monitor for signs and symptoms of infusion-related reactions. Interrupt, slow the rate of, or permanently discontinue IMFINZI based on the severity. See Dosing and Administration for specific details. For Grade 1 or 2 infusion-related reactions, consider using pre-medications with subsequent doses. Infusion-related reactions occurred in 2.2% (42/1889) of patients receiving IMFINZI, including Grade 3 (0.3%) adverse reactions.

Complications of Allogeneic HSCT after IMFINZI

Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/L-1 blocking antibody. Transplant-related complications include hyperacute graft-versus-host-disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease (VOD) after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/L-1 blockade and allogeneic HSCT. Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/L-1 blocking antibody prior to or after an allogeneic HSCT.

Embryo-Fetal Toxicity

Based on its mechanism of action and data from animal studies, IMFINZI can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with IMFINZI and for at least 3 months after the last dose of IMFINZI.

Lactation

There is no information regarding the presence of IMFINZI in human milk; however, because of the potential for adverse reactions in breastfed infants from IMFINZI, advise women not to breastfeed during treatment and for at least 3 months after the last dose.

Adverse Reactions

- In patients with Stage III NSCLC in the PACIFIC study receiving IMFINZI (n=475), the most common adverse reactions (≥20%) were cough (40%), fatigue (34%), pneumonitis or radiation pneumonitis (34%), upper respiratory tract infections (26%), dyspnea (25%), and rash (23%). The most common Grade 3 or 4 adverse reactions (≥3%) were pneumonitis/radiation pneumonitis (3.4%) and pneumonia (7%)
- In patients with Stage III NSCLC in the PACIFIC study receiving IMFINZI (n=475), discontinuation due to adverse reactions occurred in 15% of patients in the IMFINZI arm. Serious adverse reactions occurred in 29% of patients receiving IMFINZI. The most frequent serious adverse reactions (≥2%) were pneumonitis or radiation pneumonitis (7%) and pneumonia (6%). Fatal pneumonitis or radiation pneumonitis and fatal pneumonia occurred in <2% of patients and were similar across arms

The safety and effectiveness of IMFINZI have not been established in pediatric patients.

Please see Brief Summary of complete Prescribing Information on adjacent pages.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.FDA.gov/medwatch or call 1-800-FDA-1088.

References: 1. Faivre-Finn C, Vicente D, Kurata T, et al. Durvalumab after chemoradiotherapy in stage III NSCLC: 4-year survival update from the phase 3 PACIFIC trial. Presented at: 2020 ESMO Virtual Congress; September 19-21, 2020. **2.** IMFINZI® (durvalumab) [Prescribing Information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2020. **3.** Antonia SJ, Villegas A, Daniel D, et al. Durvalumab after chemoradiotherapy in stage III non–small-cell lung cancer. *N Engl J Med.* 2017;377(20):1919-1929. **4.** Gray JE, Villegas AE, Daniel DB, et al. Three-year overall survival update from the PACIFIC trial. Poster presented at: 2019 ASCO Annual Meeting; May 31-June 4, 2019; Chicago, IL. **5.** Antonia SJ, Villegas A, Daniel D, et al. Overall survival with durvalumab after chemoradiotherapy in stage III NSCLC. *N Engl J Med.* 2018;379(24):2342-2350.

AstraZeneca

IMFINZI®
durvalumab
Injection for Intravenous Use 50 mg/mL

IMFINZI® (durvalumab) injection, for intravenous use

Brief Summary of Prescribing Information. For complete prescribing information consult official package insert.

INDICATIONS AND USAGE

Non-Small Cell Lung Cancer

IMFINZI is indicated for the treatment of adult patients with unresectable Stage III non-small cell lung cancer (NSCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy.

DOSAGE AND ADMINISTRATION

Recommended Dosage

The recommended dosages for IMFINZI as a single agent and IMFINZI in combination with chemotherapy are presented in Table 1 *[see Clinical Studies (14) in the full Prescribing Information]*.

IMFINZI is administered as an intravenous infusion over 60 minutes.

Table 1. Recommended Dosages of IMFINZI

Indication	Recommended IMFINZI dosage	Duration of Therapy
Unresectable stage III NSCLC	Patients with a body weight of 30 kg and more: 10 mg/kg every 2 weeks or 1500 mg every 4 weeks Patients with a body weight of less than 30 kg: 10 mg/kg every 2 weeks	Until disease progression, unacceptable toxicity, or a maximum of 12 months

Dosage Modifications for Adverse Reactions

No dose reduction for IMFINZI is recommended. In general, withhold IMFINZI for severe (Grade 3) immune-mediated adverse reactions. Permanently discontinue IMFINZI for life-threatening (Grade 4) immune-mediated adverse reactions, recurrent severe (Grade 3) immune-mediated reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to 10 mg or less of prednisone or equivalent per day within 12 weeks of initiating corticosteroids.

Dosage modifications for IMFINZI for adverse reactions that require management different from these general guidelines are summarized in Table 2.

Table 2. Recommended Dosage Modifications for Adverse Reactions

Adverse Reaction	Severity[1]	Dosage Modification
Immune-Mediated Adverse Reactions *[see Warnings and Precautions (5.1) in the full Prescribing Information]*		
Pneumonitis	Grade 2	Withhold[2]
	Grade 3 or 4	Permanently discontinue
Colitis	Grade 2 or 3	Withhold[2]
	Grade 4	Permanently discontinue
Hepatitis with no tumor involvement of the liver	ALT or AST increases to more than 3 and up to 8 times the ULN or total bilirubin increases to more than 1.5 and up to 3 times ULN	Withhold[2]
	ALT or AST increases to more than 8 times ULN or total bilirubin increases to more than 3 times the ULN	Permanently discontinue
Hepatitis with tumor involvement of the liver[3]	AST or ALT is more than 1 and up to 3 times ULN at baseline and increases to more than 5 and up to 10 times ULN or AST or ALT is more than 3 and up to 5 times ULN at baseline and increases to more than 8 and up to 10 times ULN	Withhold[2]
	AST or ALT increases to more than 10 times ULN or Total bilirubin increases to more than 3 times ULN	Permanently discontinue
Endocrinopathies	Grade 3 or 4	Withhold until clinically stable or permanently discontinue depending on severity
Nephritis with Renal Dysfunction	Grade 2 or 3 increased blood creatinine	Withhold[2]
	Grade 4 increased blood creatinine	Permanently discontinue
Exfoliative Dermatologic Conditions	Suspected SJS, TEN, or DRESS	Withhold[2]
	Confirmed SJS, TEN, or DRESS	Permanently discontinue
Myocarditis	Grade 2, 3, or 4	Permanently discontinue
Neurological Toxicities	Grade 2	Withhold[2]
	Grade 3 or 4	Permanently discontinue
Other Adverse Reactions		
Infusion-related reactions *[see Warnings and Precautions (5.2) in the full Prescribing Information]*	Grade 1 or 2	Interrupt or slow the rate of infusion
	Grade 3 or 4	Permanently discontinue

ALT = alanine aminotransferase, AST = aspartate aminotransferase, DRESS = Drug Rash with Eosinophilia and Systemic Symptoms, SJS = Stevens Johnson Syndrome, TEN = toxic epidermal necrolysis, ULN = upper limit normal

[1] Based on National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03.

[2] Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone 10 mg per day or less (or equivalent) within 12 weeks of initiating steroids.

[3] If AST and ALT are less than or equal to ULN at baseline in patients with liver involvement, withhold or permanently discontinue IMFINZI based on recommendations for hepatitis with no liver involvement.

Preparation and Administration

Preparation

- Visually inspect drug product for particulate matter and discoloration prior to administration, whenever solution and container permit. Discard the vial if the solution is cloudy, discolored, or visible particles are observed.
- Do not shake the vial.
- Withdraw the required volume from the vial(s) of IMFINZI and transfer into an intravenous bag containing 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP. Mix diluted solution by gentle inversion. Do not shake the solution. The final concentration of the diluted solution should be between 1 mg/mL and 15 mg/mL.
- Discard partially used or empty vials of IMFINZI.

Storage of Infusion Solution

- IMFINZI does not contain a preservative.
- Administer infusion solution immediately once prepared. If infusion solution is not administered immediately and needs to be stored, the total time from vial puncture to the start of the administration should not exceed:
  - 24 hours in a refrigerator at 2°C to 8°C (36°F to 46°F)
  - 8 hours at room temperature up to 25°C (77°F)
- Do not freeze.
- Do not shake.

Administration

- Administer infusion solution intravenously over 60 minutes through an intravenous line containing a sterile, low-protein binding 0.2 or 0.22 micron in-line filter.
- Do not co-administer other drugs through the same infusion line.

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Immune-Mediated Adverse Reactions

IMFINZI is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death-receptor 1 (PD-1) or the PD-ligand 1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance and inducing immune-mediated adverse reactions. Important immune-mediated adverse reactions listed under Warnings and Precautions may not include all possible severe and fatal immune-mediated reactions.

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue. Immune-mediated adverse reactions can occur at any time after starting treatment with a PD-1/PD-L1 blocking antibody. While immune-mediated adverse reactions usually manifest during treatment with PD-1/PD-L1 blocking antibodies, immune-mediated adverse reactions can also manifest after discontinuation of PD-1/PD-L1 blocking antibodies.

Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1 blocking antibodies. Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

Withhold or permanently discontinue IMFINZI depending on severity *[see Dosage and Administration (2.2) in the full Prescribing Information]*. In general, if IMFINZI requires interruption or discontinuation, administer systemic corticosteroid therapy (1 mg to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroid therapy.

Toxicity management guidelines for adverse reactions that do not necessarily require systemic steroids (e.g., endocrinopathies and dermatologic reactions) are discussed below.

Immune-Mediated Pneumonitis

IMFINZI can cause immune-mediated pneumonitis. The incidence of pneumonitis is higher in patients who have received prior thoracic radiation.

In Patients Who did Not Receive Recent Prior Radiation

In patients who received IMFINZI on clinical trials in which radiation therapy was generally not administered immediately prior to initiation of IMFINZI, the incidence of immune-mediated pneumonitis was 2.0% (28/1414), including fatal (<0.1%), and Grade 3-4 (0.4%) adverse reactions. Events resolved in 15 of the 28 patients and resulted in permanent discontinuation in 5 patients. Systemic corticosteroids were required in 17 patients (17/28) with pneumonitis who did not receive chemoradiation prior to initiation of IMFINZI.

