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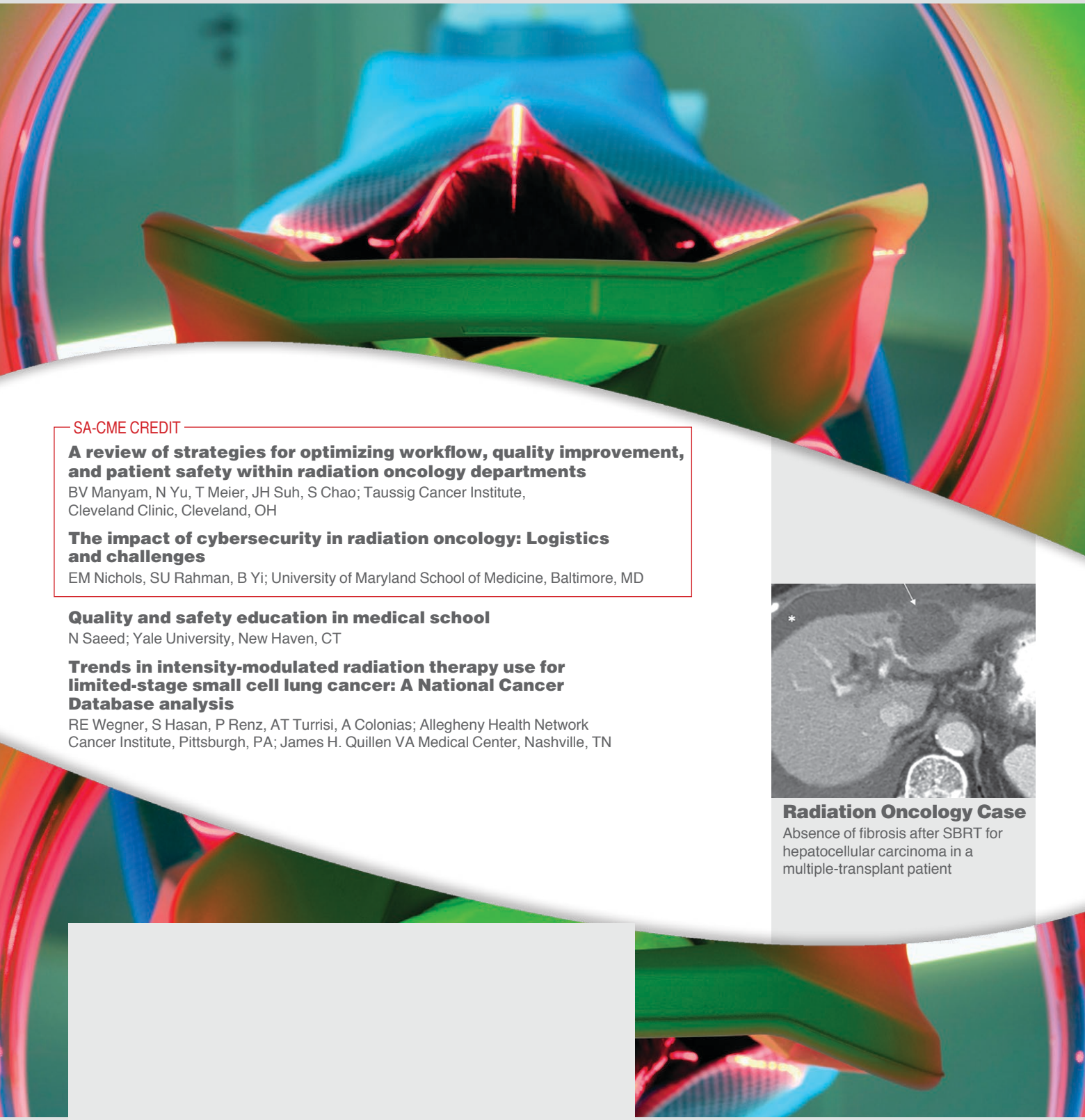

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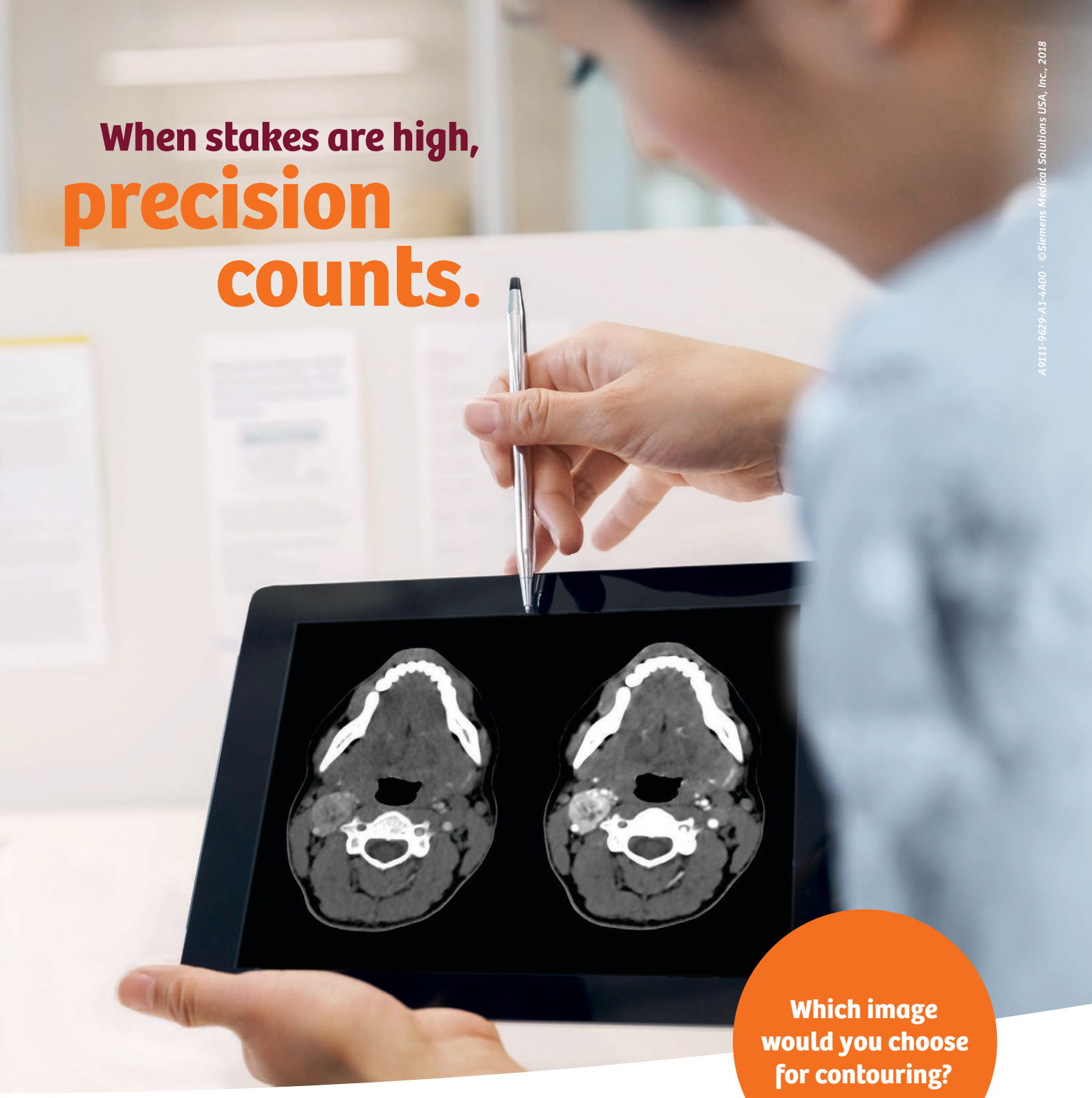

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John Suh, MD, FASTRO

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Circulation Director
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TEL: 908-301-1995
FAX: 908-301-1997

info@appliedradiationoncology.com
www.appliedradiationoncology.com

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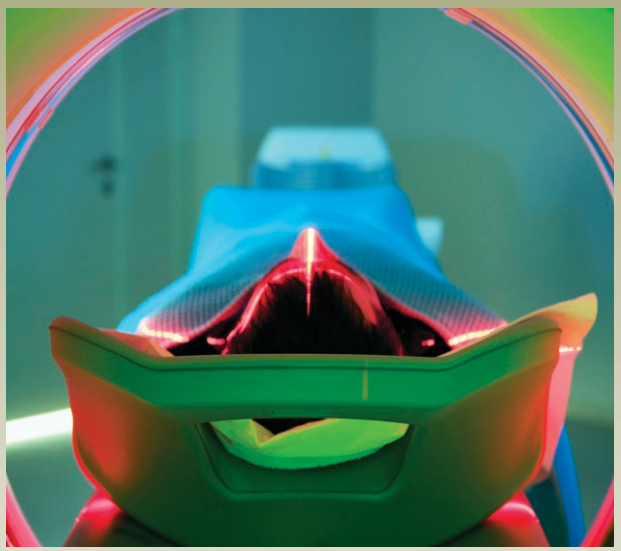

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EDITORIAL

Cybersecurity, workflow and quality

John Suh, MD, FASTRO
Editor-in-Chief

Hacking, phishing, spoofing – these and other types of cyberattacks are often one click away from potentially disastrous consequences. Damage can include crippling computer viruses, extortion, personal privacy violations, and cancelled treatments – and it can happen to anyone. Unfortunately, such breaches in cybersecurity are on the rise in radiation oncology and healthcare overall.

Exploring this topic, University of Maryland's Elizabeth Nichols, MD, and colleagues, present the eye-opening review article, *The impact of cybersecurity in radiation oncology: Logistics and challenges*. Presented as part of this month's focus on quality and safety, the SA-CME-approved article describes experiences and unique considerations in radiation oncology that can help prevent and overcome a costly, exhausting cyber disaster. Strategies focus on radiation oncology IT infrastructure, electronic medical records, automatic time outs, treatment planning and delivery, plan verification, screen locking and more.

Also part of our safety theme is *A review of strategies for optimizing workflow, quality improvement, and patient safety within radiation oncology departments* by Cleveland Clinic's Bindu V. Manyam, MD, and colleagues. This well-written, comprehensive article identifies initiatives to mitigate errors related to workflow changes, misinformation transfers, heavier workloads, greater treatment complexity and other causes. Also outlined are specific efforts for incorporating quality improvement and patient safety into resident education.

We are also pleased to feature the review, *Quality and safety education in medical school* by Nadia Saeed, BA, Yale School of Medicine. This thoughtful article targets an important topic that, happily, is gaining much-needed attention. Key dimensions of quality and safety training in medical education are discussed, including quality and safety training specific to radiation oncology.

Rounding out this issue is *Enhancing quality, safety and efficiency in treatment planning with health information technology (HIT) and artificial intelligence (AI)*. Industry experts share advice in this Technology Trends installment on how to best leverage medical error reporting systems, patient safety databases, machine learning, human factor engineering, and related AI and HIT efforts to underscore quality and safety measures.

Please also enjoy this issue's novel case reports; research article on intensity-modulated radiation therapy (IMRT) usage in lung cancer; and Resident Voice editorial, which showcases an inspired way to meet information overload head on.

Finally, stay tuned for announcements of the 2018 winners for best case report ($500 prize), review article ($1,000 prize) and research article ($1,000 prize). Votes are underway, and we are excited to share news on these top *ARO* papers soon.

As we enter the new year, we wish to thank you for your continuous support of the journal and its many online offerings. Your input and contributions have fueled our growth and helped to shape our goals of continuous improvement and innovation. Our very best wishes to you for a joyous holiday season and peaceful, bright, and memorable 2019!

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

RESIDENT VOICE

Embracing information overload

Laura Dover, MD, MSPH

Laura Dover, MD, MSPH

Caleb Dulaney, MD

***Dr. Dover** is a PGY-5 resident physician in the Department of Radiation Oncology at the University of Alabama at Birmingham (UAB). **Dr. Dulaney** is a practicing radiation oncologist at Anderson Regional Cancer Center in Meridian, MS. Drs. Dover and Dulaney are co-creators of QuadShot News (www.quadshotnews.com).*

The reasons we each pursue a career in oncology are in some ways overlapping and in other ways distinct. But, as we look toward the future, we are all faced with the same challenges that lie ahead. What makes oncology arguably the most exciting field of 21st century medicine is also what makes it so formidable to its practitioners: its rapid pace of advancement.

If I am honest, early in my training, this fast pace disheartened more than invigorated me. I was constantly bombarded with new publications, while at the same time struggling to learn the current standard of care. Each time I opened my inbox, I felt I was losing ground. What's worse, I came to realize there was no light at the end of the tunnel. There was no point I would reach in my career where I would finally have time to catch up. As an oncologist, it is unsettling to continually worry there may be a breakthrough your patient will never hear about simply because her physician was unaware of it.

The fact is that growth in the number of reported scientific results over the last decade alone has been logarithmic, posing a growing critical barrier for practicing oncologists striving to stay current on the best available cancer care.[1] This is also, without doubt, a contributing factor to rising rates of resident physician burnout.[2] At the same time, practicing physicians have a growing disgruntlement with mandated, formalized continuing medical education (CME) that is often costly—both in monetary value and time spent—without affording corresponding educational value.[3]

The upside? Big problems are often the gateways to big advancements. My first reaction to information overload was the same as mine to any challenge: to commiserate with my co-residents, of course. While I was bemoaning our crumbling system of effective oncology education, my co-resident Caleb was opening an email newsletter conveniently describing the most pertinent highlights of the day's national news. He posed the question, "Wouldn't it be great if we had a resource like this for *cancer* news?" To my ears this was reminiscent of my partner's universal response to any variety of my complaining, "There are no problems, only solutions."

That day in the resident room, QuadShot News was born. QuadShot News is a web-based daily newsletter for oncologists to easily and efficiently stay informed of recent medical literature and policy developments that influence

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clinical practice. Unlike existing platforms that deliver tables of contents with a list of verbose titles, we understand that combining ease and entertainment with education enhances learning.[4] With this in mind, we intentionally format succinct blurbs to enable readers to learn in a quick, engaging manner with as little medical jargon as possible.

In the past year, QuadShot News has steadily grown to reach over 10% of practicing radiation oncologists nationwide. I attribute our initial success to two key factors: a powerful mission and powerful collaboration. For the past year, Caleb and I have been mission-obsessed. We are always brainstorming ways we can make our educational platform more effective, more efficient, and more engaging. Focusing on our mission rather than our product ensures we solve what we set out to do.

Finally, continual collaboration with our co-residents, mentors, colleagues and friends at other institutions frees us from being limited to our own strengths. Together we can capitalize on information overload to become a stronger, more equipped field as we inevitably enter the next era of oncology.

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SA–CME Information

A REVIEW OF STRATEGIES FOR OPTIMIZING WORKFLOW, QUALITY IMPROVEMENT, AND PATIENT SAFETY WITHIN RADIATION ONCOLOGY DEPARTMENTS

Description
With increases in complexity of radiation delivery and patient volume, vulnerable sources for errors may exist within radiation oncology workflow. Patterns of care recommendations are outlined by the American College of Radiology and the National Comprehensive Cancer Network guidelines; however, departmental and institutional policies and standards for quality and patient safety may vary. This article examines initiatives to mitigate errors and enhance safety, and describes efforts to incorporate quality improvement and patient safety into resident education.

Learning Objectives
After completing this activity, participants will be able to:

1. Identify areas within radiation oncology workflow that may be susceptible to errors.
2. Implement strategies at the personnel and systems level that will mitigate errors, enhance safety, and improve quality of care.

Authors
Bindu V. Manyam, MD, is a resident, **Naichang Yu, PhD**, is a medical physicist, **Tim Meier, RTT**, is a radiation therapist, and **John H. Suh, MD**, and **Samuel T. Chao, MD**, are radiation oncologists at the Department of Radiation Oncology, Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH.

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As part of this CME activity, the reader should reflect on how it will impact his or her personal practice and discuss its content with colleagues.

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A review of strategies for optimizing workflow, quality improvement, and patient safety within radiation oncology departments

Bindu V. Manyam, MD; Naichang Yu, PhD; Tim Meier, RTT; John H. Suh, MD; Samuel T. Chao, MD

Safety challenges within the field of radiation oncology have gained increasing attention in the mainstream media and among organizations such as the Food and Drug Administration (FDA), American Society for Radiation Oncology (ASTRO), and the American Association of Physicists in Medicine (AAPM) over the last decade.[1,2] Prior data has suggested that changes in workflow, transfer of misinformation, increasing workload of radiation oncology services and complexity of treatment delivery are frequent sources of errors, underscoring the importance of established processes for patient safety and mechanisms for quality improvement for ensuring the safe delivery of radiation therapy.[3-6]

***Dr. Manyam** is a resident, **Dr. Yu** is a medical physicist, **Mr. Meier** is a radiation therapist, and **Dr. Suh** and **Dr. Chao** are radiation oncologists at the Department of Radiation Oncology, Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH.* *Disclosure: The authors have no conflicts of interest to disclose. None of the authors received outside funding for the production of this original manuscript and no part of this article has been previously published elsewhere.*

Patterns of care recommendations are outlined in the American College of Radiology (ACR) Appropriateness Criteria and the National Comprehensive Cancer Network (NCCN) guidelines; however, dedicated procedures at the departmental and institutional level are essential as well.[2] The ACR Practice Parameters discuss typical components of a quality improvement program including peer review, periodic auditing of radiation oncology medical records, review of physics quality improvement, review of incident reports and deviations, and patient outcomes.[2] Suggested components include new patient review, chart review (both clinical and physics), image verification review, and incident reporting and learning system to facilitate quality improvement projects. The International Atomic Energy Agency (IAEA) has identified that optimization of patient safety within radiation therapy require personnel-, system-, and equipment-level initiatives.[4] Voluntary error reporting systems and comprehensive quality assurance programs have been shown to significantly decrease error rates within radiation oncology.[7] This article will review areas susceptible to error within radiation oncology workflow, present primarily personnel- and system-level initiatives implemented within our department and other institutions to mitigate errors and enhance safety, and to describe efforts to incorporate quality improvement and patient safety into resident education.

Incident Reporting Systems

The systematic documentation, reporting and analysis of incidents is a critical first step in the quality improvement process. A national system for incident reporting within radiation oncology has been proposed by the Canadian Partnership for Quality in Radiation (CPQR) therapy to standardize taxonomy and classification of severity

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Table 1. Simulation Verification Checklist at the Cleveland Clinic

1st Page to Physician Team from Simulation Team When Patient is En Route to Simulation

1. Verify patient name and date of birth
2. Verify not pregnant, if female
3. Access consent form within electronic medical record
    a. Verify treatment site
4. Access prescription within Mosaiq integrated information software
    a. Verify diagnosis, category, stage, treatment intent, protocol, treatment site, and prescription dose
5. Access simulation request and verify:
    a. Set-up
    b. Site and laterality (must match consent)
    c. Position
    d. Immobilization
    e. Markers
    f. Bolus
    g. Contrast
    h. Motion management
    i. Superior and inferior borders of CT scan
    j. Treatment start date
6. Verify site technique (ie, 2- or 3-field)
7. Start CT simulation

2nd Page to Physician Team from Simulation Team: Ready to Place Isocenter

Key: CT = computed tomography

of incidents. A list of 26 core elements was generated, which included event description, severity classification with a medical acute injury and dosimetric scale, hazards, and mitigating factors, and was reviewed by a panel of experts for consensus.[8] Similarly, ASTRO and AAPM implemented the Radiation Oncology Incident Learning System (ROILS) in 2014, with 425 facilities across the United States, which facilitates collection of incidents within a national database with generation of quarterly aggregate reports on events throughout the country with suggestions on process improvement.[6,9] As there is likely variation across institutions regarding descriptions and classifications of incidents, initiatives such as these serve as a model for a systematic method for incident reporting, which can improve multi-institutional data collection and implementation of interventions across systems.

The Workflow Enhancement (WE) Team serves, in part, as a structured reporting system for incidents and errors specific to our department, separate from our institution's incident reporting system.[10] Errors are reported anonymously online through the department's intranet site or can be reported at the biweekly process improvement meeting. Errors can be reported by physicians, radiation therapists, dosimetrists, medical physicists, residents, nurses, and administrative staff. Forms contain patient identifiers, including name and medical record number, error category/type, and description of the error, and all forms are recorded into a secure Excel database. An analysis of all incidents submitted to the WE Team in 2013 demonstrated 10 incidents. The number of patients treated per day was significantly associated with increased risk of incidents ($p < 0.003$) and the ratio of patients to physicians was significantly associated with errors ($p < 0.03$).[5] Increased workload as a risk factor for error has been identified within other institutional reporting systems as well.[11] Additionally, communication breakdown and changes in workflow are also well-established sources of error in the literature.[3-6] Workflow processes, communication protocols, systematic checks to mitigate these sources of errors and departmental stressors are discussed below.

Implemented Initiatives

CT Simulation Time-out/ Checklist Procedure

The efficacy of safety checklist procedures in reducing errors is well established in the surgical literature and is now a national patient safety goal standard.[7,12] The computed tomography (CT) simulation procedure is one of the first steps within the radiation therapy treatment planning process and its accurate completion is critical. Failure to complete this step can lead to substantial downstream effects, including additional, unnecessary testing; patient treatment delays; and errors in treatment delivery. An analysis of incident reports through the WE Team at our institution identified 136 simulation-related events reported between 2014 and 2016. Examples of simulation-related events included wrong site imaged, failure to administer contrast, failure to place mouthpiece, etc. A safety check-

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Table 2. Rates of Quarterly Noncompliance to Daily and Weekly Metrics Before and After QMAP Implementation at the Cleveland Clinic

Metric	Definition	Miss rate Pre-QMAP 2011	Miss rate Post-QMAP 2016
Plan completion	Plan ready 4 hours before scheduled treatment	14.8%	4.0%
CBCT review	Physician reviewed CBCT on day of acquisition	8.0%	<1.0%
Weekly physics check	Completed on or before the 5th fraction of each 5-fraction block	10.2%	<1.0%
Weekly physician on treatment visit	Completed on or before the 5th fraction of each 5-fraction block	6.1%	2.0%

Key: QMAP = Quantitative Metric and Automatic Auditing Program, CBCT = cone-beam computed tomography

list and time-out procedure were implemented to address the errors noted in the simulation process. A pocket safety checklist card was distributed to all physicians (**Table 1**) and verbal communication between the radiation therapist and physician was required prior to the patient's simulation.[13] One year after implementation of this safety procedure, the number of simulation-related events reported to the WE Team decreased by 57% ($p < 0.0001$).[13] Specific safety checklists have now been introduced for prostate and gynecologic brachytherapy, intraoperative radiation therapy (IORT), and stereotactic radiosurgery (SRS) procedures.

Quantitative Metric and Automatic Auditing Program (QMAP)

Process consistency, automation, workflow standardization, and frequent checks and reminders are effective mechanisms for reducing errors and streamlining processes involving multiple teams. At our institution, our incident reporting system identified timely checks of cone-beam CTs, plan completion, weekly physics checks, and weekly physician on treatment visits, as areas of improvement, with quarterly late checks of these tasks ranging from about 6% to 15%. Timely and accurate completion of these tasks is imperative to identifying potential errors and optimizing patient safety. To mitigate this, our department implemented a Quantitative Metric and Automatic Auditing Program (QMAP). Acceptable time frames for completing each task were agreed upon. A software program was developed using Mosaiq (Elekta, Stockholm, Sweden) integrated information software to generate an automatic timestamp upon completion of each critical clinical task, as well as reminders if a task was not completed. In addition to reminding the responsible party, a designated triage team is also notified to help mitigate a workflow delay before it occurs. The rates of timely completion of daily and weekly metrics before and after QMAP implementation are summarized in **Table 2.**

Similarly, the University of Michigan reported on the development of a Plan-Checker Tool (PCT) within the Eclipse Scripting Application Programming Interface (Varian, Palo Alto, California) as another effort to automate workflow, improve efficiency, and reduce treatment delays.[14] Their software includes a system of automated and manual checks of a plan's suitability for treatment. The highest frequency error identified was within the category of secondary check software, with examples including a plan not exported to the treatment planning system and a reference point not having a location to calculate MUs (18%). Other examples include a mislabeled field name, scheduling errors, and plan and prescription inconsistencies. They were able to automate 19 of 33 checklist items, which led to a 60% reduction in the number of patient delays due to errors in the treatment planning process after 6 months of PCT implementation. PCT did not reduce the number of errors found during the physics check; however, it increased the identification of errors that help avoid treatment delays and, most importantly, potential errors in treatment delivery.[14] Automation is an important tool for improving quality and workflow.

Structured Peer Review

Across providers, there can be substantial variability in patient positioning, target volume delineation, choice of dose fractionation, and normal tissue dose constraints within the radiation treatment planning process. The AAPM and the European Organization for Research and Treatment of Cancer

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(EORTC) have recommended quality assurance rounds with treatment plan peer review to ensure patient outcomes are not affected by interprovider variability.[15] The impact of structured peer review is well illustrated by a study of 1,247 plans reviewed in quality assurance rounds from 2004 to 2010 in a Canadian radiation oncology department. Plans were peer reviewed and graded as being adequate (A), needing minor suggestions of change to a plan for a future patient (B), or requiring significant change before delivery of the next fraction (C). They determined that 6% of plans were graded B and 1% were grade C and that mean years of experience were less for the plans graded C compared to those graded A ($p = 0.02$), highlighting the importance of peer review for physician education.[16] Treatment plan peer review often occurs after a patient has started treatment, so as to avoid treatment delays. Despite increased logistical concerns, there may be value in prospective peer review before a patient starts treatment. Mitchell et al published their experience with prospective peer review of 422 cases over 2 years and identified that 20.6% of cases were marked as having a variation, with 0.7% having a major deviation. They found that a change in contours was recommended in 10% of cases, with peer review requiring, on average, 7 minutes per case.[17] Their data suggests that prospective peer review is a feasible practice and influences changes in practice.

Our institution has implemented several established processes for structured peer review, which requires the following in order to be effective: active participation from providers; a supportive and respectful environment; support from leadership to maintain dedicated time and reduced interruptions; and availability of facilities and technology to access images, electronic medical record data, planning images, and remote capabilities for off-site participants. Most time is dedicated to our weekly retrospective chart review of all new patient treatment starts, which includes participation of physicians, physics, dosimetry, and therapists. To increase consistency of practice patterns across hospitals within our integrated healthcare system, we have implemented monthly, disease-site specific, retrospective peer review. Prospective peer review efforts include all stereotactic body radiation therapy (SBRT) treatment plans and head and neck treatment plans and, most recently, review of challenging cases across hospitals within our integrated healthcare system. This includes a voluntary review of contours and dosimetry using disease-site-specific teams of experts. The ultimate goal of prospective peer review is to standardize treatment plans and establish the same quality of care throughout the enterprise. In addition, the reduction in variability potentially may reduce treatment errors through consistency.

Quality Improvement, Patient Safety in Radiation Oncology Resident Education

The Accreditation Council for Graduate Medical Education (ACGME) mandates resident and fellow participation in quality and patient safety education; however, release of the Clinical Learning Environment Review demonstrated that trainee knowledge of formal methods for patient safety reporting and analysis can be improved.[18] Our department encourages resident participation in the WE Team and, in keeping in line with ACGME requirements, a resident-led quality and patient safety project is implemented within the department annually. Examples of resident-led initiatives in our department include standardization of disease-site-specific simulation request templates, creation of dosimetric score cards to standardize treatment plan evaluation, and implementation of atlas-based auto-segmentation to standardize normal tissue contouring. Encouraging education of the science and methods of quality improvement and patient safety for trainees will promote these processes in practice and lead to lasting change. Also, developing a mindset of quality improvement and safety will lead to ongoing continuous improvement as residents graduate and enter practice.

Implementing and Sustaining Change

Although these initiatives were in a large academic, tertiary care center, many of these strategies can be implemented in much smaller centers by utilizing all members in the department including physicists, dosimetrists, therapists, nurses, and administrative staff. For instance, our WE Team employs all members of the department to discuss issues and develop multidisciplinary solutions to minimize recurrence. To implement and sustain these strategies, a safety culture with a blame-free environment must be developed. With this in place, an effective incident learning and reporting system can be developed. Ford et al summarizes the key components of an incident learning system, including identifying and addressing cognitive bias, which can impede effective solutions.[19] This bias includes imagining that a wrong decision is being made at that time to identify cognitive missteps, considering the opposite (ie, imagining that the opposite conclusion is correct), recalibration whereby one acknowledges that bias can calibrate thinking, and crowd wisdom.