In Patients Who Received Recent Prior Radiation

The incidence of pneumonitis (including radiation pneumonitis) in patients with unresectable Stage III NSCLC following definitive chemoradiation within 42 days prior to initiation of IMFINZI in PACIFIC was 16.6% (79/475) in patients receiving IMFINZI and 13.2% (31/234) in patients receiving placebo. Of the 79 patients who received IMFINZI, 1.1% were fatal and 2.5% were Grade 3-4 adverse reactions. Events resolved in 43 of the 79 patients and resulted in permanent discontinuation in 24 patients.

Systemic corticosteroids were required in 60 patients (60/79) with pneumonitis who had received chemo-radiation prior to initiation of IMFINZI, while 2 patients required use of infliximab with high-dose steroids.

The frequency and severity of immune-mediated pneumonitis in patients who did not receive definitive chemoradiation prior to IMFINZI were similar whether IMFINZI was given as a single agent in patients with various cancers in a pooled data set or in patients with ES-SCLC when given in combination with chemotherapy.

Immune-Mediated Colitis

IMFINZI can cause immune-mediated colitis that is frequently associated with diarrhea. Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies.

Immune-mediated colitis occurred in 1.6% (31/1889) of patients receiving IMFINZI, including Grade 4 (0.1%) and Grade 3 (0.3%) adverse reactions. Events resolved in 23 of the 31 patients and resulted in permanent discontinuation in 8 patients. Systemic corticosteroids were required in all patients with immune-mediated colitis, while 2 patients (2/31) required other immunosuppressants (e.g., infliximab, mycophenolate).

Immune-Mediated Hepatitis

IMFINZI can cause immune-mediated hepatitis.

Immune-mediated hepatitis occurred in 1.0% (19/1889) of patients receiving IMFINZI, including fatal (<0.1%) and Grade 3 (0.6%) adverse reactions. Events resolved in 12 of the 19 patients and resulted in permanent discontinuation of IMFINZI in 4 patients. Systemic corticosteroids were required in all patients with immune-mediated hepatitis, while 1 patient (1/19) required use of mycophenolate with high-dose steroids.

Immune-Mediated Endocrinopathies

Adrenal Insufficiency:

IMFINZI can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold or permanently discontinue IMFINZI based on the severity *[see Dosage and Administration (2.2) in the full Prescribing Information]*.

Immune-mediated adrenal insufficiency occurred in 0.4% (7/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions. Adrenal insufficiency did not lead to permanent discontinuation of IMFINZI in any patients. Systemic corticosteroids were required in all patients with adrenal insufficiency; of these, the majority remained on systemic corticosteroids.

Hypophysitis:

IMFINZI can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field cuts. Hypophysitis can cause hypopituitarism. Initiate symptomatic treatment including hormone replacement as clinically indicated. Withhold or permanently discontinue IMFINZI depending on severity *[see Dosage and Administration (2.2) in the full Prescribing Information]*.

Grade 3 hypophysitis/hypopituitarism occurred in <0.1% (1/1889) patients who received IMFINZI. Treatment with systemic corticosteroids was administered in this patient. The event did not lead to permanent discontinuation of IMFINZI.

Thyroid Disorders:

IMFINZI can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement therapy for hypothyroidism or institute medical management of hyperthyroidism as clinically indicated. Withhold or discontinue IMFINZI based on the severity *[see Dosage and Administration (2.2) in the full Prescribing Information]*.

Thyroiditis: Immune-mediated thyroiditis occurred in 0.4% (7/1889) of patients receiving IMFINZI. Events resolved in 3 of the 7 patients and none resulted in permanent discontinuation. Systemic corticosteroids were required in 3 patients (3/7) with immune-mediated thyroiditis, while 5 patients (5/7) required endocrine therapy.

Hyperthyroidism: Immune-mediated hyperthyroidism occurred in 1.4% (27/1889) of patients receiving IMFINZI. Events resolved in 20 of the 27 patients. Systemic corticosteroids were required in 9 patients (9/27) with immune-mediated hyperthyroidism, while 21 patients (21/27) required endocrine therapy.

Hypothyroidism: Immune-mediated hypothyroidism occurred in 7.3% (137/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions. Systemic corticosteroids were required in 10 patients (10/137) and the majority of patients (134/137) required long-term thyroid hormone replacement.

Type 1 Diabetes Mellitus, which can present with diabetic ketoacidosis: Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold or permanently discontinue IMFINZI based on the severity *[see Dosage and Administration (2.2) in the full Prescribing Information]*.

Grade 3 immune-mediated type 1 diabetes mellitus occurred in <0.1% (1/1889) of patients receiving IMFINZI. This patient required long-term insulin therapy and IMFINZI was permanently discontinued.

Immune-Mediated Nephritis with Renal Dysfunction

IMFINZI can cause immune-mediated nephritis.

Immune-mediated nephritis occurred in 0.3% (5/1889) of patients receiving IMFINZI, including Grade 3 (0.1%) adverse reactions. Events resolved in 3 of the 5 patients and resulted in permanent discontinuation in 4 patients. Systemic corticosteroids were required in all patients with immune-mediated nephritis.

Immune-Mediated Dermatology Reactions

IMFINZI can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens Johnson Syndrome (SJS), drug rash with eosinophilia and systemic symptoms (DRESS), and toxic epidermal necrolysis (TEN), has occurred with PD-1/L-1 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Withhold or permanently discontinue IMFINZI depending on severity *[see Dosage and Administration (2.2) in the full Prescribing Information]*.

Immune-mediated rash or dermatitis occurred in 1.6% (30/1889) of patients receiving IMFINZI, including Grade 3 (0.4%) adverse reactions. Events resolved in 18 of the 30 patients and resulted in permanent discontinuation in 2 patients. Systemic corticosteroids were required in all patients with immune-mediated rash or dermatitis.

Other Immune-Mediated Adverse Reactions

The following clinically significant, immune-mediated adverse reactions occurred at an incidence of less than 1% each in patients who received IMFINZI or were reported with the use of other PD-1/PD-L1 blocking antibodies.

Cardiac/vascular: Myocarditis, pericarditis, vasculitis.

Nervous system: Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, autoimmune neuropathy.

Ocular: Uveitis, iritis, and other ocular inflammatory toxicities can occur. Some cases can be associated with retinal detachment. Various grades of visual impairment to include blindness can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada-like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss.

Gastrointestinal: Pancreatitis including increases in serum amylase and lipase levels, gastritis, duodenitis.

Musculoskeletal and connective tissue disorders: Myositis/polymyositis, rhabdomyolysis and associated sequelae including renal failure, arthritis, polymyalgia rheumatic.

Endocrine: Hypoparathyroidism

Other (hematologic/immune): Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenia, solid organ transplant rejection.

Infusion-Related Reactions

IMFINZI can cause severe or life-threatening infusion-related reactions.

Monitor for signs and symptoms of infusion-related reactions. Interrupt, slow the rate of, or permanently discontinue IMFINZI based on the severity *[see Dosage and Administration (2.2) in the full Prescribing Information]*. For Grade 1 or 2 infusion-related reactions, consider using pre-medications with subsequent doses.

Infusion-related reactions occurred in 2.2% (42/1889) of patients receiving IMFINZI, including Grade 3 (0.3%) adverse reactions.

Complications of Allogeneic HSCT after IMFINZI

Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/L-1 blocking antibody. Transplant-related complications include hyperacute graft-versus-host-disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease (VOD) after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/L-1 blockade and allogeneic HSCT.

Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/L-1 blocking antibody prior to or after an allogeneic HSCT.

Embryo-Fetal Toxicity

Based on its mechanism of action and data from animal studies, IMFINZI can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, administration of durvalumab to cynomolgus monkeys from the onset of organogenesis through delivery resulted in increased premature delivery, fetal loss and premature neonatal death. Advise pregnant women of the potential risk to a fetus.

Advise females of reproductive potential to use effective contraception during treatment with IMFINZI and for at least 3 months after the last dose of IMFINZI *[see Use in Specific Populations (8.1, 8.3) in the full Prescribing Information]*.

ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the labeling.

- Immune-Mediated Adverse Reactions *[see Warnings and Precautions (5.1) in the full Prescribing Information]*.
- Infusion-Related Reactions *[see Warnings and Precautions (5.2) in the full Prescribing Information]*.

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data described in the Warnings and Precautions section reflect exposure to IMFINZI in 1889 patients from the PACIFIC study (a randomized, placebo-controlled study that enrolled 475 patients with Stage III NSCLC), Study 1108 (an open-label, single-arm, multicohort study that enrolled 191 patients with urothelial carcinoma and 779 patients with other solid tumors), and additional open-label, single-arm trial that enrolled 444 patients with metastatic lung cancer, an indication for which durvalumab is not approved. In these trials, IMFINZI was administered at a dose of 10 mg/kg every 2 weeks. Among the 1889 patients, 38% were exposed for 6 months or more and 18% were exposed for 12 months or more. The data also reflects exposure to IMFINZI in combination with chemotherapy in 265 patients from the CASPIAN study (a randomized, open-label study in patients with ES-SCLC). In the CASPIAN study, IMFINZI was administered at a dose of 1500 mg every 3 or 4 weeks.

The data described in this section reflect exposure to IMFINZI in patients with Stage III NSCLC enrolled in the PACIFIC study.

Non-Small Cell Lung Cancer

The safety of IMFINZI in patients with Stage III NSCLC who completed concurrent platinum-based chemoradiotherapy within 42 days prior to initiation of study drug was evaluated in the PACIFIC study, a multicenter, randomized, double-blind, placebo-controlled study. A total of 475 patients received IMFINZI 10 mg/kg intravenously every 2 weeks. The study excluded patients who had disease progression following chemoradiation, with active or prior autoimmune disease within 2 years of initiation of the study or with medical conditions that required systemic immunosuppression *[see Clinical Studies (14.2) in the full Prescribing Information]*.

The study population characteristics were: median age of 64 years (range: 23 to 90), 45% age 65 years or older, 70% male, 69% White, 27% Asian, 75% former smoker, 16% current smoker, and 51% had WHO performance status of 1. All patients received definitive radiotherapy as per protocol, of which 92% received a total radiation dose of 54 Gy to 66 Gy. The median duration of exposure to IMFINZI was 10 months (range: 0.2 to 12.6).