Conclusion

Avoiding harm and providing the best care is the responsibility of the health care system. As such, quality and patient safety should be priorities, which, in turn, can be improved by a safe environment and structured

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system to report near misses and errors, standardization and automation of workflow, and a structured peer review process. Commitment to these processes is a collective effort on both the individual and system level.

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SA–CME Information

THE IMPACT OF CYBERSECURITY IN RADIATION ONCOLOGY: LOGISTICS AND CHALLENGES

Description
Breaches in cybersecurity can levy drastic consequences in radiation treatment delivery and health care overall. This review article describes experiences and unique needs and strategies pertaining to radiation oncology IT infrastructure, electronic medical records, automatic time outs, treatment planning and delivery, plan verification, screen locking and more to help prevent and overcome a cyber disaster.

Learning Objectives
After completing this activity, participants will be able to:
1. Recognize critical areas of cybersecurity risk in the radiation oncology department/clinic.
2. Adopt strategies to bolster cybersecurity within the radiation oncology department.

Authors
Elizabeth M. Nichols, MD, is assistant professor and clinical director, **Shafiq Ur Rahman, MBA, MS**, is director of radiation oncology IT, and **Byongyong Yi, PhD**, is a professor, University of Maryland School of Medicine, Department of Radiation Oncology.

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The impact of cybersecurity in radiation oncology: Logistics and challenges

Elizabeth M. Nichols, MD; Shafiq Ur Rahman, MBA, MS; Byongyong Yi, PhD

In May 2016, a large metropolitan health care organization consisting of 10 hospitals and numerous outpatient facilities was subject to a ransomware attack.[1] When employees logged onto their workstations, a pop-up message demanded a payment of 45 bitcoin (roughly $19,000) to unlock patient-related data (access to electronic medical records [EMRs]). In response, all computer systems/networks and interfaces of health system "X" were shut down, including those at a radiation oncology facility. It took several days for the health care organization to regain full functionality, including the radiation oncology practice (herein called XRO).

Dr. Nichols *is assistant professor and clinical director,* ***Mr. Rahman*** *is director of radiation oncology IT, and* ***Dr. Yi*** *is a professor, University of Maryland School of Medicine, Department of Radiation Oncology.* *Disclosure: The authors have no conflicts of interest to disclose. None of the authors received outside funding for the production of this original manuscript and no part of this article has been previously published elsewhere.*

XRO had to cancel 36 treatment appointments on day 1 of the attack as well as all appointments on days 2 and 3 post-attack. On day 3 post-attack, XRO began to contact another local major health care system with an established radiation oncology practice (herein YRO) to discuss the potential of patient transfers for continuation of treatment as the radiation oncologists felt that the unintentional break coupled with the unknown time of when the network would return would be potentially detrimental to patient outcomes. YRO and XRO were subsequently tasked with how to make this transition possible without access to the record and verify system, the tried and true record of radiation delivery. As these discussions took place, the XRO computer network was restored on day 4 post-attack and patient transfers were not required. While this scenario may seem like "something that could never happen to me," any radiation oncologist or practice could experience it at any time, especially those in metropolitan areas.

A 2014 study by Filkins et al showed that 94% of health care institutions have been victims of cyberattacks.[2] Of attacks aimed at the health care industry, 72% were directed against hospitals, clinics, large group practices and individual providers, while 28% of malware attacks were directed at provider organizations, health plans, pharmaceutical companies and other health care entities.[3] Health-related cyberattacks are generally categorized into four groups: data loss, monetary theft, attacks on medical devices and infrastructure attacks.[4]

As a result of increased health-related cyberattacks, the FDA issued a safety communication in June 2013 titled, "Cybersecruity for Medical Devices and Hospital Networks," which called for greater private-sector involvement and the establishment of a risk-based regulatory framework. Unfortunately, the guideline lacked specific details or regulations on how

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healthcare networks could accomplish these goals.[5] The Ponemon study suggested, however, that networks focusing on cybersecurity with a specific recommendation to hire and empower a chief information security officer and establish incident response capabilities can reduce potential cybersecurity risks by 42%.[6] Cybersecurity is a major focus of health care as a result of these staggering statistics, and the FDA has ongoing efforts focused on cybersecurity and public health, including public workshops (www.fda.gov/medicaldevices/digitalhealth/ucm373213.htm).

In this article, we will discuss logistics of cybersecurity particularly as they pertain to radiation oncology, as well as resultant challenges. We also will describe how our organization has navigated some of these logistics and challenges, as this may prove helpful to other organizations.

Challenges of Cybersecurity in Radiation Oncology

The healthcare industry has been the target of increasing cyberattacks over the last several decades. The complexity of the healthcare industry as well as laws surrounding patient privacy make cybersecurity a top priority resulting in extensive and robust hospital IT departments. Similar to radiology, radiation oncology has specific software required to utilize and operate machinery/departments. This requires unique IT expertise to assist users, troubleshoot problems and manage/store large amounts of data. For sites where radiation oncology has its own IT group, it is critical to define roles and responsibilities, workflows, and monitoring systems to align with hospital-based policies and procedures.

Radiation Oncology IT Infrastructure

Some of the general topics required for a successful radiation oncology IT group (or integration into the hospital IT system) are to organize, develop, document and disseminate personnel roles and define access to control policies. Much like hospital-based EMRs, "super-users" or "builders" must be defined and limited to ensure data quality. Policies and procedures must be developed in accordance with hospital-based policies and also revised at regular intervals. For example, if the hospital-based EMR has a time-out policy of 10 minutes, radiation oncology software should follow the same policy. Hospital IT departments typically have clear procedures for monitoring/auditing of the EMR by monitoring system accounts and user access to ensure patient privacy. They also have procedures for granting and revoking access around employee hires, terminations, etc. It is critical that radiation oncology IT follows similar procedures as these are often not controlled by the hospital-based IT group.

Radiation oncology IT must collaborate with multiple EMR systems with several teams in managing the appropriate functioning of these applications (hospital, machine vendor, treatment planning system [TPS] vendor, etc.). There are also significant challenges with interfaces from radiation oncology technology to hospital systems in part because hospital IT departments generally lack knowledge regarding radiation oncology workflows and technological needs, which can make interface development and maintenance difficult.

Radiation oncology is a research-oriented field with increasing demands from institutional research bodies as well as national research governing bodies such as the NRG. For example, many patients enrolled in NRG trials need to have DICOM information as well as numerous demographic and cancer characteristics sent to centralized databases. Developing safe, efficient workflows around these processes is quite challenging.

Lastly, there is also a need to monitor and maintain these systems with routine upgrades. These require significant work efforts in conjunction with vendor support. Many future vendor upgrades focus specifically on cybersecurity.

Logistics of Cybersecurity in Radiation Oncology

Radiation oncology is undoubtedly one of the most technical fields in medicine both in terms of radiation technology as well as information technology infrastructure. Linear accelerators (linacs) require frequent maintenance and quality assurance with standard schedules. Several manufacturers have taken new approaches of remote access to fix technical issues and perform routine maintenance. Treatment areas/rooms are equipped with vendor-controlled networks behind their firewall for their certified configuration and security. Many hospital systems have firewalls in place to prevent this type of access as the concern is that malware from the manufacturer could potentially enter the hospital network through this type of access.

At our institution, this has been raised as a cybersecurity concern to the hospital environment and special permission had to be obtained from hospital leadership to allow vendor access. Our radiation oncology IT team designed a subnetwork for each treatment room in the hospital network that effectively separates each treatment room and vendor-controlled firewall with a hospital-managed firewall, allowing for secure transmission of data (two layers of firewalls). Both the vendor-supported and hospital-based firewalls have controlled access to allow for continuous treatments. This design ensures the radiation oncology treatment rooms are securely isolated from other sections of the hospital IT infrastructure in the event of malware.

In the past, many radiation oncology vendors also utilized USB disks for data transfers. USBs can pose a significant cybersecurity threat if left unencrypted/unsecure as malware attached

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to the USB can be transferred between computers and systems. Vendors have made significant improvements to limit the need for USB transfers; however, this need has not been completely eliminated. Continuous product improvement is needed in this arena among vendors and clients to further minimize these risks. When a USB must be used it is critical that it is encrypted and secure.

Electronic Medical Records

Commercially available hospital EMRs cannot be the sole EMR system for radiation oncology practices due to their inability to operate linacs. As such, all radiation oncology practices require radiation oncology software such as ARIA (Varian, Palo Alto, California), MOSAIC (Elekta, Stockholm, Sweden), or others. Most hospital-based practices have been asked to integrate to the hospital EMR, posing significant challenges to the workflow and operations of radiation oncology practices, especially as most of these software programs have no integration with radiation oncology EMRs. Major vendors such as Varian and Elekta have now devoted specific resources to assist with this integration; however, much of this still depends on custom-built interfaces, which expose both systems to risk. Additionally, hospital systems must make decisions regarding uni- or bi-directional interfaces, each of which poses risks to the EMR systems.

More recently, Epic Systems Inc. (Verona, Wisconsin), developer of one of the most popular EMR systems used in the United States, says it is developing a module specific to radiation oncology. While this undoubtedly will not replace radiation oncology EMR systems, it will hopefully ease the burden on radiation oncology EMR integration.

Standard components of hospital-based EMR systems are hospital data governance, compliance audits and firewall testing, all of which support health system security. At this point, these features are not standard in radiation-oncology-based EMRs. For radiation oncology practices in which the EMR system is not governed by the hospital, it is critical to have the same level of auditing and testing to ensure appropriate cybersecurity.

Automatic Time Outs

One of the basic tenets of cybersecurity is automatic time outs and/or locking of computers both for reduced access/opportunity for malware/viruses as well as compliance with the Health Insurance Portability and Accountability Act (HIPAA). These pose unique challenges for some of the workflows in radiation oncology.

Treatment Delivery

Radiation therapists need to have several computer screens/operations functioning to treat patients safely. The treatment control system (TCS), EMR, and other secondary treatment systems (eg, BrainLab, AlignRT) all must open simultaneously for safe, quality patient treatment. As therapists are often in and out of rooms and sometimes attending to patients for > 5 to 10 minutes without attending to a computer screen, automatic time outs result in lost work and decreased efficiency. This inadvertently can increase treatment times, as every time a therapist must log into the computer and EMR system, roughly 30 to 90 seconds are lost. Multiplied across 20 treatment sessions in a day, it is equivalent to an entire treatment slot. As hospitals are focused on quality and efficiency, this can be viewed as an opportunity for lost revenue in terms of "one less patient treated" as well as potentially increased cost of therapy staff time.

Treatment Planning

Treatment planning and plan optimization algorithms take significant amounts of time. Plan optimization can require several hours depending on plan complexity and the radiation technique (such as proton therapy). In many cases, dosimetrists may set complex plan optimization to occur overnight to increase their workflow efficiency. However, automatic time outs prevent dosimetrists from doing this as in many cases the TPS closes once the time out is performed. In our proton center, for example, if a plan optimization does not start by the early afternoon, the dosimetrist must choose between working extremely late (while touching their computer every 30 minutes to prevent the time out) vs. waiting another day to start the optimization. Similar to therapy, this can cause significant workflow challenges.

Plan Verification

While plan verification systems have also become quicker and more efficient, the same issues can apply to the physics workflow as described above for treatment planning.

Locking Screens in Unattended Computer Systems

Another tenet of cybersecurity and HIPAA compliance in the EMR era is locking a computer screen when the computer is unattended, even for a moment. This requires the user to lock the screen; however, if the EMR is accessed for a particular patient record, then that record can remain "locked," preventing another from saving information in the record. This can result in many challenges for the radiation oncology workflow for all radiation oncology users. For example, two to three therapists work on a machine. If one therapist logs into the EMR and locks the screen but another therapist needs to document in the chart, this can cause save-back issues in which one individual's work can be lost. This is potentially common for the therapy group that is constantly in and out of rooms, and again, can significantly obstruct workflow.

Our Approach to Cybersecurity and IT

The University of Maryland Medical System is comprised of 13 hospitals

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across the state along with numerous outpatient practices. As a general matter, all of the hospitals operate Epic EMRs, although as of press time, several hospitals were transitioning from their legacy system. The University of Maryland Radiation Oncology Department consists of six practices, three in system hospitals and three freestanding. One of these practices is a proton center. All practices use Varian linacs, and the proton center uses a Varian cyclotron. We use ARIA as our radiation oncology EMR, and both the Varian Eclipse and RayStation (RaySearch laboratories, Stockholm, Sweden) treatment planning systems.

All six locations use a single, central ARIA database and all linacs are commissioned to the same standard, which allows for ease of patient transfers between practice locations. The ARIA application was integrated to include all of our network sites several years ago, which has significantly lowered system-level operational costs.

Five of our six practices have interfaces built between Epic and ARIA, and one continues to operate the Meditech (Westwood, Massachusetts) system but will transition in the future. In our hospital system, Epic is considered the "source of truth." Our clinicians perform all clinical documentation except for on-treatment notes and end-of treatment notes in Epic. All orders (lab, medication, imaging) are also performed in Epic. On-treatment and end-of-treatment notes are initiated in ARIA and interfaced to Epic. This workflow was chosen to allow for the auto-population function of dose/fractionation provided by ARIA.

A critical component for interfacing is having the correct account number attached to the note. The hospital system allows only unidirectional interfaces and, as a result, many workarounds were created for patient workflow. For example, since patient treatment times and machines often fluctuate, patient treatment appointments are not interfaced to Epic. The downside is that our medical oncology colleagues cannot see the radiation oncology treatment schedule. Consult and follow-up visits are scheduled in Epic and interfaced to ARIA. A reconciliation process is performed every night to ensure all visits are interfaced. While working with Epic can initially be demanding, we have created workflows that minimize duplication of staff/faculty effort and have successfully reduced duplicative efforts by 70%.