IMFINZI was discontinued due to adverse reactions in 15% of patients. The most common adverse reactions leading to IMFINZI discontinuation were pneumonitis or radiation pneumonitis in 6% of patients. Serious adverse reactions occurred in 29% of patients receiving IMFINZI. The most frequent serious adverse reactions reported in at least 2% of patients were pneumonitis or radiation pneumonitis (7%) and pneumonia (6%). Fatal pneumonitis or radiation pneumonitis and fatal pneumonia occurred in < 2% of patients and were similar across arms. The most common adverse reactions (occurring in ≥ 20% of patients) were cough, fatigue, pneumonitis or radiation pneumonitis, upper respiratory tract infections, dyspnea, and rash.

Table 5 summarizes the adverse reactions that occurred in at least 10% of patients treated with IMFINZI.

Table 5. Adverse Reactions Occurring in ≥ 10% Patients in the PACIFIC Study

	IMFINZI N = 475		Placebo[1] N = 234	
Adverse Reaction	**All Grades (%)**	**Grades 3-4 (%)**	**All Grades (%)**	**Grades 3-4 (%)**
Respiratory, Thoracic, and Mediastinal Disorders				
Cough/Productive Cough	40	0.6	30	0.4
Pneumonitis[2]/Radiation Pneumonitis	34	3.4	25	3
Dyspnea[3]	25	1.5	25	2.6
Gastrointestinal Disorders				
Diarrhea	18	0.6	19	1.3
Abdominal pain[4]	10	0.4	6	0.4

Table 5. Adverse Reactions Occurring in ≥ 10% Patients in the PACIFIC Study (cont'd)

	IMFINZI N = 475		Placebo[1] N = 234	
Adverse Reaction	**All Grades (%)**	**Grades 3-4 (%)**	**All Grades (%)**	**Grades 3-4 (%)**
Endocrine Disorders				
Hypothyroidism[5]	12	0.2	1.7	0
Skin and Subcutaneous Tissue Disorders				
Rash[6]	23	0.6	12	0
Pruritus[7]	12	0	6	0
General Disorders				
Fatigue[8]	34	0.8	32	1.3
Pyrexia	15	0.2	9	0
Infections				
Upper respiratory tract infections[9]	26	0.4	19	0
Pneumonia[10]	17	7	12	6

1 The PACIFIC study was not designed to demonstrate statistically significant difference in adverse reaction rates for IMFINZI, as compared to placebo, for any specific adverse reaction listed in Table 4
2 Includes acute interstitial pneumonitis, interstitial lung disease, pneumonitis, pulmonary fibrosis
3 Includes dyspnea, and exertional dyspnea
4 Includes abdominal pain, abdominal pain lower, abdominal pain upper, and flank pain
5 Includes autoimmune hypothyroidism and hypothyroidism
6 Includes rash erythematous, rash generalized, rash macular, rash maculopapular, rash papular, rash pruritic, rash pustular, erythema, eczema, rash, and dermatitis
7 Includes pruritus generalized and pruritus
8 Includes asthenia and fatigue
9 Includes laryngitis, nasopharyngitis, peritonsillar abscess, pharyngitis, rhinitis, sinusitis, tonsillitis, tracheobronchitis, and upper respiratory tract infection
10 Includes lung infection, pneumocystis jirovecii pneumonia, pneumonia, pneumonia adenoviral, pneumonia bacterial, pneumonia cytomegaloviral, pneumonia haemophilus, pneumonia klebsiella, pneumonia necrotising, pneumonia pneumococcal, and pneumonia streptococcal

Other adverse reactions occurring in less than 10% of patients treated with IMFINZI were dysphonia, dysuria, night sweats, peripheral edema, and increased susceptibility to infections.

Table 6 summarizes the laboratory abnormalities that occurred in at least 20% of patients treated with IMFINZI.

Table 6. Laboratory Abnormalities Worsening from Baseline Occurring in ≥ 20% of Patients in the PACIFIC Study

	IMFINZI		Placebo	
Laboratory Abnormality	**All Grades[1] (%)[2]**	**Grade 3 or 4 (%)**	**All Grades[1] (%)[2]**	**Grade 3 or 4 (%)**
Chemistry				
Hyperglycemia	52	8	51	8
Hypocalcemia	46	0.2	41	0
Increased ALT	39	2.3	22	0.4
Increased AST	36	2.8	21	0.4
Hyponatremia	33	3.6	30	3.1
Hyperkalemia	32	1.1	29	1.8
Increased GGT	24	3.4	22	1.7
Hematology				
Lymphopenia	43	17	39	18

1 Graded according to NCI CTCAE version 4.0
2 Each test incidence is based on the number of patients who had both baseline and at least one on-study laboratory measurement available: IMFINZI (range: 464 to 470) and placebo (range: 224 to 228)

Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to durvalumab to the incidence of antibodies to other products may be misleading.

Of 2280 patients who received IMFINZI 10 mg/kg every 2 weeks or 20 mg/kg every 4 weeks as a single-agent, 69 patients (3%) tested positive for treatment-emergent anti-drug antibodies (ADA) and 12 (0.5%) tested positive for neutralizing antibodies. The development of ADA against durvalumab appears to have no clinically relevant effect on its pharmacokinetics or safety.

Of 201 patients in the CASPIAN study who received IMFINZI 1500 mg every 3 weeks in combination with chemotherapy for four doses followed by IMFINZI 1500 mg every 4 weeks no patients tested positive for treatment-emergent ADA.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk summary

Based on its mechanism of action and data from animal studies, IMFINZI can cause fetal harm when administered to a pregnant woman *[see Clinical Pharmacology (12.1) in the full Prescribing Information]*. There are no data on the use of IMFINZI in pregnant women.

In animal reproduction studies, administration of durvalumab to pregnant cynomolgus monkeys from the confirmation of pregnancy through delivery resulted in an increase in premature delivery, fetal loss, and premature neonatal death *(see Data)*. Human immunoglobulin G1 (IgG1) is known to cross the placental barrier; therefore, durvalumab has the potential to be transmitted from the mother to the developing fetus. Apprise pregnant women of the potential risk to a fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Animal Data

As reported in the literature, the PD-1/PD-L1 pathway plays a central role in preserving pregnancy by maintaining maternal immune tolerance to the fetus. In mouse allogeneic pregnancy models, disruption of PD-L1 signaling was shown to result in an increase in fetal loss. The effects of durvalumab on prenatal and postnatal development were evaluated in reproduction studies in cynomolgus monkeys. Durvalumab was administered from the confirmation of pregnancy through delivery at exposure levels approximately 6 to 20 times higher than those observed at the recommended clinical dose of 10 mg/kg (based on AUC). Administration of durvalumab resulted in premature delivery, fetal loss (abortion and stillbirth), and increase in neonatal deaths. Durvalumab was detected in infant serum on postpartum Day 1, indicating the presence of placental transfer of durvalumab. Based on its mechanism of action, fetal exposure to durvalumab may increase the risk of developing immune-mediated disorders or altering the normal immune response and immune-mediated disorders have been reported in PD-1 knockout mice.

Lactation

Risk Summary

There is no information regarding the presence of durvalumab in human milk, the effects on the breastfed infant, or the effects on milk production. Human IgG1 is excreted in human milk. Durvalumab was present in the milk of lactating cynomolgus monkeys and was associated with premature neonatal death *(see Data)*. Because of the potential for adverse reactions in breastfed infants, advise women not to breastfeed during treatment with IMFINZI and for at least 3 months after the last dose.

Data

In lactating cynomolgus monkeys, durvalumab was present in breast milk at about 0.15% of maternal serum concentrations after administration of durvalumab from the confirmation of pregnancy through delivery at exposure levels approximately 6 to 20 times higher than those observed at the recommended clinical dose of 10 mg/kg (based on AUC). Administration of durvalumab resulted in premature neonatal death.

Females and Males of Reproductive Potential

Contraception

Females

Based on its mechanism of action and data from animal studies, IMFINZI can cause fetal harm when administered to a pregnant woman *[see Use in Specific Populations (8.1) in the full Prescribing Information]*. Advise females of reproductive potential to use effective contraception during treatment with IMFINZI and for at least 3 months following the last dose of IMFINZI.

Pediatric Use

The safety and effectiveness of IMFINZI have not been established in pediatric patients.

Geriatric Use

Of the 476 patients treated with IMFINZI in the PACIFIC study, 45% were 65 years or older, while 7.6% were 75 years or older. No overall differences in safety or effectiveness were observed between patients 65 years or older and younger patients. The PACIFIC study did not include sufficient numbers of patients aged 75 years and over to determine whether they respond differently from younger patients.

PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Immune-Mediated Adverse Reactions

Inform patients of the risk of immune-mediated adverse reactions that may require corticosteroid treatment and interruption or discontinuation of IMFINZI *[see Warnings and Precautions (5.1) in the full Prescribing Information]*, including:

- Pneumonitis: Advise patients to contact their healthcare provider immediately for any new or worsening cough, chest pain, or shortness of breath.
- Hepatitis: Advise patients to contact their healthcare provider immediately for jaundice, severe nausea or vomiting, pain on the right side of abdomen, lethargy, or easy bruising or bleeding.
- Colitis: Advise patients to contact their healthcare provider immediately for diarrhea, blood or mucus in stools, or severe abdominal pain.
- Endocrinopathies: Advise patients to contact their healthcare provider immediately for signs or symptoms of hypothyroidism, hyperthyroidism, adrenal insufficiency, type 1 diabetes mellitus, or hypophysitis.
- Nephritis: Advise patients to contact their healthcare provider immediately for signs or symptoms of nephritis.
- Dermatological Reactions: Advise patients to contact their healthcare provider immediately for signs or symptoms of severe dermatological reactions.
- Other Immune-Mediated Adverse Reactions: Advise patients to contact their healthcare provider immediately for signs or symptoms of aseptic meningitis, immune thrombocytopenia, myocarditis, hemolytic anemia, myositis, uveitis, keratitis, and myasthenia gravis.

Infusion-Related Reactions:

- Advise patients to contact their healthcare provider immediately for signs or symptoms of infusion-related reactions *[see Warnings and Precautions (5.2) in the full Prescribing Information]*.

Complications of Allogeneic HSCT:

- Advise patients of potential risk of post-transplant complications *[see Warnings and Precautions (5.3) in the full Prescribing Information]*.