Several additional medical software systems are integrated in our model. In the Epic EMR system, secure data transmission is through HL7 (in-bound interfaces are ADT [admissions, discharges and transfers] and SIU [scheduling information unsolicited]) into ARIA and MDM (medical document management), while the outbound interfaces to Epic are for MDM, DFT-UPC (detailed financial transactions-universal product code). In our workflows with Meditech and other systems, interfaces for imaging reports, labs, SIU, DFT and MDM are also present. Creating secure communication lines requires education in various software systems and analysis of how custom-built interfaces will work together without duplicating patient records.

Regarding data governance and compliance audits, our department has its own data governance group for ARIA modeled after the hospital-based one. New hospital policies and procedures are reviewed in real-time and appropriate modifications are made. For example, when our hospital changed to an 8-minute time-out policy, this was modified in ARIA. Our hospital system engages a third-party vendor who performs cybersecurity audits on an annual basis for departments using separate EMR software. All our practice locations are firewall protected and undergo periodic testing at the hospital-system level.

To address challenges discussed above, we have created unique groups with unique rights depending on group member workflows. For example, the dosimetry location is not accessible to the general public. As a result, we have recently disabled the time-out procedure for dosimetry due to the difficulties it causes with plan optimization, especially at our proton center where this is known to take hours. While this was a difficult decision, it was felt that since the area was not accessible to the public and if users "locked" their screens, plans could still run in a secure manner without significant risk of a malware attack. In the treatment control areas, however, since patients and their family members can often see the computers, we did not feel comfortable making these changes. As a result, therapists are subject to some inconveniences in workflows discussed above.

While we live in a hybrid environment with vendor-provided devices, radiation oncology IT is responsible for the supporting infrastructure and an antivirus environment. Vendors frequently have exceptions to their software capabilities, which can pose risks to our IT environment. For example, the Elekta GammaKnife has a very secure system that prevents transmission of data even within our own local area network (LAN) to another system (such as ARIA). As a result, the only way users can transfer data is through a USB disk, which has a much higher risk for hackers/viruses/malware. These exceptions can pose a large risk to our environment and extra precautions are taken in these scenarios.

In addition, we have designed our system in a redundant style, serving our applications from two physical locations (main data center and our disaster recovery [DR] location). Depending on each kind of a disaster/attack (critical, medium, low), we have developed our DR plans to ensure patients can receive treatment. Our system is redundant in terms of database delivery, image and file delivery as well as different technologies

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involved to deliver applications, such as domain controllers (DCs), Citrix controllers, data collectors, etc. We are actively working on a concept of a separate DR plan in case of an attack similar to that described in the beginning of this paper.

In radiation oncology, we cannot eliminate the importance of QA protocols for our daily/every treatment. We are delivering all of our QA applications from a central location with the same redundancy level.

Another healthcare institute experienced a cyberattack, and within 90 seconds their 15000 servers were infected and rendered unusable. This was the result of a single user clicking a wrong link. This highlights the importance of education of users as one of the best and first lines of protection. All ARIA users attend a mandatory RadOnc IT annual inservice where we speak about technology and cybersecurity. We also send notices to staff as needs arise to educate them on ways to avoid cyber risks. These are often in addition to any hospital-based emails/notifications.

The focus of radiation oncology IT is to ensure our mission of safe patient care will remain aligned by considering sizing needs, infrastructure and function/workflows.

Conclusion

Radiation oncology is a unique specialty with unique needs regarding cybersecurity. In our experience, most of the radiation oncology software lags behind that of hospital-based EMRs in regard to cybersecurity features and, as a result, the onus is on the user to ensure that appropriate measures are taken for the safety of our patients and staff. Future upgrades are prepared to enhance cybersecurity features; however, we would encourage all radiation oncology practices to develop a "disaster strikes" plan on how to handle such situations.

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Quality and safety education in medical school

Nadia Saeed, BA

Compared to many other fields, quality and safety is a relatively new discipline within medicine. Many efforts to improve quality and safety in healthcare are aimed at training practicing physicians and residents, through efforts such as safety courses, quality improvement project participation, and continuing medical education sessions.[1,2] However, there has been increasing interest in beginning quality and safety education earlier in physicians' training. Upstream interventions during medical school can introduce future physicians to this crucial aspect of medical practice early in their careers and have the potential to significantly improve patient safety and quality of healthcare delivery. This article will discuss the considerations and dimensions of quality and safety training in medical education.

There are many aspects of safety and quality within the context of healthcare. The field encompasses a range of skills and behaviors, including technical skills, crisis management, and personal and professional behaviors and qualities such transparency, communication, and teamwork. Some of these, such as technical safety skills, anticipation and preparedness, and organizational skills are easily trainable, while others are less so, adding to the complexity of imparting quality and safety education to medical students.[3] Thus, the question of how to best teach these principles and skills remains debated.

***Ms. Saeed** is a medical student at Yale University, New Haven, CT.* *Disclosure: The author has no conflicts of interest to disclose. The author has received no outside funding for the production of this original manuscript and no part of this article has been previously published elsewhere.*

Although an increasing number of medical schools have implemented a patient safety curriculum over the past several years, there still exists a need to improve quality and safety teaching at this stage of training. Results from the 2012 Clerkship Directors in Internal Medicine Survey found that less than half of medical schools in North America had a formal patient safety curriculum. While this number has increased since the time of the survey, there are still deficits in reported satisfaction with medical students' competency in the areas of quality and safety at the end of their training.[4-6]

Not only is effective quality and safety training integral for medical students in their future practice as physicians, this training can also help students play an immediate and integral role in reducing harm, identifying medical errors, and promoting patient safety while in medical school.[7] Thus, establishing curricula that foster the development of safety skills in medical students is an immediate priority. Faculty development and institutional culture are essential elements to consider as well and will be discussed in this article.

Past and Current Educational Interventions for Quality and Safety

Quality and safety is a dynamic and interdisciplinary field, encompassing many areas including systems-based analysis, quality improvement methodology, and development of communication and teamwork skills.[8] As such, there are several methods for its integration into medical school education, including formal didactic- and workshop-based curricula to teach the concepts of quality and safety, activities aimed at helping students develop skills related to quality and safety, and participation in quality improvement and patient safety projects.[9] In developing quality and safety curricula, attention should be paid to the learning methods medical students perceive to be most helpful in acquiring knowledge and skills in this domain. Survey

analyses of medical student attitudes toward safety and quality improvement education have found that they prefer real-life examples of quality improvement projects, participation in these projects with patients, problem-solving and brainstorming components, and real-life examples of medical errors, suggesting the value of integrating quality and safety teaching into clinical education.[10,11] Indeed, many interventions have capitalized on the clinical experiences in medical school to present the principles of safety and quality.[12-14]

While the clinical stages of medical school provide an appropriate opportunity to teach about this topic, introduction to quality and safety principles during pre-clinical training can supplement more downstream interventions. Workshops and didactics during this time provide a foundation upon which students can later build during their clerkships and can prepare students to become active participants in promoting patient safety during their clinical rotations. For example, first- and second-year medical students participate in a surgical safety and quality improvement program at the Ohio State University Medical Center, completing a self-paced online module on patient-centered care and safety, leadership and teamwork, and quality improvement, followed by an orientation and use of the Surgical Safety Checklist.[15] Following the program, students not only showed improved knowledge of quality improvement methodology, they displayed an attitudinal change that all health professionals are responsible for promoting quality improvement. Brown et al demonstrated the efficacy and feasibility of a pre-clerkship quality improvement initiative, in which first year medical students learned about the principles of quality improvement by identifying areas for improvement within their own curriculum. Students subsequently demonstrated increased knowledge about quality improvement and motivation to engage in future quality improvement projects in the healthcare system.[16]

Longitudinal interventions that expose students to different components of the domain throughout the various stages of their medical education—including the pre-clinical and clinical years—are likely to provide a more comprehensive and enduring foundation in quality and safety practices compared to shorter interventions. For example, medical students at the Case Western Reserve University are first exposed to quality-of-care and patient safety principles during their first block of medical school, including through lectures and exercises on medical errors, root cause analysis, and medical micro and macro systems.[17] They subsequently engage in clinical improvement projects during their inpatient or ambulatory experience, and during their clerkship years complete an interprofessional small group learning experience on root cause analysis. Similarly, a longitudinal curriculum spanning across all four years at Mayo Medical School was developed to teach students about medical errors and systems issues they may encounter in clinical practice.[18]

In addition to implementing safety and quality education throughout the different stages of medical school, utilizing a variety of teaching methods can engage students more fully in their quality and safety training. In the Case Western Reserve University curriculum mentioned above, students learn through didactics as well as small and large group exercises. At Mayo, the safety curriculum is taught using simulations, lectures, case discussions, video sessions with debriefings, and exercise-based discussions. A 3-day patient safety curriculum implemented at Johns Hopkins School of Medicine in 2012 taught students through case studies, small group exercises, simulations, and skills demonstrations, and reported significantly improved safety knowledge, systems-thinking, and communication and safety skills.[19] A mandatory quality safety course for upper year medical students at Vanderbilt University School of Medicine consisting of three one-month blocks utilizes didactics and weekly assignments along with experiential learning activities, including a quality improvement poster project that students presented at the conclusion of the course.[20] Such methods actively engage the learner and provide real-world context for the principles of quality and safety.

Developing curricula requires time, faculty, and financial resources, and may be the largest barrier to integrating more safety and quality teaching in medical education. In 2010, the World Health Organization's Alliance for Patient Safety developed a standard medical curriculum for patient safety—the WHO Patient Safety Curriculum Guide for Medical Schools—which includes a step-by-step instructor manual and comprehensive curriculum.[21] This blueprint provides a starting point for schools looking to integrate quality and safety into their education.

The Role of Simulation

Simulation is becoming increasingly recognized as a valuable resource for quality and safety training during medical education.[22] Many forms exist and continue to emerge, from robotic human-like mannequins to standardized patient interactions to high-tech simulation suites. These resources are commonly used by medical schools to teach important clinical skills and foster interprofessional learning; and medical students may indirectly learn about quality and safety in evaluating patient cases and practicing teamwork and communication skills during simulation trainings.[23] However, more explicit use of simulations to teach specifically on the principles of quality improvement and patient safety can help students build

competency in this area prior to residency. Importantly, simulations allow students to recognize common patient safety issues and make their own medical errors in a low-risk setting before entering their own clinical practice.[24] King et al argue that actively encouraging errors during simulation-based team training can help students develop better foresight and emotional control to manage similar situations in future clinical settings.[25]

Several studies have been published on the use of simulation in quality and safety training specifically. For example, Thomas et al report on the efficacy of a ward round simulation incorporating distractions and interruptions—a significant contributor to error-making in clinical practice—in helping students minimize medical error.[26] Participation in the distraction-laden simulation significantly reduced medical errors in a subsequent simulation, and receipt of immediate feedback on the management of distractors reduced error-making to an even greater degree. Additionally, a simulation-based model that presents common hospital-based safety threats (such as medication errors, fall risks, and risks from upper extremity restraint or catheter use) and asks students to identify as many as possible has shown to be a feasible and efficacious method of providing safety-focused education to medical students.[27] The use of simulations, moreover, ultimately protects patients—and thus directly promotes patient safety—by shifting some learning environments from the real-world setting with real patients to simulated ones, reducing the probability of inadvertent harm.[28] The ethical benefits provide a strong imperative for the increased use of simulations in medical education, particularly in the context of quality and safety training.[29] Future research should also aim at further identifying how simulation objectively impacts students' long-term attitudes and behaviors regarding quality and safety.[24]

Interprofessional Learning and Safety Education

All healthcare professionals—not just physicians—are responsible for practicing in ways that maximize patient safety and quality of service. As teamwork and communication are necessary skills for preventing medical errors, there has been a shift toward integrating quality and safety teaching among different health professional students. Many methods can accomplish this, including the use of simulations, joint didactics and small group exercises, clinical teachings, and interprofessional service learning projects.[30] Headrick et al, for example, made interprofessional learning a key aspect of the Retooling for Quality and Safety initiative, aimed at incorporating patient safety and quality improvement into medical and nursing school education.[31] Curricular components included classroom activities, clinical activities, and simulations, and the majority involved students working together from both schools. The efficacy of applying the Team Strategies and Tools to Enhance Performance and Patient Safety (TeamSTEPPS) communication training model to train interprofessional teams of students has been reported as well.[32] In the study by Brock et al, upper-year medical, nursing, pharmacy, and physician assistant (PA) students participated in training that included didactic, simulation, and feedback components, and were found to have demonstrated attitudinal and knowledge shifts in areas such as communication and situation monitoring among others. Similarly, a course aimed at providing interprofessional education on patient safety among upper-level medical, nursing, and pharmacy students at the University of Maryland found high levels of interest in interprofessional learning and improvements in patient safety knowledge from participation.[33] Sessions included case-based discussions and a mock root cause analysis.

Longitudinal interprofessional training in particular can potentially further break down hierarchical barriers that contribute to ineffective teamwork in the healthcare setting. For example, a three-year interprofessional curriculum focused on quality improvement, patient safety, and teamwork was developed through collaboration between a medical, nursing, and physician assistant school in New England.[34] One component in the second year involves a medical error simulation, followed by planned unsuccessful and successful interactions with a dismissive authority figure, helping prepare students to navigate the hierarchical challenges to addressing safety issues in the clinic.

Developing interprofessional curricula is no easy task, requiring significant coordination between different schools with varying schedules and a large cohort of students. Thus, pre-developed educational materials to teach patient safety and quality to students in different health professional schools can be useful. For example, the use of courses offered by the Institute of Health's Open School has been implemented in an interprofessional setting among medical and other health students at University of South Dakota, for an inexpensive and feasible method of integrating interprofessional quality and safety education.[35] Interprofessional programs can provide foundational skills in cooperative and communicative care—an essential component of safe future practice.

Faculty Development and Role Modeling

One challenge to establishing quality and safety education in medical schools is finding instructors specifically trained in these disciplines. The cost, resources, and infrastructure necessary to train faculty in this domain may hinder curricular change. Thus, integration of quality and safety into medical school curricula necessitates feasible

and effective faculty development programs. Myers et al created an academy aimed at training medical educators to introduce quality improvement and patient safety principles into their own programs.[36] The three-day, in-person program consisted of instruction in not only quality and safety, but curriculum development, change management, and professional development. Expansion of faculty development programs in these areas can hopefully improve curricular change in quality and safety.