Embryo-Fetal Toxicity:

- Advise females of reproductive potential that IMFINZI can cause harm to a fetus and to inform their healthcare provider of a known or suspected pregnancy *[see Warnings and Precautions (5.4) and Use in Specific Populations (8.1, 8.3) in the full Prescribing Information]*.
- Advise females of reproductive potential to use effective contraception during treatment and for at least 3 months after the last dose of IMFINZI *[see Use in Specific Populations (8.3) in the full Prescribing Information]*.

Lactation:

- Advise female patients not to breastfeed while taking IMFINZI and for at least 3 months after the last dose *[see Warnings and Precautions (5.4) and Use in Specific Populations (8.2) in the full Prescribing Information]*.

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EXPANDING THE SCOPE of practice in regard to training

Regarding Residency: Perspectives from a Program Director

BY EMMA FIELDS, MD, PRESIDENT OF THE ASSOCIATION FOR DIRECTORS OF RADIATION ONCOLOGY PROGRAMS

THE ASTRO SCOPE OF PRACTICE SURVEY[1] SHOWED that radiation oncologists, particularly those earlier in their careers, were interested in expanding their scope of practice to include radiopharmaceuticals, palliative care, systemic therapies and running an inpatient service. From my perspective as a program director, there are certainly improvements to be made in the training of our residents to make them leaders in oncology. There is also a lot of work to be done to promote our specialty and continue to recruit excellent medical students to our programs. However, I am not convinced that the results of this survey will direct the future of residency training. For a start, not all of these areas are truly expansions of our scope. Additionally, I do not think that any or all of these expansions of scope would affect recruitment. More importantly, residency training should include learning about teamwork, emotional intelligence and leadership skills, so that wherever a trainee's career takes them, they will be prepared.

In the survey, about a fifth of providers were interested in expanding their scope of practice. However, many RO providers already offer these services based on demand at their site and availability of providers who may more regularly supply those services. In my practice, and in the survey results, the major barrier to expanding scope is not education but political infeasibility. The use of radiopharmaceuticals is not new to RO, as residents are required by the ACGME to complete cases of unsealed sources for graduation. In accordance with the scope of practice survey, ACGME recently increased the number of cases required for graduation from six to eight, and ASTRO has released several training courses. Residents should certainly feel comfortable using radiopharmaceuticals, and this is a good expansion of practice, as these treatments fit well in many RO clinics.

However, I think providers have to be careful what they wish for with expansion of scope in some areas, such as running an inpatient service. Residency training is very compressed as is and includes apprentice-based clinical training, radiation biology, physics, clinical education, keeping up with evolving technology and performing research, etc. Even if it may seem like a good idea to have an inpatient service, this would generally be a deterrent to many trainees and faculty alike who have not practiced general medicine for years. From a training perspective, having an inpatient service would add a great deal of instruction time and resources. It would be the death of small programs and put average sized programs in jeopardy, as they would lack the faculty to devote to the increased teaching demand while maintaining a thriving practice. The benefit of radiation oncology, in addition to long and caring patient relationships, multidisciplinary care, use of technology, research and more, remains the favorable lifestyle of having outpatient clinic hours.

In my opinion, the major issue with attracting residents into our field is not our scope of practice. We are now in our third year of a downtrend in number of applications to radiation oncology programs. This is multi-factorial but largely related to bad publicity about our specialty on highly trafficked public forums for medical students.[2] Many of the potential RO applicants' concerns are based on the job market, board passing rates and residency expansion, as highlighted in a paper by ARRO, published in the Red Journal.[3] To combat this, we need to get into medical schools, both in the classroom and clinic, to increase exposure to RO and foster mentorship.[4] Within our society, we should look at residency expansion and ensure we are training appropriate numbers of quality residents and not just adding bodies to help with clinical service.

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Should We Expand the Scope of Practice? A Resident's Perspective

BY ELIZABETH B. JEANS, MED, MD, VICE-CHAIR, ASSOCIATION OF RESIDENTS IN RADIATION ONCOLOGY (ARRO)

IN THE ARTICLE BY FUNG ET AL.[1], practicing radiation oncologists were queried about their interest in expanding their current scope of practice. The surveyed cohort comprised a wide variety of practicing radiation oncologists consisting of private practitioners and academicians trained over many decades and practicing across a variety of locations. Variability was seen in current practice patterns in regard to the delivery of radiopharmaceuticals/theranostics, anticancer therapies and additional patient care measures, including a dedicated inpatient service and the ability to prescribe medical marijuana. While the authors note the independence of radiation oncology from diagnostic radiology over several decades, they also note the continued need for radiation oncology to determine its place in being leaders in oncologic care, an important sentiment by nearly all survey respondents (>95%).

The inquiry into scope of practice highlights the interconnectedness in cancer care, which has substantially progressed over the past several years. As novel therapeutic strategies emerge, the role of a practicing radiation oncologist becomes more complex, as one must have a wide breadth of knowledge to provide adequate counseling and delivery of care to patients. Determining the interest in untangling the modern-day scope of practice for a practicing radiation oncologist is important; however, the ultimate decision to support the expansion of the current practice should be tempered by determining its importance in the educational milieu and the ability to effectively educate trainees.

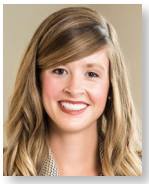
A survey administered by the Association of Residents in Radiation Oncology (ARRO) in 2019 highlighted top concerns of trainees within the field of radiation oncology.[2] Of greatest concern were board examinations and the current state of graduate medical education. Seventy-eight percent agreed that a lack of clarity in importance of educational topics, accompanied by lack of transparency in board examination, could be clarified by the development and maintenance of a comprehensive radiation oncology curriculum. A call was made for ASTRO to develop a subcommittee of graduate medical education to improve the educational practice and provide clarity and focus within resident training and assessment.

Similarly, an additional editorial published in 2020 by educational expert and practicing radiation oncologist Daniel Golden, MD, MHPE,[3] highlighted that continued training and development of residents without a United States radiation oncology curriculum has left both educators and residents with a lack of focus in what content to teach. The lack of clarity provided by any stakeholder organization has led to a paradigm of "the tail wagging the dog," a scenario in which residents and educators use examinations to determine importance of content.

Inherent to both these publications is the element that expansion of radiation oncology foci in the past several decades (clinical, radiation and cancer biology, and medical physics) without a correlative consensus on importance has set back trainees and educators. The breadth of knowledge required of trainees in the modern era is so vast that failure to develop a radiation oncology curriculum through deliberative educational curricular techniques has led to pages of accumulating topics provided to educators and trainees. The current process of training and assessing radiation oncology residents is faulted without a comprehensive top-down radiation oncology curriculum. Currently, the Radiation Oncology Educational Collaborative Study Group (ROECSG) has initiated a deliberative inquiry into a radiation oncology specific core curriculum.[4]

Illustrated in the scope of practice survey, trainees in the modern era, represented by recent graduates, are excited to acquire new knowledge and further develop their skillsets to be a comprehensive resource for their patients. However, it is necessary to survey radiation oncology trainees to understand the current exposure of training that residents have in these areas of potential expansion. Failure to assess the current level of exposure as well as current content-specific resident education in these areas would further the education problem in residency learning and assessment. A clear understanding of the current exposure, the availability of programs to provide dedicated learning, and deliberative inquiry into how these topics would fit into a comprehensive radiation oncology curriculum is needed. It is crucial that the expanded training topics be weighed against the other important aspects of training prior to expanding the scope of practice.

As trainees, we aim to be at the forefront of practice and seek to find the void in treatment strategies, culminating in the development of further cancer-specific therapies. Our hope is to provide patients with the best care, and doing so requires the comprehension of multiple different subjects. However, with the current training paradigm, expanding any further into additional fields of practice would fail without an adequate educational development plan alongside a dedicated deliberative inquiry into how said topics fit into the greater radiation oncology curriculum.



Elizabeth B. Jeans, MEd, MD, is a radiation oncologist resident at the Mayo Clinic Rochester, Minnesota, and serves on the Executive Committee of ARRO.

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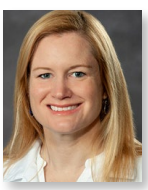
Within residency programs, we must train our residents so that they are prepared to lead programs, develop new initiatives and feel confident taking on new challenges, no matter what our scope of practice entails. There is a hidden curriculum, in which residents learn by observing their mentors in the field. We need to be cognizant of this and ensure that we are modeling collegiality, leadership and good interprofessional dynamics. As stated in the discussion of the study,[1] the goal should be to "promote a *culture* of meaningful multidisciplinary teamwork" and to "collaborate with mutual respect and … share the common goal of consistently upholding the patient's best interest." Along these lines, the Radiation Oncology Education Collaborative Study Group (ROECSG) is developing a curricular framework with Entrustable Professional Activities to give trainees and faculty a standardized tool for resident assessment on the necessary skills for independent practice.

The scope of practice article[1,5] opens with a quote from the 1975 ASTRO presidential address by Dr. del Regato motivating the newly minted therapeutic radiologists by saying, "No one is as deserving of the title of oncologist as you are," while noting that many didn't have their own departments or recognition as a distinct specialist. Dr. del Regato concluded the speech by saying, "You have come a long way, indeed! ... but it behooves you to anticipate new pitfalls that might be awaiting you." Now, in 2020, we have certainly come a long way! While we may have more pitfalls ahead, by ensuring we promote ourselves accurately, provide mentorship at all stages along the path and recruit and train future leaders, I think we will have a thriving future.



Emma Fields, MD, is an associate professor and residency program director of radiation oncology at Virginia Commonwealth University in Richmond, Virginia, and serves as president of ADROP.