Moreover, all medical educators—not just those trained to teach on quality and safety—also play an implicit role in the quality and safety development of medical students through role-modeling. In a survey analysis, Martinez et al found that both training on how to respond to medical errors as well as exposure to positive role-modeling had positive influences on students' attitudes regarding error disclosure.[37] In contrast, negative role modeling was significantly associated with negative attitudes as well as a higher likelihood of students handling errors in a nontransparent manner, highlighting the need for medical educators who set positive examples in these domains for students.

In addition to teaching students, faculty also play a key role in driving curricular reform to further incorporate quality and safety principles.[38] Thus, it is crucial to not only provide all future medical professionals with the skills to promote quality and safety within their own medical practices, but to train future leaders in the field of quality and safety. While there are several quality and safety training programs offered at different institutions, many of these are fellowships at the graduate level separate from medical school. The Pritzker School of Medicine at the University of Chicago has implemented a 4-year scholarly track in quality and patient safety for medical students, incorporating an elective on quality-improvement skills, participation in the Institute for Healthcare Improvement Open School, and a mentored research project.[39] Medical school scholarly tracks such as this can help train future leaders in quality and safety, who can also serve as the next generation of educators to introduce curricular change.

Establishing Safety Culture

Formal instruction alone is insufficient to train future physicians in the domain of quality and safety; trainees should operate within a culture that promotes safety starting in medical school. The workplace environment plays an integral role in this regard; climates that promote quality and accountability not only encourage error reporting among medical students but can also help ingrain positive and transparent behaviors when it comes to clinical error and patient safety for future practice.

Many medical students may feel uncomfortable questioning authority and reporting medical errors they witness during their clinical experiences. For example, a survey analysis of students at the University of California, San Francisco, found that a majority of students said they felt mistakes were held against them, and that they would not speak up if they saw a possible adverse event.[40] Moreover, more than half of students surveyed were afraid to ask questions if the felt they were witnessing something that did not seem right.

Establishing a culture that promotes transparency is integral for patient well-being and the development of future physicians. However, changing institutional culture can be challenging. Several measures can be taken to address the individual dynamics that contribute to culture. Leadership should prioritize patient safety in tangible ways, setting clear institutional goals and allocating resources for quality improvement.[41] Additionally, urging medical educators to encourage error and safety reporting without consequence among students can contribute to changing institutional culture. Moreover, an emphasis on interprofessional training enhances the teamwork and communication skills that are essential to ensuring patient safety, as was discussed in the previous section. Leape et al enumerate key concepts integral to creating a culture of safety and quality in healthcare organizations, including transparency, establishment of an integrated care platform, promoting joy and meaning in providers' work, and reforming medical education to include safety and improvement science, systems thinking, leadership, and teamwork—all necessary for developing quality and safety skills.[42]

Additionally, it should be noted that provider burnout has been linked to medical error and diminished safety climate.[43,44] Efforts to reduce burnout among physicians during all stages of their training—from medical school onward—can ultimately impact patient safety. Increasing recognition of the importance of self-care in preventing burnout and establishing measures to ensure medical student well-being can create greater engagement and meaning in work and eventually improve quality and safety culture.

Quality and Safety Training in Radiation Oncology

In recent years, attention to quality and safety within radiation oncology has increased. In 2010, the American Society of Radiation Oncology (ASTRO) launched Target Safely, a national campaign focused on improving patient safety and reducing errors.[45] The campaign included a recommendation to expand educational interventions on quality and safety, as well as to incorporate quality and safety content into ASTRO meetings.

Radiation oncology is an inherently interdisciplinary specialty involving communication and coordination between many different professionals, making quality and safety concerns a

particularly critical component of care. Interventions that involve all members of the care team—including physicians, physicists, nurses, PAs, therapists, and dosimetrists—may have the greatest potential in generating change. Success has been shown with implementation of a mandatory program in radiation oncology departments, even in large, multisite centers. Woodhouse et al report on a longitudinal quality and safety culture education program initiated in 2010 at the University of Pennsylvania.[46] The program consists of lectures, meetings, and interactive workshops for all department members across all Penn radiation locations. Achieving 100% participation rates, the program demonstrated significantly improved scores on content-based questionnaires following participation, with the largest improvements among radiation therapists. Moreover, high knowledge retention was shown on subsequent periodic assessments, indicating the longitudinal benefit as well as feasibility of such a program.

Simulation, discussed previously, may also play an important role in quality and safety training in radiation oncology, improving adherence to practice guidelines and ultimately patient safety. For example, a simulation-based training intervention for radiation oncology professionals at the University of North Carolina at Chapel Hill was found to significantly improve procedural compliance without impacting subjective workload.[47] In particular, simulation-based exercises may aid in learning new knowledge and skills in radiation, increasing the chance for error in a low-stakes simulated setting rather than in clinic.

Residency training has also become an increasingly recognized target for quality and safety educational interventions in radiation oncology. The need for improved education in quality and safety during residency has been documented. A survey analysis of radiation oncology residents' experience with patient safety and quality improvement concepts found that more than 60% of respondents had little to no exposure of critical quality and safety concepts, including incident learning systems, root cause analysis, failure mode and effects analysis, and human factors engineering.[48] Moreover, only a small number (27%) felt confident that they received adequate patient safety training in their residency program.

Thus, there has been interest in identifying universal competencies and developing frameworks that can be used in quality and safety programs in radiation oncology residency. Yeung and Greenwalt report on a framework for quality improvement and patient safety education in radiation residency programs, citing both didactic and project-based experiences as necessary components for an effective educational intervention.[49] They argue that didactic components should not only teach the basic principles of quality improvement, but also focus on specific institutional goals. Moreover, role modeling by quality improvement faculty in everyday clinical practice is necessary for behavioral change aimed at promoting patient safety, as discussed. In helping define the content necessary for inclusion in such interventions, the 2015 international Delphi Study was conducted to develop a competency profile for quality and safety curricula in radiation oncology residency.[50] The study identified 90 items consisting of 18 key competencies, representing a potential minimum standard for safety and quality programs for radiation residencies. Such frameworks may provide a starting point for developing and implementing institutional-specific interventions.

Shorter initiatives that provide a foundation in quality and safety may be feasibly incorporated into radiation oncology residencies, and later expanded into more comprehensive, longitudinal interventions. For example, Fogh et al report on a quality and safety mini-course for medical and physics radiation oncology residents at the University of California, San Francisco.[51] Consisting of a series of didactics followed by interactive group discussions, the course was streamlined so it could be taught within a single day, and was found to significantly improve residents' perception of quality and safety. Quality and safety education for medical physics residencies has gained increasing attention as well.[52] Programs specific for physics residencies and those specific for medical residencies may inform each other and complement more general, department-wide quality and safety education interventions.

Conclusions

The need for improved quality and safety education in medical curricula has been well documented. While an increasing number of schools are integrating essential components of this field into their teachings, debate remains over which methods are most effective. Moreover, curricular development alone is not sufficient enough to impart these skills to future physicians—creating a culture that promotes patient safety and quality improvement is equally important. Faculty development has posed a challenge to curricular reform, but programs aimed at training instructors are continuing to be created and improved upon. Interprofessional learning is another essential component of safety training and can help students develop skills in communication and teamwork essential to safe practice. Future studies should aim to qualitatively and quantitatively evaluate the longitudinal impact of quality and safety educational interventions in medical students.

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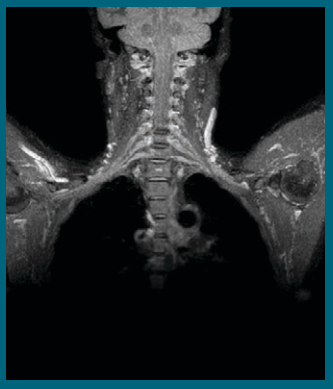

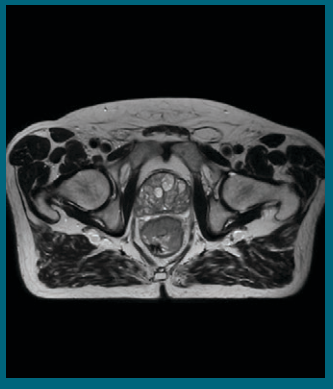

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Trends in intensity-modulated radiation therapy use for limited-stage small cell lung cancer: A National Cancer Database analysis

Rodney E. Wegner, MD; Shaakir Hasan, DO; Paul Renz, DO; Andrew T. Turrisi, MD; Athanasios Colonias, MD

Abstract

Purpose: The standard of care for limited-stage small cell lung cancer (SCLC) is concurrent chemoradiation, which can be delivered using 3-dimensional conformal radiation therapy (3D CRT) or intensity-modulated radiation therapy (IMRT). We sought to use the National Cancer Database (NCDB) to identify predictors and trends in IMRT use for limited-stage SCLC.

Methods and Materials: We queried the NCDB from 2004-2014 for limited-stage SCLC patients that received chemotherapy and definitive doses of radiation to the chest using either 3D CRT or IMRT. Univariable and multivariable analyses were performed to identify sociodemographic, treatment, and tumor characteristics predictive of IMRT use and overall survival (OS). Propensity-adjusted Cox proportional hazard ratios for survival were used to account for indication bias.

Results: We found 9970 patients treated as above, with 59% being treated with 3D CRT and 41% being treated with IMRT. The use of IMRT increased steadily between 2004 and 2014, starting at a rate of 11% and ending at 57%. Patients with higher education and treatment at an academic center were more likely to have received IMRT, as were those receiving higher radiation dose and BID (twice daily) fractionation. IMRT use did not predict for overall survival (OS). Predictors for OS on propensity-adjusted Cox analysis were BID treatment, younger age, female gender, and private insurance.

Conclusions: The use of IMRT in limited-stage SCLC has steadily increased over the past 10 to 15 years. We expect these rates to continue to climb based on extrapolation from recommendations for non-small cell lung cancer (NSCLC).

Dr. Wegner *is a radiation oncologist,* ***Dr. Hasan*** *is a resident physician in radiation oncology,* ***Dr. Renz*** *is the chief resident in radiation oncology, and* ***Dr. Colonias*** *is a radiation oncologist, at Allegheny Health Network Cancer Institute, Division of Radiation Oncology, Pittsburgh, PA.* ***Dr. Turrisi*** *is a radiation oncologist at James H. Quillen VA Medical Center, Department of Radiation Oncology, Nashville, TN.*
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Small cell lung cancer (SCLC) is an aggressive, high-grade neuroendocrine tumor that accounts for about 15% of all lung cancers and 20 000 to 30 000 new cases per year.[1] SCLC typically presents as extensive stage, with limited stage accounting for about 30% of new diagnoses. Limited stage is classically defined as disease limited to the ipsilateral hemithorax and regional nodes that can be encompassed in a safe radiation therapy field. The standard of care treatment approach for limited-stage SCLC is chemoradiation typically using a platinum-based agent in combination with etoposide.[2-5] Multiple treatment options exist in terms of radiation fractionation, including daily treatment, twice daily treatment, and occasionally a concomitant boost technique. At the time of this writing, Radiation Therapy Oncology Group (RTOG) trial 0538 remains open to help determine which scheme is most efficacious.

The technique used to deliver radiation to targets in the lung can likewise differ and varies from 3-dimensional conformal radiation therapy (3D CRT) and intensity-modulated radiation therapy (IMRT) (which use photons), to even use of protons.[6,7] IMRT is used to deliver a highly conformal dose of radiation with rapid falloff to spare surrounding critical structures in the chest such as the normal lung, spinal cord, esophagus, and heart. The goal of IMRT is to help reduce treatment-related toxicity, but the technique has also been used to dose escalate. RTOG trial 0617 was a landmark non-small cell lung cancer (NSCLC) study that examined dose escalation and targeted therapy use. In that study, IMRT was utilized in about 50% of cases, and the technique was associated with less pneumonitis and a decreased heart dose, which was shown to be an important predictor for overall survival.[8,9] Since the dose of radiation used with daily treatment for SCLC is similar to that of NSCLC, IMRT has been used to treat those patients as well. There are some institutional series comparing the technique in NSCLC and SCLC, potentially showing decreased toxicity.[10,11] Currently, the overall utilization rate of IMRT in SCLC is unreported, although it is presumably increasing based on extrapolation of results from RTOG 0617.

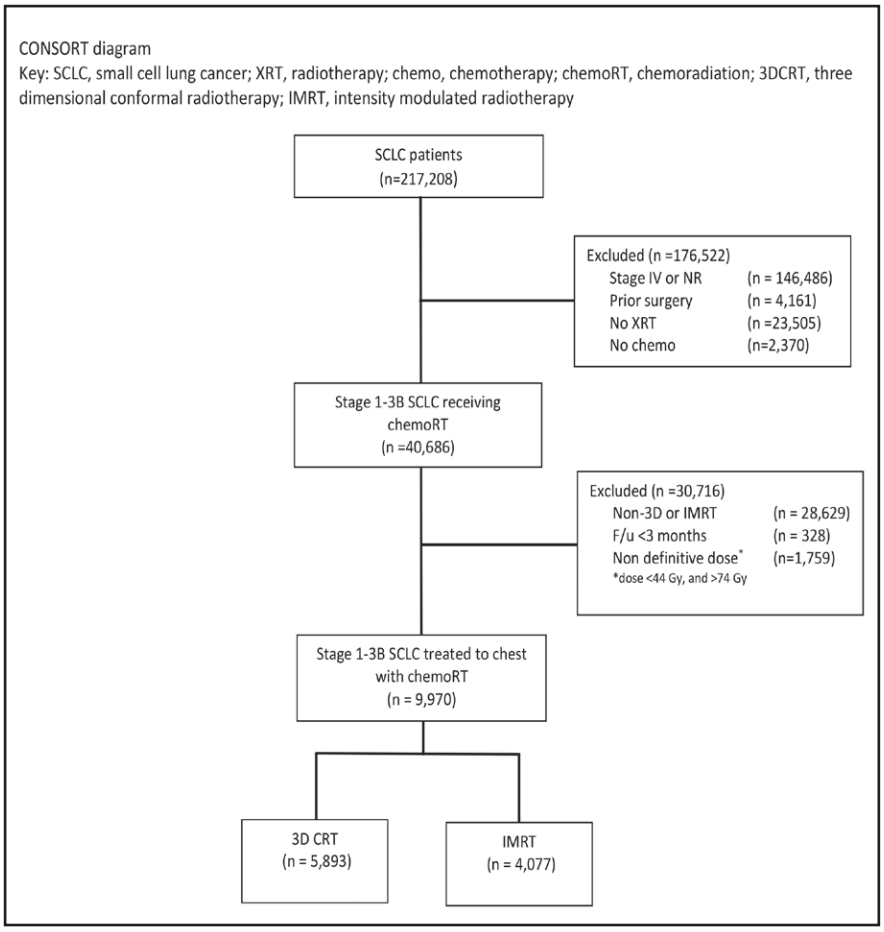

FIGURE 1. *CONSORT diagram*

In the present study, we aim to use the National Cancer Database (NCDB) to examine trends in use of IMRT in limited-stage SCLC over time, and to see if those trends impact outcome.

Methods and Materials

We conducted a retrospective review using de-identified data from the National Cancer Database (NCDB), which is exempt from institutional review board (IRB) oversight. The NCDB is a tumor registry maintained by the American Cancer Society and the American College of Surgeons (ACS) for more than 1500 hospitals accredited by the Commission on Cancer. The database captures up to an estimated 70% of newly diagnosed malignancies each year in the United States. We queried the database for patients with American Joint Committee on Cancer (AJCC) clinical stage 1-3B small cell lung cancer diagnosed between 2004 and 2014. **Figure 1** is a Consolidated Standards of Reporting Trials (CONSORT) diagram outlining the cohort selection criteria. We excluded patients with documented stage IV disease or unrecorded stage. Patients with prior surgery, no documented radiation, or no documented chemotherapy were also excluded. We excluded patients treated

Table 1. Patient Demographics and Clinical Characteristics at Baseline (n=9,970)

Characteristics	No. (%)
Sex	
Male	4,384 (44)
Female	5,586 (56)
Race	
White	8,982 (90)
African American	792 (8)
Other	196 (2)
Comorbidity Score	
0	6,022 (60)
1	2,771 (28)
≥2	1,177 (12)
Insurance	
Not Insured	333 (3)
Private Payer	3,213 (32)
Government	6,324 (63)
Unrecorded	100 (2)
Education %	
≥29	1,593 (16)
20 to 28.9	2,945 (30)
14 to 19.9	3,482 (35)
<14	1,824 (18)
Unrecorded	13 (1)
Treatment Facility type	
Community cancer program	1,019 (10)
Comprehensive community cancer program	5,060 (51)
Academic/research program	3,845 (38.5)
Unrecorded	46 (0.5)
Treatment facility location	
Metro	7,691 (78)
Urban	1,786 (18)
Rural	228 (2)
Unrecorded	265 (2)
Income, US dollars	
<30,000	2,014 (20)
30,000 to 35,000	2,847 (29)
35,000 to 45,999	2,761 (28)
>46,000	2,216 (22)
Unrecorded	132 (1)
Distance to treatment facility, miles	
≤9.6 miles	4,896 (49)
>9.6 miles	5,074 (51)
Age distribution, years	
≤65	5,053 (51)
>65	4,917 (49)
Year of Diagnosis	
2004-06	1,170 (12)
2007-09	2,267 (23)
2010-12	3,433 (34)
2013-14	3,100 (31)
Stage Grouping	
1A/B	979 (10)
2A/B	1,127 (11)
3A	4,471 (45)
3B	3,393 (34)

with unknown radiation type or non-3D, non-IMRT techniques. To account for immortal time bias, patients were also excluded if follow-up was < 3 months, the maximum allowable time from diagnosis to start radiation therapy.[12] We also used dose cutoffs of ≤ 44 Gy and > 74 Gy to define a "definitive" dose for our cohort. Patients also had to have radiation directed at the chest or thorax as coded by the NCDB, and not another anatomic site.

Race was categorized as white, African-American, or other. Comorbidity was quantified using the Charlson/Deyo comorbidity index.[13] Stage was defined according to the 7th edition of the AJCC's clinical group. Socioeconomic data in the patients' residence census tract were provided as quartiles of the percentage of persons with less than a high school education and median household income. The facility type was assigned according to the CoC accreditation category. Locations were assigned based on data provided by the U.S. Department of Agriculture Economic Research Service. Insurance status is documented in the NCDB as it appears on the admission page. The data used in the study are derived from a de-identified NCDB file. The ACS and the CoC have not verified and are not responsible for the analytic or statistical methodology employed or the conclusions drawn from these data by the investigator.

Data were analyzed using MedCalc Version 18 (Ostend, Belgium). Summary statistics are presented for discrete variables. χ^2 tests compared sociodemographic, treatment, and tumor characteristics between the treatment groups. Overall survival was calculated in months from time of diagnosis to date of last contact or death. Kaplan-Meier curves were used to calculate cumulative probability of survival.[14] Log-rank statistics were used to test whether there was a statistically significant difference in the cumulative proportions across groups.

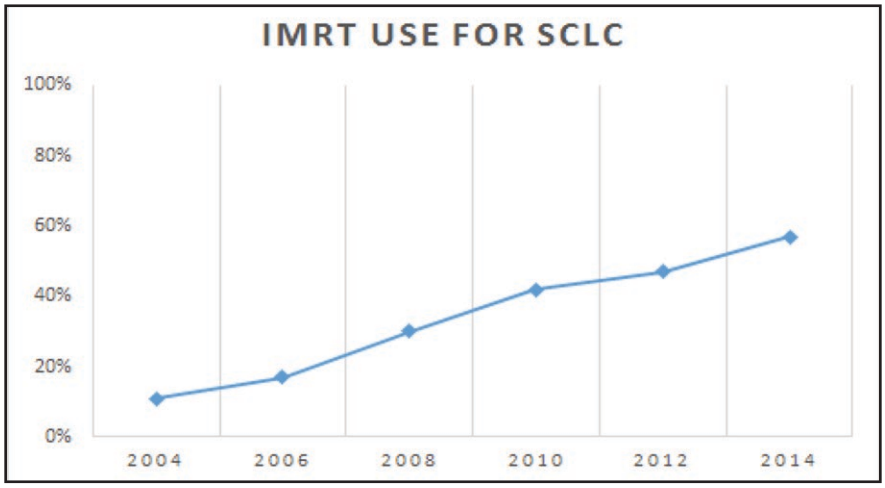

FIGURE 2. *Percentage of patients treated with intensity-modulated radiation therapy (IMRT) by year.*

A Cox proportional hazards model was used for multivariable survival analysis.[15] Due to the large nature of the dataset, factors significant on univariable analysis were entered using a stepwise backward elimination process. Adjusted hazard ratios and 95% confidence intervals are reported, using an α level of 0.05 to indicate statistical significance.

Propensity score-matched survival analysis was used to account for indication bias due to lack of randomization between patients receiving 3D CRT and IMRT.[16] Multivariable logistic regression was used to calculate a propensity score indicative of conditional probability of receiving IMRT compared to 3D CRT. The propensity model included observable variables associated with treatment selection on multivariable logistic regression. A Cox proportional hazards model was then constructed incorporating the propensity score, but also excluding factors included in the propensity score calculation to avoid overcorrection. The assumption of balance was further validated by stratifying the data into propensity score-based quintiles and confirming that the difference in propensity score mean per quintile was < 0.10.

Results

Baseline patient characteristics are outlined in **Table 1**. Briefly, most patients (79%) were stage 3A/B. The median age for our cohort was 65 (range: 27-90). The median radiation dose to the chest/thorax was 60 Gy (interquartile range, 54-63 Gy). Twice daily fractionation was used in 1045 cases (11%). Radiation to the chest was started at a median 42 days after diagnosis (interquartile range, 28-71 days). Chemotherapy was started at a median 21 days after diagnosis (interquartile range, 12-35 days). IMRT was utilized in 11% of cases in 2004, and steadily rose to 57% usage by 2014 (**Figure 2**). Overall, IMRT was used in 4,077 of 9,970 cases (40%). The odds of receiving IMRT increased with "other" race, treatment at an academic facility, BID (twice daily) fractionation, dose > 62 Gy, increased distance to facility, treatment at an academic facility, and increasing year. The likelihood of receiving IMRT decreased with urban location and with decreased education (**Table 2**). On multivariable regression analysis, all predictors remained significant except for distance to treatment facility. (**Figure 3**).

The median follow-up time was 19.1 months (range: 3 to 154 months). The median OS was 21 months. Survival at 3 years was 32% for the entire cohort. There was no statistically significant difference in survival between patients treated with IMRT or 3D CRT (median OS 21 months in each arm). On univariable analysis, predictors for increased OS included age < 65, BID treatment, lower comorbid score, increased distance to facility, type of facility, income, private insurance, race (African-American), female gender, stage, and more recent year of treatment. For multivariable Cox proportional hazards analysis, age < 65, BID treatment, lower comorbid score, increased income, private insurance type, race (African-American), female gender, lower stage, and more recent year of treatment were found to be predictors of OS (**Table 3**). A second multivariable Cox proportional hazards model was used including factors significant on univariable analysis plus the propensity score. The propensity score-adjusted multivariable analysis identified age < 65, BID fractionation, female gender, and nongovernment insurance as predictors for improved OS, and treatment modality remained insignificant (**Table 3**).

Discussion

SCLC remains a very aggressive thoracic malignancy, presenting as true limited stage only about one-third of the time.[1] For those patients, despite the challenging prognosis, true "cure" remains the goal and standard of care therapy is chest radiation with concurrent chemotherapy.[2] Traditionally, 3D CRT has been used for the treatment of thoracic malignancies. With the advent of IMRT, astute radiation oncologists recognized the potential advantages the technique could provide when treating lung cancer.[17] Namely, those advantages involve delivery of a highly conformal dose of radiation with rapid falloff to help spare surrounding organs at risk (reduce toxicity), and perhaps even the ability to dose escalate.

The report herein appears to be the first of its kind to examine trends in IMRT use for limited-stage SCLC across the United States.

Table 2. Comparative Use of IMRT by Baseline Characteristics in Patients Receiving Concurrent Chemoradiotherapy

Characteristic	3D CRT (n=5,893) (%)	IMRT (n=4,077) (%)	Odds Ratio	95% CI	p
Sex					
Male	2,599 (44)	1,785 (44)	1	Ref	
Female	3,294 (56)	2,292 (56)	1.01	0.96-1.06	0.75
Race					
White	5,341 (91)	3,641 (89)	1	Ref	
African American	458 (8)	334 (8)	1.07	0.92-1.24	0.37
Other	94 (1)	102 (3)	1.59	1.20-2.11	0.0013
Comorbidity Score					
0	3,523 (60)	2,499 (61)	1	Ref	
1	1,669 (28)	1,102 (27)	0.93	0.85-1.02	0.13
≥2	701 (12)	476 (12)	0.96	0.84-1.09	0.50
Age					
≤65	2,988 (51)	2,065 (51)	1	Ref	
>65	2,905 (49)	2,012 (49)	1.00	0.93-1.09	0.96
Insurance					
None	196 (3)	137 (3)	1	Ref	
Private Payer	1,972 (33)	1,241 (30)	0.90	0.72-1.13	0.37
Government	3,671 (62)	2,653 (65)	1.03	0.83-1.29	0.77
Unknown	54 (2)	46 (2)	1.22	0.78-1.91	0.39
Education					
≥29%	835 (14)	757 (19)	1	Ref	
20 to 28.9	1,759 (30)	1,186 (29)	0.74	0.66-0.84	<0.0001
14 to 19.9	2,099 (36)	1,383 (34)	0.73	0.64-0.82	<0.0001
<14	1,111 (20)	713 (18)	0.71	0.62-0.81	<0.0001
Facility Type					
Community Cancer Program	605 (10)	414 (10)	1	Ref	
Comprehensive Cancer Program	3,168 (54)	1,892 (47)	0.87	0.76-1.00	0.0522
Academic/research program	2,099 (36)	1,746 (43)	1.22	1.06-1.40	0.0064
Facility Location					
Metro	4,498 (78)	3,193 (80)	1	Ref	
Urban	1,107 (19)	679 (17)	0.86	0.78-0.96	0.0068
Rural	131 (3)	97 (3)	1.04	0.80-1.36	0.76
Income, USD					
<30,000	1,164 (20)	850 (21)	1	Ref	
30,000-35,000	1,678 (29)	1,169 (29)	0.95	0.85-1.07	0.43
35,000-45,999	1,729 (30)	1,032 (26)	0.82	0.73-0.92	0.0008
>46,000	1,233 (21)	983 (24)	1.09	0.97-1.23	0.16
Fractionation					
Daily	5,314 (90)	3,611 (89)	1	Ref	
BID	579 (10)	466 (11)	1.18	1.04-1.35	0.0102
Radiation Dose					
≤62 Gy	4,530 (77)	2,729 (67)	1	Ref	
>62 Gy	1,363 (23)	1,348 (33)	1.64	1.51-1.79	<0.0001
Distant to facility					
≤9.6 miles	3,067 (52)	2,007 (60)	1	Ref	
>9.6 miles	2,826 (48)	2,070 (40)	1.12	1.03-1.21	0.0057
Year of Diagnosis					
2004-06	997 (21)	173 (20)	1	Ref	
2007-09	1,579 (20)	861 (20)	2.51	2.09-3.02	<0.0001
2010-12	1,898 (19)	1,535 (20)	4.67	3.91-5.55	<0.0001
2013-14	1,419 (22)	1,681 (20)	6.83	5.72-8.14	<0.0001
Stage Grouping					
1A/B	591 (10)	388 (10)	1	Ref	
2A/B	716 (12)	411 (10)	0.87	0.73-1.04	0.14
3A	2,644 (45)	1,827 (45)	1.05	0.86-1.34	0.48
3B	1,942 (33)	1,451 (35)	1.14	0.98-1.32	0.08

Note: Education is quartiles of the percentage of persons with less than a high school education in the patients' residence census tract. Income is median household income in the patients' residence census tract.