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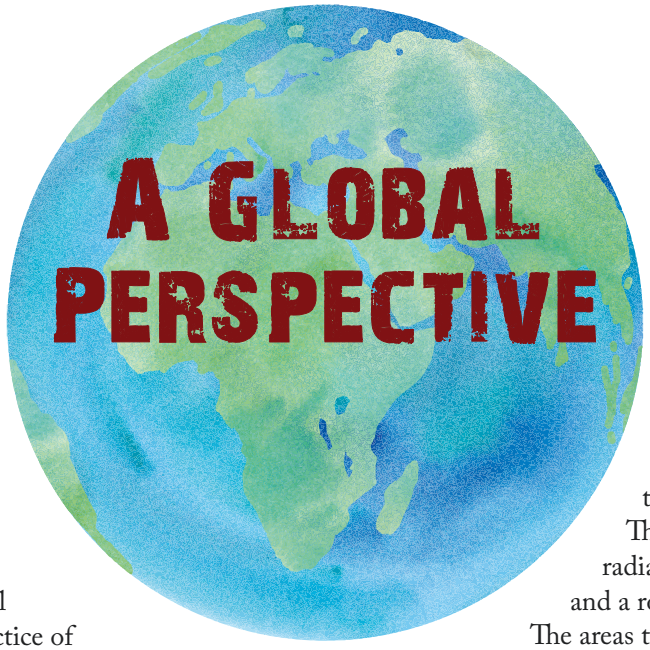
The Scope of Practice of Radiation Oncology:



BY SIMON S. LO, MB, CHB, FASTRO, AND SUSHIL BERIWAL, MD, MBA, FASTRO

THE SCOPE OF PRACTICE DESCRIBES THE PROCEDURES allowed by hospitals and clinics and are based on residency training, competency and experience. In the U.S., cancer care is provided by specialists in surgical, medical and radiation oncology. The practice of U.S. radiation oncologists is largely limited to independent opinion within the radiotherapy scope, including planning radiotherapy, supervision of radiation delivery, management of side effects from radiotherapy and post-radiotherapy follow-up.

A recent ASTRO scope of practice study showed that 82.5% of participating radiation oncologists felt that the ideal approach to patient care was to provide an independent opinion on radiation therapy and other treatment options. Over 16% (16.1) felt that an independent opinion on radiation therapy but not outside of it would be the ideal approach. However, the vast majority of radiation oncologists felt that they should be leaders in oncology care. In reality, actual practice fully matched the ideal approach in only 18.2% of respondents. Most radiation oncologists in the U.S. do not administer systemic therapy, admit inpatients or serve as a primary care physician. Only a minority of radiation oncologists in the U.S. administer radioactive isotopes for treatment, which is usually handled by a nuclear medicine physician.

Radiation oncology training varies across the globe, and in some countries, radiation oncologists are trained in administration of systemic therapy and they regularly manage inpatient admitted for oncology care. Furthermore, in some countries, radiation oncologists routinely administer radionuclide therapy.

Is it time for us to look at best practices for training across the globe and revisit radiation oncology training to increase scope of practice? The enhanced training may give radiation oncologists wider access and a role in management of cancers. The areas to explore would be the administration of concurrent chemotherapy, immunotherapy and targeted therapy with radiation therapy and being involved in decisions on and the administration of radionuclides. This may be important as the field of radiopharmaceuticals is advancing, such as the use of ^{177}Lu-PSMA-based radioligand therapy for prostate cancer. These changes would require significant changes in residency structure but may be important for our role in oncology care in the future. To provide a broader perspective, this article will review the scope of practice of radiation in some countries across the globe.

Canada, United Kingdom (UK), Australia and New Zealand

Medical training in Canada bears the closest resemblance to that in the U.S. As such, medical schools in Canada are not regarded as foreign medical schools, as they are also accredited by the Association of American Medical Colleges (AAMC). Training in radiation oncology in Canada is under the governance of The Royal College of Physicians of Canada and is recognized by the American Board of Radiology for the purpose of board certification. Based on information obtained from radiation oncologists from major academic centers in Ontario and British Columbia, radiation oncologists admit their own inpatients. They

also prescribe and manage iodine-131, radium-223, strontium-89, and lutetium-177 at some sites, although nuclear medicine does the ordering and administration of the isotopes. However, radiation oncologists only administer hormones, not chemotherapy, targeted therapy or immunotherapy.

In the UK, despite that The Royal College of Radiologists (RCR) governs the training, doctors who pass the fellowship examination and fulfill the post-fellowship requirements are called clinical oncologists, as both the training and examination cover both radiation and medical oncology. In other words, clinical oncologists admit their own inpatients and are responsible for making recommendations on and administering radiotherapy and hormonal therapy, chemotherapy, targeted therapy and immunotherapy. Furthermore, they also make recommendations on and are responsible for the administration of radioactive iodine in certain specialist centers

In Australia and New Zealand, training and board certification in radiation oncology are governed by The Royal Australian and New Zealand College of Radiologists (RANZCR). Practice varies regionally, but radiation oncologists typically admit their inpatients. Australian radiation oncologists do not administer any systemic therapy. Radiopharmaceuticals are administered only in specialized centers that have rooms to give treatments.

In New Zealand, the majority of radiation oncologists prescribe androgen deprivation therapy for prostate cancer, and some prescribe abiraterone as well. For breast cancer, some of them prescribe hormonal therapy, and a majority of them also prescribe temozolomide for central nervous system tumors. They admit their inpatients to manage the side effects of treatment and for those needing inpatient radiotherapy. New Zealand radiation oncologists prescribe radioisotopes, including iodine-131, but this can overlap with the endocrinologist.

Continental Europe: Switzerland, Germany, The Netherlands, Italy, Denmark and Turkey

Training in radiation oncology in Switzerland includes radiation and medical oncology. As a result, radiation oncologists typically administer hormonal therapy, whereas the administration of chemotherapy, targeted therapy and immunotherapy is variable across centers. Whether radiation oncologists admit inpatients is institution dependent. They do not administer radiopharmaceuticals.

In Germany, radiation oncologists administer and supervise all systemic therapy, especially concurrent with radiotherapy, and they admit inpatients. They do not administer radiopharmaceuticals. Interestingly, some radiation oncologists assume the role of primary care doctors.

The scope of practice in the Netherlands is very similar to that in the U.S. in that radiation oncologists do not administer systemic therapy, admit inpatients (except for large centers with a large pulse dose rate practice and their own wards) or administer radiopharmaceuticals.

Radiation oncology training in Italy also includes medical oncology. Radiation oncologists typically administer hormones, whereas the administration of chemotherapy, targeted therapy and immunotherapy is variable across centers, generally limited to larger academic institutions and in the context of concurrent combinations. Inpatient radiation oncology service is again hospital dependent. Radiation oncologists are trained in administration of radiopharmaceuticals, but they are not always given by radiation oncologists.

Like in the UK, Danish oncologists are educated in both radiation and medical oncology, and medical license covers both medical and radiation oncology. A majority of oncologists practice both radiation and medical oncology, whereas a minority practice mainly radiation oncology, although they manage concurrent chemotherapy. Oncology centers in Denmark have their own hospital wards and can admit radiotherapy patients to their ward if needed. Radioisotopes are administrated in collaboration with specialists in nuclear medicine. There are some differences across Denmark, but in general the oncologist prescribes and the nuclear medicine specialist handles the preparation and infusion. Generally, they serve as primary care doctors depending on the tumor type.

Radiation oncologists in Turkey have medical oncology/hematological oncology/internal medicine rotations for a total duration of one year in their five-year residency program and were exclusively prescribing chemotherapy previously in the era of limited number of medical oncologists. Currently, Turkish radiation oncologists have the license to administer chemotherapy in the setting of concurrent chemoradiotherapy as well as first line hormonal therapy (except second generation) when required. They also admit inpatients. Although they are given permission to administer radiopharmaceuticals, it is generally performed by nuclear medicine doctors. Interestingly, they also serve as primary care doctors.

Continued on the following page

East Asia: Japan, Taiwan, Hong Kong and Singapore

Japanese radiation oncologists provide medical oncology care in a limited capacity, in that they administer only chemotherapy, immunotherapy and targeted therapy for limited disease sites. They also admit their inpatients and administer radiopharmaceuticals to cancer patients. One unique aspect in the scope of practice in Japan is that most radiation oncologists also assume the role of medical physicists dealing with the technical aspects of radiotherapy, particularly dose planning and optimization.

In Taiwan, only a minority of radiation oncologists administer systemic therapy. Likewise, a minority of them admit inpatients or assume the role of primary care doctors, respectively. They do not administer radiopharmaceuticals.

Hong Kong is a former British colony and as a result, the practice of radiation oncology is influenced by the British system. In Hong Kong, radiation oncologists are clinical oncologists who pass the conjoint fellowship examination of Royal College of Radiologists and Hong Kong College of Radiologists, fulfill post-fellowship requirements and subsequently pass a final exit examination. As the training encompasses radiation and medical oncology, clinical oncologists in Hong Kong handle all non-surgical oncology care, including radiopharmaceuticals, as in the UK.

Although Singapore was also a British colony, the scope of practice is different from that in the UK. The training either follows the RCR or the RANZCR stream, depending on the site of training. Radiation oncologists (if certified by RANZCR) or clinical oncologists (if certified by RCR) do not administer any systemic therapy except hormones, and they do not admit inpatients or administer radiopharmaceuticals.

Brazil

In Brazil, radiation oncologists do not administer systemic therapy or radiopharmaceuticals. However, in some regions they are responsible for adverse effect management during combined radical treatment. The majority of radiation oncologists do not admit inpatients There are also some radiation oncologists who serve as primary care doctors.

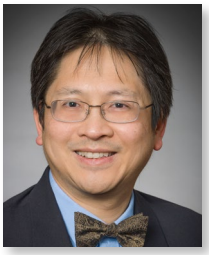
India and Sub-Sahara Africa

Apart from practicing radiation oncology, Indian radiation oncologists also administer systemic therapy and admit their own inpatients. However, they do not administer radiopharmaceuticals.

Similar to radiation oncologists in India, radiation oncologists in Sub-Sahara Africa administer systemic therapy and admit their own inpatients. However, they do not administer radiopharmaceuticals. They assume the role of primary care doctors for their patients.

It is enlightening to look at best practices and how they evolved across the globe with an eye to the future. Now is the time for us to pick up best training and practices from across the world and revisit our residency training structure. These changes will require significant but necessary changes in residency structure, but they may help us expand scope of practices and be leaders in oncology care.