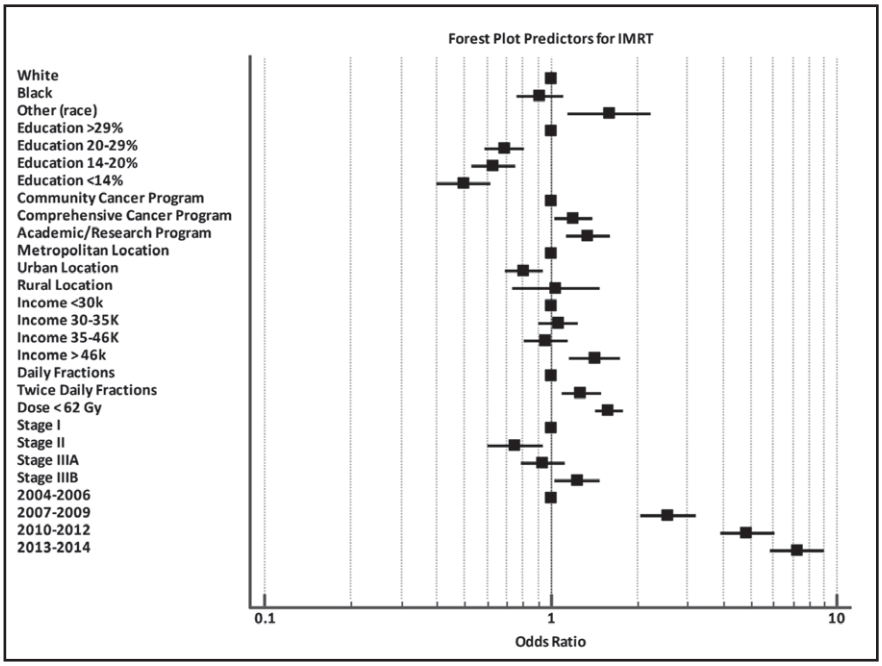

FIGURE 3. *Forest plot showing significant predictors for intensity-modulated radiation therapy (IMRT) use in limited-stage small stage lung cancer (SCLC) on multivariable logistic regression.*

Our results show a steady increase in the utilization of IMRT in this patient population, with > 50% of patients being treated in that manner as of 2014, while only 11% received the technique in 2004. Along those lines, the odds ratio of receiving IMRT in 2013-2014 was 6.83 compared to 2004-2006. Indicators/predictors for IMRT use in this study were higher education and treatment at an academic facility, with urban patients less likely to receive IMRT. These findings likely indicate that these patients had access to more recent technology or perhaps academic radiation oncologists subspecializing in lung cancer who were more comfortable using the technique. Similarly, that urban patients were less likely to receive IMRT may indicate lack of access or other undocumented socioeconomic factors, which we can only assume played into that association.

The increase in IMRT use likely relates to extrapolation from the results of RTOG 0617, which compared 60 Gy to 74 Gy in NSCLC.[8] On secondary analysis, 47% of patients in that study were treated using IMRT. Results presented in 2017 showed that patients with larger radiation therapy volumes and more advanced stage were treated with IMRT.[9] Despite treating larger volumes and more advanced disease, IMRT usage allowed for a decrease in grade 3 pneumonitis and decreased heart dose, which was shown to correlate with OS. Concordantly, in our analysis, we did show a trend toward IMRT use with more advanced disease, although it was not statistically significant ($p = 0.08$). The authors of RTOG 0617 concluded that those results support the routine use of IMRT in NSCLC, which is frequently extrapolated to SCLC. Additionally, IMRT may provide better esophageal sparing compared with conventional techniques to mitigate this limiting toxicity of BID treatment.[2]

Our study did not show a survival difference with the use of IMRT, perhaps not surprisingly, as the main benefit/goal for IMRT use is to help decrease serious toxicity (data which is not included in the NCDB). We could postulate, however, that with the trend toward more advanced disease in patients receiving IMRT, a decrease in toxicity through the use of IMRT could reasonably result in an otherwise improved outcome compared to standard techniques. Our results showed that treating to a dose > 62 Gy was also a predictor for IMRT use. This indicator makes sense as treating to higher doses would make it more difficult to meet organ at risk (OAR) constraints using traditional 3D CRT. Of note, in this analysis, increasing radiation dose did not predict for improved OS. However, one could speculate that using IMRT to deliver a higher dose perhaps increased local control (not reported in NCDB), but not OS as patients with SCLC have high risk for distant disease, which is often their ultimate cause of death. A single-institution study from 2016 compared and examined outcomes in over 600 patients treated with either 3D (206 patients) or IMRT (446 patients), and showed a slight OS benefit, local control benefit, and reduced toxicity with IMRT use.[11] Granted, those results were not seen in randomized data from RTOG 0617, which did not show an increase in local control or OS for NSCLC with dose escalation. We must also keep in mind that SCLC is more radiosensitive comparatively, and dose escalation in that setting will likely have diminishing returns. There is one single-institution series from MD Anderson comparing IMRT and 3D CRT for SCLC.[10] Those authors reviewed outcomes in over 200 patients with limited-stage SCLC and did not show any difference in OS or disease-free survival (DFS) with IMRT. They did, however, show that IMRT patients required significantly fewer percutaneous feeding tube placements, ie, less toxicity.

We would be remiss not to mention that in our study BID fractionation was shown to have better OS compared to daily treatment (HR: 0.78, $p < 0.0001$).

Table 3. Multivariable Cox Proportional Hazards Models for Overall Survival in Patients Receiving Chemoradiotherapy for Limited Stage SCLC

Significant Characteristic	Hazard of Death (95% CI)	p
Cox model without propensity score		
Age		
≤65	Reference	
>65	1.29 (1.22-1.36)	<0.0001
BID treatment		
No	Reference	
Yes	0.82 (0.76-0.89)	<0.0001
Comorbidity Score		
0		Reference
1	1.12 (1.067-1.19)	<0.0001
2	1.31 (1.21-1.42)	<0.0001
3	1.56 (1.35-1.80)	<0.0001
Income, USD		
<30,000	Reference	
30,000-35,000	1.06 (1.00-1.11)	0.0366
35,000-45,999	0.97 (0.91-1.05)	0.53
>46,000	0.97 (0.90-1.04)	0.38
Insurance		
None	Reference	
Private	0.86 (0.80-0.90)	<0.0001
Government	1.01 (0.89-1.16)	0.82
Race		
White	Reference	
African American	0.88 (0.80-0.96)	0.0037
Other	0.94 (0.79-1.13)	0.55
Sex		
Male	Reference	
Female	0.79 (0.75-0.83)	<0.0001
Stage Group		
1A/B	Reference	
2A/B	1.19 (1.07-1.32)	0.0015
3A	1.51 (1.39-1.65)	<0.0001
3B	1.70 (1.56-1.86)	<0.0001
Years of Diagnosis		
2004-06	Reference	
2007-09	0.93 (0.87-1.01)	0.112
2010-12	0.93 (0.88-0.98)	0.0089
2013-14	0.91 (0.86-0.97)	0.0053
Cox model with propensity score		
Propensity Score	0.80 (0.67-0.97)	0.026
Age		
≤ 65	Reference	
> 65	1.24 (1.16-1.32)	<0.0001
Fractionation		
Daily	Reference	
BID	0.78 (0.71-0.85)	<0.0001
Sex		
Male	Reference	
Female	0.80 (0.76-0.85)	<0.0001
Insurance		
None	Reference	
Private	0.91 (0.78-1.09)	0.0584
Government	1.16 (1.09-1.24)	<0.0001

CI, confidence interval; BID, twice daily;

This was not the intention of the current study, nor was it taken into account when defining our cohort. In addition, this question was initially addressed with the Turrisi trial,[2] and readdressed in the CONVERT trial using a higher daily dose.[4] The results of the current RTOG trial will help further address that issue. Furthermore, in 2015, there was an NCDB analysis looking for differences in OS based on fractionation scheme (daily, concomitant boost, and BID), showing no significant difference among the three regimens.[18]

The NCDB provides a unique platform to perform well-powered retrospective analyses on a large number of patients. Nevertheless, it is subject to several limitations, namely selection bias given its retrospective, nonrandomized nature. Additionally, initial treatment response, toxicity data, salvage therapies, and disease recurrence are not included in the NCDB, all of which may affect interpretation of results. We also lack data on any follow-up radiation therapy such as prophylactic cranial irradiation (PCI), which has been shown to have an OS benefit in limited-stage SCLC and may not have been balanced between treatment arms.[19] In addition, there is potential for miscoding within the data set. In that vein, we elected to exclude patients coded as being treated with photons, protons, or radiation not otherwise specified (NOS), as those codes could have been 3D CRT or IMRT and there was no reliable way to distinguish.

In summary, this study shows increased use of IMRT in limited-stage SCLC over time, with rates now eclipsing 50%. This increase in use is not unreasonable given the benefits seen when applied to our NSCLC patients. In addition, other NCDB and institutional analyses show a similar rise in IMRT use across multiple other disease sites.[20,21]

Conclusions

The results of this NCDB analysis show a steady increase in the use of IMRT for the treatment of limited-stage SCLC. We expect the proportion of patients with limited-stage SCLC to continue to increase based on recent data showing reduced lung toxicity and heart dose in NSCLC.

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Enhancing quality, safety and efficiency in treatment planning with health information technology (HIT) and artificial intelligence (AI)

Mary Beth Massat

Across every step of the radiation therapy process, checks are performed to ensure patient safety. From verifying the linear accelerator calculations to examining treatment plans to ensuring proper patient positioning, all members of the multidisciplinary treatment staff have a specific role in safeguarding patients as well as reporting errors and near misses.

In 2010, the American Society for Radiation Oncology (ASTRO) launched the Target Safely initiative to focus its resources on improving patient safety and reducing the potential for medical errors. A key aspect of the initiative was the 2014 development of the Radiation Oncology Incident Learning System (RO-ILS), a national medical error reporting system and patient safety database created in partnership with the American Association of Physicists in Medicine (AAPM). Target Safely also included another AAPM/ASTRO-sponsored initiative, Integrating the Healthcare Enterprise-Radiation Oncology (IHE-RO), which aims to improve the compatibility of system-to-system connections, especially among different radiation oncology vendors' equipment and information systems.

***Ms. Massat** is a freelance healthcare writer based in Crystal Lake, IL.*

***FIGURE 1**. Elekta (Stockholm, Sweden) and IBM Watson Health (King of Prussia, Pennsylvania) combine the MOSAIQ oncology information system (OIS) for treatment planning and automation with artificial intelligence (AI) capabilities to provide deep learning algorithms and cognitive computing. photo/courtesy Elekta*

David Hoopes, MD, associate professor at the University of California San Diego (UCSD) School of Medicine and medical director at 4S Ranch cCare (San Diego), is one of four physicians appointed to the RO-ILS Radiation Oncology Healthcare Advisory Council (RO-HAC), the group that analyzes data from RO-ILS. Based on analyses of these data, the most common pitfalls that can lead to a safety event or near-miss in radiation oncology departments are set-up errors, iso-center problems and suboptimal contours.

"What causes these errors really boils down to communication among the staff and the patient safety culture in the clinic," Dr. Hoopes says. "It is important that anything that doesn't go as it should—whether it reaches the patient and causes an incident or not—should be reported to RO-ILS."

What causes errors really boils down to communication among the staff and the patient safety culture in the clinic.

David Hoopes, MD

Participating in a system such as RO-ILS is a big step toward improving communication, he adds. In addition to the incident being recorded in the database, it is also discussed by the treatment team.

"That discussion is a great step for improving communication," Dr. Hoopes adds, noting that successful interdepartmental communication relies on strong physician leadership that champions open, free dialog. "When the team sees that it is a nonpunitive environment and that their ideas are taken seriously when they propose a solution, they are more likely in the future to communicate well and take care of issues the way they need to be done. So just participating in RO-ILS can help drive better communication and a culture of safety in the department."

To date, more than 480 facilities nationwide have joined RO-ILS. To further encourage participation, RO-ILS provides reports of aggregated data and in-depth case examinations to all ASTRO members and the public. These reports include free continuing medical education (CME) credits.

"RO-ILS continues to grow and add new practices," says Dr. Hoopes. "Certainly our goal is to continue growing, and while we would love to have all facilities nationally participate, we have facilities from almost every state."

One technology-related area that Dr. Hoopes would like to see improved is the development of software modules to help connect treatment planning systems or oncology-specific electronic medical records (EMRs) to RO-ILS. Currently, reporting to RO-ILS involves a separate system. In the future, Dr. Hoopes says enabling connectivity could simplify error reporting by allowing for automatic population of patient and treatment information to the incident learning system.

The ability to perform high-quality, electronic peer review is another area where Dr. Hoopes sees a gap in technology. His hope is that vendors will create a module allowing peer review to be part of treatment planning system. "While many departments do peer review, it is inefficient," he says.

Education and Training

Safety in radiation oncology is not a new topic, but interest has resurged as its link to payment and accreditation has grown. Many clinics are now putting more resources toward accreditation programs from ACR, ASTRO or the American College of Radiation Oncology (ACRO).

In light of this increased focus, one group from the University of Washington (Seattle) examined the education and training that residents received regarding patient safety and quality improvement in radiation therapy. According to lead author Matthew Spraker, MD, PhD, who is now assistant professor of radiation oncology at Washington University School of Medicine (St. Louis, MO), the study found that residents are not exposed to training in patient safety and quality improvement programs, including incident learning programs, even though physicians and physicists are expected to assume leadership roles in these areas.[1]

"Radiation oncology residents are not being trained to lead these credentialing programs," says Dr. Spraker. "On top of that, they reported that they don't feel that they are prepared in this specific respect."

In a follow-up survey of directors of radiation oncology and medical physics residency programs accredited by the Accreditation Council for Graduate Medical Education (ACGME), Dr. Spraker and co-authors reported that most directors believe residents are adequately exposed to patient safety and quality improvement tools.[2] However, this perception differs from the results of Dr. Spraker's prior study and other independent studies.

There were several interesting takeaways from the program directors' responses, says Dr. Spraker. Many programs don't have educators experienced in designing curricula to address patient safety and quality improvement. Residents undergo a grueling curriculum to learn how to manage all cancers and, therefore, many program directors are concerned about the time and resources to build these concepts into the curricu-

> Radiation oncology residents are not being trained to lead credentialing programs. On top of that, they reported that they don't feel they are prepared in this specific respect.
>
> Matthew Spraker, MD, PhD

lum, even if they have the expertise.