Special thanks to Dr. Alexander Louie; Dr. Mitchell Liu; Dr. Kristopher Dennis; Dr. Emma Dunne; Associate Professor Shankar Siva; Dr. Matthew Foote; Dr. Ramesh Pandey; Dr. Matthias Guckenberger; Dr. Anca-Liga Grosu; Professor Ben Slotman; Professor Frank Lohr; Professor Umberto Ricardi; Professor Morten Hoyer; Professor Ugur Selek; Professor Yasushi Nagata; Professor Hiroshi Onishi; Dr. Yuan-Hung Wu; Professor Anne WM Lee; Dr. Kevin Chua; Dr. Balamurugan Vellayappan; Dr. Fabio Ynoe de Moraes; Dr. Alan Dal Pra; Dr. Anusheel Munshi; and Dr. Parthosarthy Mukherjee.



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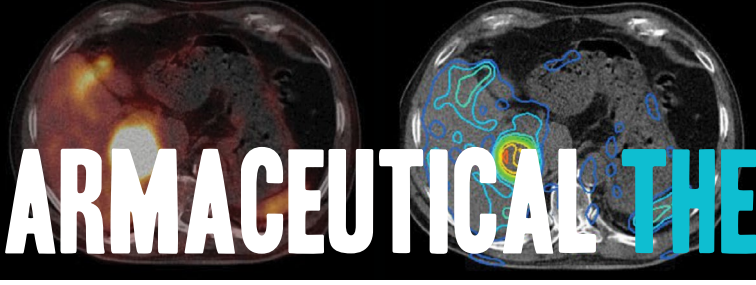

RADIOPHARMACEUTICAL THERAPIES

Breakthroughs in RPTs are emerging as new treatments for various cancers, and radiation oncologists are certified to deliver these RPTs. Here, three experts weigh in and provide updates on these advances.

Radiopharmaceutical Therapy: A New Frontier for Radiation Oncologists

BY SUSAN KNOX, MD, PHD

RADIOPHARMACEUTICAL THERAPY (RPT) is a form of systemically targeted radiation delivered by radionuclides either unconjugated (e.g., Ra-223) or linked to carriers (e.g., peptides, antibodies or microspheres) that bind specifically to tumors or accumulate in tumors. Many are now approved, with others at various stages of development for the treatment of a variety of tumor types. Treatment of patients with metastatic castration resistant prostate cancer (mCRPC) with Lu-177 Prostate Specific Membrane Antigen (PSMA) agents is very promising, with Lu-177-PSMA-617 showing efficacy and tolerability in a phase II study. Results from a randomized phase III study of Lu-177-PSMA-617, VISION trial (NCT03511664) are eagerly anticipated and may result in FDA approval of this agent in the relatively near future. This will be an important new addition to the treatment armamentarium for mCRPC.

Radiation oncologists are well positioned to not only administer this therapy but to take a leadership role in the development of similar therapies. Involvement in a scientific role beyond just being authorized users of RPT could be transformative to our specialty. Radiation oncologists played an important role in the development of radioimmunotherapy, and some practices administer free radionuclide therapies such as I-131 and other forms of RPT. As a field, we have expertise in radiobiology, radiation effects on tumors and normal tissues, management of radiation-associated toxicities and dosimetry.

The growth of RPT requires an interdisciplinary approach and collaboration and is an opportunity for radiation oncologists to expand practice and further develop this important new service line. We are ideally suited to treat, follow and care for patients treated with RPT and have referral pathways to both oncologic specialists and supportive care providers.

Our understanding of individualized dosimetry and close collaboration with medical physics will facilitate optimization of the therapeutic index for RPTs, with delivery of targeted high dose radiation to tumors with maximal sparing of normal tissues. ASTRO and other organizations will be providing training to facilitate this expanded scope of practice for many radiation oncologists. This is a tremendous opportunity for our field and an exciting new therapy to be able to offer to our patients. We need to "get in the game."

Susan Knox, MD, PhD, is associate professor of radiation oncology, emerita, at Stanford University.

Radiopharmaceuticals: Radiation Therapy Enters the Molecular Age

BY CHARLES A. KUNOS, MD, PHD

IN THE PERSONALIZED MEDICINE ERA, the National Cancer Institute (NCI) Division of Cancer Treatment and Diagnosis (DCTD) Cancer Therapy Evaluation Program (CTEP) has reconsidered its development strategies for radiopharmaceuticals. Over the past three years, this reconsideration promotes a shift away from external beam radiotherapy to a more modern use of targeted radiopharmaceuticals alone or in combination with biologically disruptive anticancer drugs. Issues that undercut the usual approaches to the development sequence are scarce patient, financial or professional resources; complex clinical trial objectives; and a belief that tolerable investigational agent toxicity brings about treatment efficacy. In an effort to overcome such barriers, the development sequence for targeted radiopharmaceuticals at NCI DCTD CTEP engages innovative phase 0 or 1 biomarker-driven trial designs recruiting smaller patient numbers, simpler

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safety and pharmacodynamic research objectives and biologically effective rather than maximally tolerated radiopharmaceutical exposures.

Radiation oncologists are firmly embedded in this radiopharmaceutical development initiative. Our specialty's footprint on clinical trial infrastructure and trial implementation marks strides taken by NCI DCTD CTEP to study "radioactive drugs." As infrastructure evolved, NCI DCTD CTEP brought in seven portfolio agents: radium-223 dichloride (Xofigo), lutetium-177 dotatate (Lutathera), tin-117m(4+) diethylenetriaminepentaacetic acid, and four thorium-227 radioimmunotherapy conjugates.[1] As clinical trials roll out, NCI DCTD CTEP intends overarching goals of optimizing the therapeutic ratio of these agents alone or in combination and of testing efficacy in other disease indications. Only 2% of the clinical trial portfolio involves radiopharmaceuticals; however, it is projected over the next five years that up to 15% of the portfolio will engage radiopharmaceuticals as primary or maintenance therapy.

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Charles A. Kunos, MD, PhD, is a medical officer in the Investigational Drug Branch, Cancer Therapy Evaluation Program, National Cancer Institute.

Dosimetry for Radiopharmaceutical Therapy

BY ROBERT HOBBS, PHD

RADIOPHARMACEUTICAL THERAPY (RPT) IS FAST BECOMING A MAINSTREAM MODALITY with the development and approval of new emitters and conjugates. Currently, FDA-approved RPTs are administered with fixed activities or using mass-based dosing. However, RPT presents an advantage over chemotherapy, with the ability to image the drug using PET/CT or SPECT/CT. By administering a small pre-therapeutic activity of the therapeutic itself — or of a companion diagnostic agent (the theranostic paradigm) — and imaging over multiple time points, the pharmacokinetics specific to the individual patient are obtained, and the therapeutic administered activity may be adjusted to normal organ dosimetric tolerance limits, resulting in a more effective therapy. An early RPT targeting lymphoma, ^{131}I-ibritumomab tiuxetan (Bexxar), implemented this approach using planar imaging and a whole body absorbed dose surrogate (75 cGy) for hematotoxicity. The administered activities for the threshold absorbed dose ranged from 50–150 mCi with a few patients able to receive upwards of 250 mCi.[1,2] This variability in pharmacokinetics is representative of RPTs and demonstrates the potential impact of rational dosimetric-based treatment planning. Recently, ^{90}Y-therasphere therapy for HCC using tumor and normal organ dosimetric thresholds (minimum and maximum, respectively) rather than whole irradiated volume absorbed dose, showed a significant benefit in patients (26.6 vs. 10.7 months median survival).[3]

ASTRO, AAPM, SNMMI, IAEA, ICRU and NCI are all strong advocates for personalized dosimetry-based treatment planning, which is expected to become the norm in the near future with a demand for qualified physicians and medical physicists to oversee and apply these methodologies. The exceptions remain alpha-particle therapies, for which the dosimetric methodologies are more complex and not fully mature for widespread use. Radiation oncology has a long history of dosimetry-based treatment planning experience from EBRT, with tools, techniques, personnel and infrastructure readily adaptable to RPT, all necessary to implement such approaches with the precision, quality assurance and standardization to ensure safety and efficacy of treatments. Conversely, radiation oncologists typically lack experience specific to the field of RPT. Now is the time to embrace continuing RPT education and training and to support collaboration with colleagues from nuclear medicine to implement advanced dosimetric-based RPTs.

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Robert Hobbs, PhD, is an associate professor of radiation oncology and molecular radiation sciences at Johns Hopkins Medicine.

BY PAUL E. WALLNER, DO, FASTRO, AND BRIAN J. DAVIS, MD, PHD

SCOPE OF PRACTICE, CERTIFICATION ASSESSMENT AND AN UPDATE ON QUALIFYING EXAMS

A DISCUSSION OF THE SCOPE OF RADIATION ONCOLOGY PRACTICE, as considered by others in this edition of *ASTROnews* and related to the ASTRO survey and its analysis by Fung et al.,[1] represents an important snapshot of the specialty. In addition to the survey, and of critical importance, is the difference between the legal and regulatory definition of "scope of practice," as promulgated by various jurisdictional legislatures and medical regulatory bodies[2] and an individual's personal interest or practice focus. While licenses to practice medicine in most U.S. jurisdictions specify either Medicine or Medicine and Surgery, legislation or regulation in those jurisdictions defines what the individual can legally do in a more granular manner. Facilities may further define an individual's practice role by institutional privileges. In the case of radiation oncology in the U.S., the legal scope of practice is further defined by regulations of the U.S. Nuclear Regulatory Commission (NRC) and individual Agreement States.[3] In defining regulatory scope of practice, these jurisdictional entities invariably look to training requirements as specified by the Accreditation Council for Graduate Medical Education (ACGME) and the assessment instruments of the 24 American Board of Medical Specialties (ABMS) member boards. Interventions not included in ACGME training requirements or ABMS member board certification instruments will typically not be included in jurisdictional scope of practice regulations. In the case of radiation oncology, the ACGME Radiation Oncology Review Committee is careful to include all areas of the specialty, whether of significant interest or individual practice focus,[4] and the ABR is careful to include all these areas in its initial certification and continuous certification assessment instruments.[5]

The ABR recognizes that for continuous certification, its Online Longitudinal Assessment (OLA) instrument may include topics such as radiopharmaceutical management, pediatric cancer care or specific organ disease sites that may not be of relevance to some or many candidates or diplomates. However, to support the scope of practice interests of all, these must continue to be included in assessment. In the absence of subspecialty certification in specific radiation oncology modalities, the Board uses indications of "relevance" as noted by OLA responders in developing item frequency, but absolute elimination of these items is not within our interest as a specialty given these practice considerations.

Qualifying exams update

In summer 2020, the ABR radiation oncology trustees proposed a significant change in eligibility policy for the qualifying (computer-based) exams. The Board of Governors recently approved a change to the timing requirements for eligibility to sit for the qualifying exams. In medical physics for radiation oncology and radiation and cancer biology, trainees can now sit for the exam after completing 24 months of residency, reduced from 36 months. For the clinical oncology qualifying exam, timing has been reduced to 44 months in residency, from 48, with both needing approval from the program director. These changes were enacted to provide programs with greater flexibility in didactic programming and to allow residents greater flexibility in managing personal and professional time. Because of personal and program disruptions caused by the COVID-19 pandemic, the qualifying and certifying exams will each be administered twice in 2021. This semiannual administration is anticipated only for 2021. Dates of administration and additional details of the policy changes can be found at www.theabr.org.

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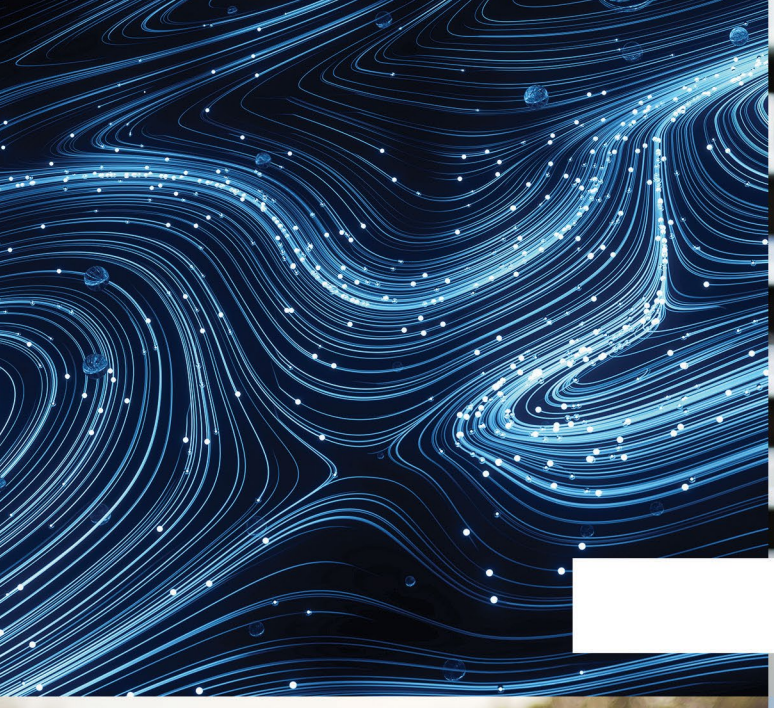

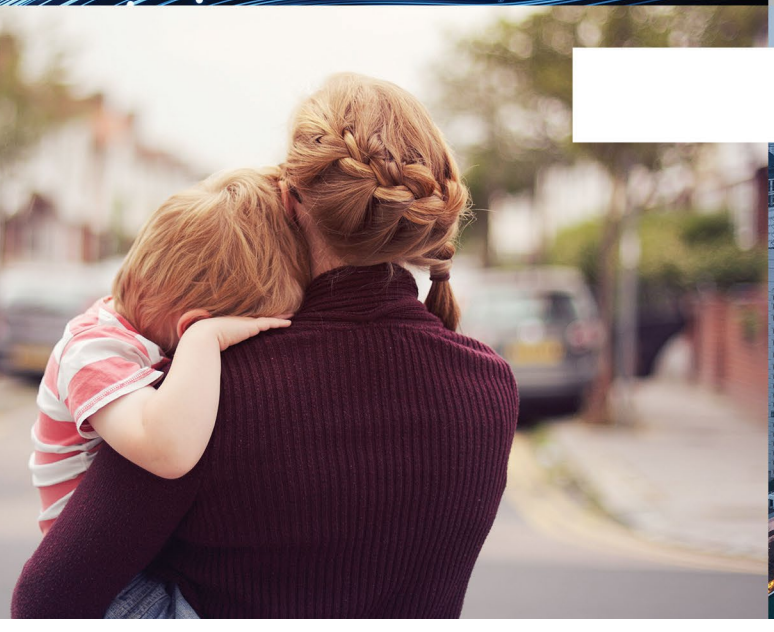

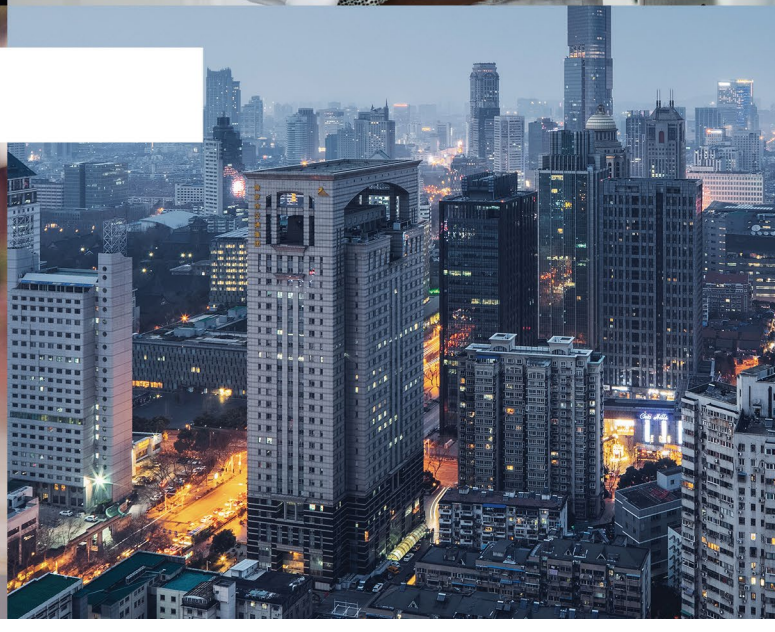

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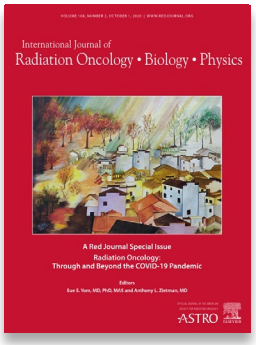
JOURNALS HIGHLIGHTS



HIGHLIGHTS FROM THE *INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY • BIOLOGY • PHYSICS*

October 1, 2020

Radiation Fractionation Schedules Published During the COVID-19 Pandemic: A Systematic Review of the Quality of Evidence and Recommendations for Future Development

Thomson et al.

Appearing in the Red Journal's special issue dedicated to COVID-19, this article assessed aggregate changes in the quality of the evidence supporting hypofractionated RT schedules. Based on a systematic review of published recommendations related to dose fractionation during the pandemic, 20 expert panelists assigned to 14 disease groups named and graded the highest quality of evidence schedule(s) used routinely for each condition and graded all COVID-era recommended schedules. Many publications recommended hypofractionated schedules across numerous major disease sites in the early days of the COVID-19 pandemic, which were supported by a lower quality of evidence than the highest quality, routinely used dose fractionation schedules.

November 1, 2020

Cardiac Irradiation Predicts Activity Decline in Patients Receiving Concurrent Chemoradiation for Locally Advanced Lung Cancer

Paul et al.

In this study, the authors explored dosimetric predictors of activity decline in a cohort of patients who underwent continuous activity monitoring during definitive concurrent chemoradiotherapy (CRT) for locally advanced lung cancer. Forty-six patients logged their steps from one week before treatment until two weeks after treatment. The extent of cardiac irradiation is associated with the rate of physical activity decline during CRT for lung cancer.

November 15, 2020

Urethra-sparing Stereotactic Body Radiation Therapy for Prostate Cancer: Quality Assurance of a Randomized Phase 2 Trial

Jaccard et al.

Between 2012 and 2015, 165 patients with prostate cancer from nine centers were randomized and treated with SBRT delivered either every other day or once a week; 36.25 Gy in 5 fractions were prescribed to the prostate with (n = 92) or without (n = 73) inclusion of the seminal vesicles (SV), and the urethra planning-risk volume received 32.5 Gy. Patients were treated either with volumetric modulated arc therapy (VMAT; n = 112) or with intensity-modulated radiation therapy (IMRT; n = 53). Deviations from protocol dose constraints, planning target volume (PTV) homogeneity index, PTV Dice similarity coefficient and number of monitor units for each treatment plan were retrospectively analyzed. Protocol deviations with potential impact on tumor control or toxicity occurred in 31% of patients in this prospective clinical trial. Protocol deviations were more frequent with IMRT.

HIGHLIGHTS FROM *PRACTICAL RADIATION ONCOLOGY*

November/December 2020

Practical Safety Considerations for Integration of Magnetic Resonance Imaging in Radiation Therapy

Hu et al.

The authors of this article note that while there is strong interest in the integration of magnetic resonance (MR) imaging into radiation therapy (RT) treatment and that there are several notable benefits, there are also many challenges that have not been fully addressed. This article provides an overview of MR safety in the RT environment. Examples of issues considered include possible effects of the magnetic field on patients and equipment, patient check-in and screening procedures, and device and equipment safety considerations. A wide variety of equipment and devices are used in RT, and many are not clearly labeled for MR safety, which in conjunction with a lack of staff familiarity with MR, can be a hazard. The authors suggest developing an MR safety program specific for RT, collaborating with the diagnostic imaging community.

Continued on the following page

Articles in Press

Radiation Therapy for Rectal Cancer: Executive Summary of an ASTRO Clinical Practice Guideline

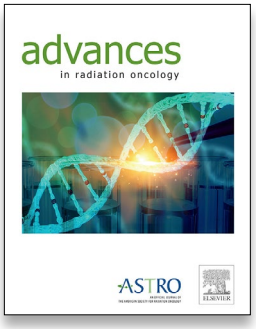
Wo et al.

This ASTRO Clinical Practice Guideline reviews the evidence and provides recommendations for the use of neoadjuvant radiation therapy (RT) in the treatment of localized rectal cancer. The guideline addresses four key questions: What are the indications for neoadjuvant RT for operable rectal cancer? What are appropriate neoadjuvant regimens for operable rectal cancer when neoadjuvant therapy is indicated? What are the appropriate indications for consideration of a nonoperative (NOM) or LE approach after definitive/preoperative chemoradiation? And what are the appropriate treatment volumes, dose constraints and techniques for patients treated with RT? This guideline is discussed on a podcast hosted by *Practical Radiation Oncology* Senior Editor Michael Buckstein, MD, PhD, which is available on the ASTRO Journals podcast channel and at https://www.practicalradonc.org/content/podcast.

VMAT Grid Therapy: A Widely Applicable Planning Approach

Grams et al.

This article describes a volumetric modulated arc therapy (VMAT) approach to spatially fractionated radiation therapy (SFRT), also known as grid therapy. The authors suggest that a VMAT approach to grid therapy will help with two major drawbacks in conventional grid therapy: When considering organ sparing, assisted by gantry and couch angles as well as multileaf collimators, the depth of maximum dose may not be within the tumor itself; and because of the single static field, a significant portion of exit dose may be delivered beyond the target into normal tissue. The approach described in the article uses the software and general approach of standard VMAT planning and delivery, which would make it accessible to institutions already utilizing VMAT. The authors use preferentially located high-dose regions to better treat deep targets that may be surrounded by critical structures and suggest that their approach is accessible and can be readily implemented once the technique, patient selection and delivery processes are established.



HIGHLIGHTS FROM *ADVANCES IN RADIATION ONCOLOGY*

September/October 2020

Reirradiation of High-grade Gliomas: A Retrospective Analysis of 198 Patients Based on the Charité Data Set

Kaul et al.

This article explores the treatment of high-grade gliomas with reirradiation. Currently, there is no standard of care for the treatment of gliomas, treatment remains a challenge and a majority of patients experience relapse despite the use of multimodal treatment approaches. The authors conducted a retrospective analysis of patients who were treated with reirradiation for high-grade gliomas from January 1997 to February 2014. The study concluded that while reirradiation was well tolerated even in cases of early reoccurrence, fewer than 8% of patients developed grade 3 or greater toxicity, and prognosis remains dismal.

Patterns of Failure After Intensity-modulated Radiation Therapy in Head and Neck Squamous Cell Carcinoma of Unknown Primary: Implication of Elective Nodal and Mucosal Dose Coverage

Kamal et al.

Metastatic head and neck squamous cell carcinoma of unknown primary disease (HN-SCCUP) is uncommon. Due to very few randomized trials, there is a lack of consensus on the treatment of the disease. This article evaluates the dosimetric and geometric based distribution of mucosal and nodal recurrences after intensity-modulated radiation therapy (IMRT) using validated typology-indicative taxonomy among a large patient cohort. The study retrospectively analyzed patients treated with curative IMRT for HN-SCCUP. It showed that most patients who developed nodal recurrences did so in the irradiated tissue, specifically in the high-dose region (type A). Future research should focus on novel radiosensitizers, dose escalation of high-risk volumes and metabolic-directed tumor segmentation.

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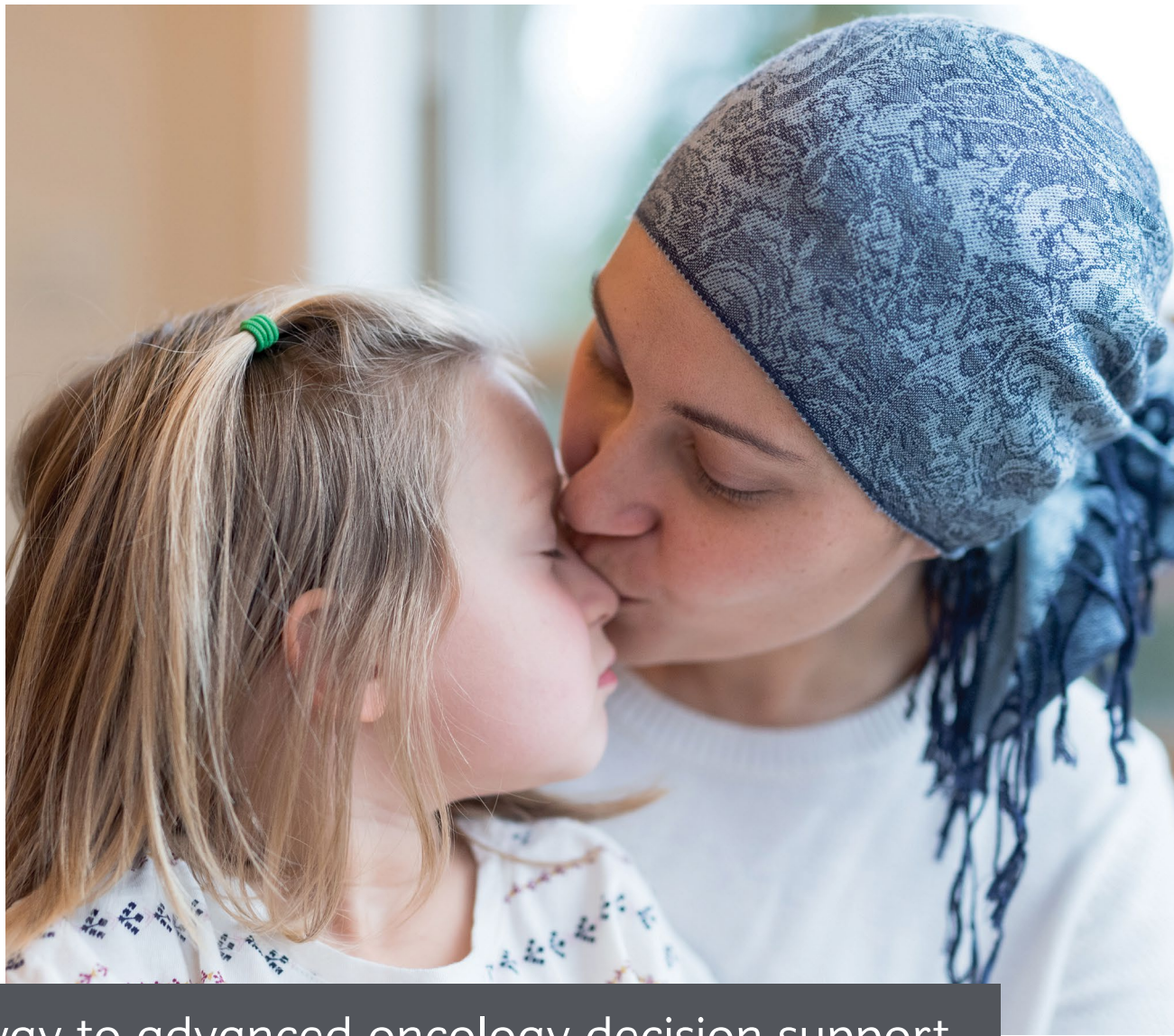

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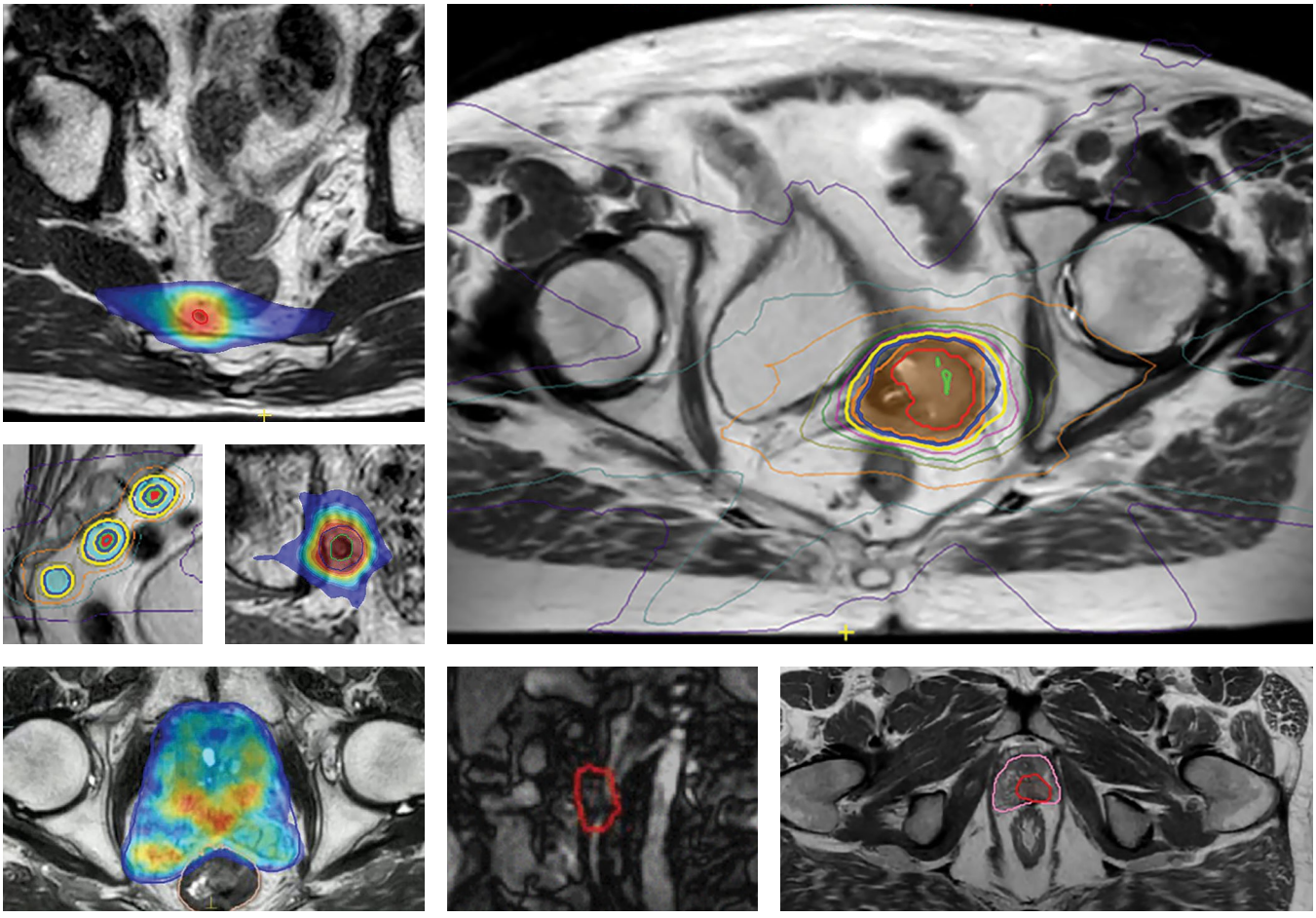

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