"This is where technology can help," Dr. Spraker says, whether it be the development of educational tools, such as online collaboration or webinars, or incident learning simulation programs.

"There is also a growing understanding of how information technology is designed and how software interfaces can lead to errors," explains Dr. Spraker, noting that it comes down to human factor engineering.

Human factor engineering is the science behind identifying and addressing safety issues that arise from the interaction of people and technology. It encompasses how systems and equipment are designed so human errors don't lead to a patient safety event.

"The idea is for industry to think about how the system works and the tools that it provides, so as people are working under certain constraints, the equipment does not contribute to errors or failures," Dr. Spraker says.

To further identity the root causes of errors, Dr. Spraker and colleagues from the University of Washington examined 300 randomly selected event reports from the international ILS, Safety in Radiation Oncology (SAFRON). Communication and human behaviors were the most common errors impacting all events; however, poor human factor engineering contributed to more high-risk than low-risk events.[3]

"Workflow is key," Dr. Spraker says. "When designing these systems, industry needs to spend time with the people using the technology and interacting with how it is used in the clinic."

Artificial Intelligence and Machine Learning

While incident reporting is an important tool for evaluating the root cause of safety-critical events and near misses, it is voluntary and post-incident. Artificial intelligence (AI) and, more specifically machine learning (ML), may help facilities identify these events pre-incident.

Deshan Yang, PhD, associate professor of radiation oncology and primary investigator in the Laboratory of Medical Imaging and Health Informatics at Washington University School of Medicine (St. Louis), has been exploring the use of machine learning in medical physics and radiation oncology. He is the recipient of a National Institutes of Health grant to develop an automated health information technology (HIT) system to improve patient safety, treatment quality and working efficiency in radiation therapy.

Dr. Yang believes that HIT and machine learning can help improve the overall quality and safety in the day-to-day workflow of medical physicists.

"By using technology to help us work more accurately and efficiently in performing daily quality checks and verifying the patient treatment plan, the hope is that we can improve the overall quality and safety of patient care," he says.

Dr. Yang is examining three types of data with HIT: patient data (tumor location, dose and prescription); image data (target and critical structures); and the treatment plan data (how good is the plan and can it be better).

"We are developing a rules-based logic solution for medical physicists that can perform the same tasks as a human but do it automatically, more accurately and more quickly," Dr. Yang explains.

It's not that radiation therapy is not safe, rather safety comes at a high price: the time and cost of the human worker. Yet, he says safety doesn't always equate to quality. Medical physicists often have a heavy workload, and Dr. Yang's goal is to develop a system that would create new workflow efficiencies so they could focus more on quality.

"If we can have a computer-based system take care of the more basic safety-related work, that would give us more time to focus on increasing the quality of the treatment," he says. "Efficiency leads to better quality care. There is always room to improve a plan, but that comes at a

If we can have a computer-based system take care of the more basic safety-related work, that would give us more time to focus on increasing the quality of the treatment.

Deshan Yang, PhD

cost of time, and that is the problem we face in our daily workflow."

Adds Dr. Yang: "The burning question is, 'What will be the expected and acceptable treatment plan for a particular patient [and] is there room for improvement?'"

That's where AI and ML can make an impact (**Figure 1**). By examining the patients treated—their treatment plan, dose distributions and the anatomic images used for planning and to contour critical structures—and using an ML model, it is possible to have a better knowledge-based understanding of the entire treatment plan, including the relationship of the patient anatomy to the previously approved treatment plan.

"We can use this technology to compare a new patient's anatomy to the machine learning model and help predict the quality of the new treatment plan and radiation dose distribution," Dr. Yang explains. "Then, we have a knowledge base and empirical ground truth to compare for the dose volume histogram matrix."

Dr. Hoopes also sees potential for AI and ML to help analyze the data from RO-ILS, particularly as the incident database continues to grow.

"Radiation therapy involves complex workflows and volumes of data," he says. "It will be difficult over time for humans to review every event. So we'll need to build machine learning algorithms to help us through this process."

Dr. Spraker agrees that ML can help by also comparing reported incidents with patient-specific features in an EMR. He cites an abstract from ASTRO 2016 that explored trigger indicators in oncology information systems (OIS) and EMRs to help identify safety-critical events. The study queried the OIS with 10 indicators over four years and correlated with the facility's ILS to find patients with reported high-grade, near-miss safety events. The study authors reported a significant correlation between the panel of indicators and safety-critical events. Future efforts will revolve around the development of an ML algorithm to refine indicator selection to find specific combinations of trigger indicators and safety-critical events.[4]

"We can use machine learning to find correlations between features in the patient's EMR and incidents in the clinic," Dr. Spraker says. "If we have a model, then triggers can be identified in the EMR that, for example, notify the user that similar patients had three incident reports." This may enable the ability to identify a potential incident before it occurs.

Dr. Yang posits that medical physicists will soon have new tools to help predict treatment plan quality. "I believe that in five years, auto segmentation of normal structures in medical images and, at some level auto treatment planning, will be ready for the clinic," he says.

If clinics can reduce the time needed for treatment planning and concurrently develop a better plan, then the potential to treat patients the same day as developing their treatment plan could become a reality. Yet, Dr. Yang cautions that benchmarks are needed to qualitatively measure the use of AI and ML in treatment planning. Without this, it will be difficult to quantitate the usefulness of these new tools.

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RADIATION ONCOLOGY CASE

Absence of fibrosis after stereotactic body radiation therapy (SBRT) for hepatocellular carcinoma (HCC) in a multiple-transplant patient

Hilario Yankey; Jordan M. Anaokar, MD; Joshua E. Meyer, MD

CASE SUMMARY

Our patient is a 58-year-old Caucasian woman with a past medical history including two liver transplantations, right kidney transplantation, recurrent hepatocellular carcinoma (HCC) and eradicated hepatitis C infection (HCV). At age 39, the patient had an orthotopic liver transplant (OLT) for HCV cirrhosis. After 11 years (age 50), she developed HCC in the transplanted liver, which was treated with transarterial chemoembolization (TACE). At age 51, the HCC was treated with a second OLT. While on immunosuppression after transplantation, the patient developed calcineurin inhibitor (CNI) toxicity and subsequently end-stage kidney failure that required hemodialysis until she received a deceased donor kidney transplant (DDKT), two years after the second OLT. Six years after her second OLT, she presented to the hospital with nausea, vomiting, and abdominal pain. Her alpha-fetoprotein (AFP) was elevated at 1067 ng/ml and 1902 ng/ml a month later.

IMAGING FINDINGS

A computed tomography (CT) scan demonstrated a large mass in the dome of the liver (segment VIII) with regions of nodular high attenuation and low-grade enhancement in all contrast phases, suspicious for atypical HCC. Magnetic resonance imaging (MRI) confirmed findings diagnostic of an atypical HCC (**Figure 1**). Chest CT and bone scans were negative for pulmonary or osseous metastases.

DIAGNOSIS

With concern of a new HCC, the patient's mycophenolate was stopped. Her subsequent immunosuppression regimen consisted of cyclosporine 50 mg BID and prednisone 5 mg once daily. Given that she had had two surgical anastomoses, chemoembolization posed a substantial risk of abscess formation, as well as vascular and chemotherapeutic injuries to the liver. The patient was also not a good surgical candidate due to the liver lesion's location between the right and middle hepatic veins, producing a future liver remnant that would be too small. The recommendation was a course of stereotactic body radiation therapy (SBRT). Fiducial marker placement was performed using CT guidance. Treatment was performed using the robotic radiosurgery system (Cyberknife, Accuray, Sunnyvale, California), with fiducial tracking. The patient was treated with 5 fractions of 900 cGy, delivered every other day. The prescription isodose line was 66%. The dose was limited by proximity to the heart.

The patient complained of some right upper quadrant pain post-SBRT, likely related to her requirement for common bile duct stent change, as it resolved post change. She also developed symptomatic atrial fibrillation,

Mr. Yankey *is a fourth-year medical student at Lewis Katz School of Medicine, Temple University, Philadelphia, PA.* ***Dr. Anaokar*** *is assistant professor of radiology, Department of Diagnostic Imaging, Fox Chase Cancer Center, Philadelphia, PA. Also at Fox Chase,* ***Dr. Meyer*** *is associate professor of radiation oncology, Department of Radiation Oncology.* *Disclosure: The authors have no conflicts of interest to disclose, and no part of this article has been previously published elsewhere. Acknowledgements: This publication was supported by grant number P30 CA006927 from the National Cancer Institute, NIH. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the National Cancer Institute or the National Institutes of Health.*

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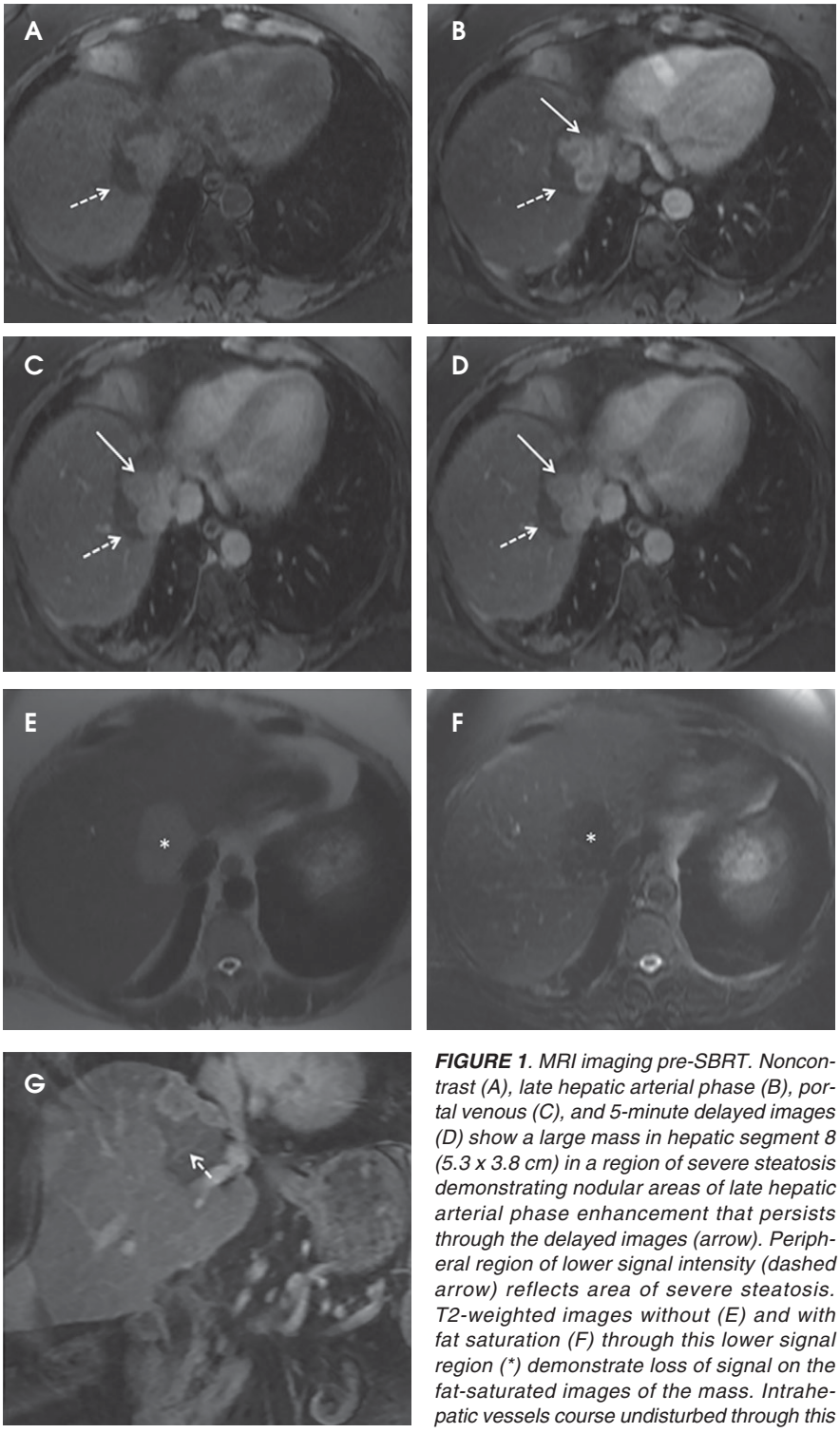

FIGURE 1. *MRI imaging pre-SBRT. Noncontrast (A), late hepatic arterial phase (B), portal venous (C), and 5-minute delayed images (D) show a large mass in hepatic segment 8 (5.3 x 3.8 cm) in a region of severe steatosis demonstrating nodular areas of late hepatic arterial phase enhancement that persists through the delayed images (arrow). Peripheral region of lower signal intensity (dashed arrow) reflects area of severe steatosis. T2-weighted images without (E) and with fat saturation (F) through this lower signal region (*) demonstrate loss of signal on the fat-saturated images of the mass. Intrahepatic vessels course undisturbed through this mass (arrowhead in G), a hallmark of steatosis. Although this enhancement pattern is atypical for hepatocellular carcinoma (HCC), in the clinical context, this was sufficient for diagnosis of recurrent HCC.*

requiring hospital admission. She had a history of paroxysmal atrial fibrillation for multiple years, and we felt that this was not likely treatment related. The patient's AFP initially decreased to 325 ng/mL approximately 6 weeks after treatment. It then rose to 450 ng/mL at approximately 6 months post-treatment and 1930 ng/ml at 8 months post-treatment. On follow-up MRI performed 6 months following completion of therapy, the treated mass had decreased substantially (**Figure 2**). More surprisingly, careful examination of the liver with MRI demonstrated no effects of the radiation treatment (**Figure 3**). This very unusual lack of treatment effect was striking to the radiologists and the treating clinicians involved in the patient's care.

DISCUSSION

Pathologically, normal liver tissue treated with SBRT will demonstrate changes like veno-occlusive disease.[1] On CT scans and other imaging, local injuries by radiation treatment are commonly seen as density changes in the liver, as well as volume loss. These changes on imaging often manifest as hypodense regions surrounding the target tumor volume. However, visualized density changes do not necessarily correlate with symptomatic toxicity.[2]

Liver injury (from radiation, for example) initiates a cascade of inflammatory and fibrogenic signals that recruit and transform hepatic stellate cells (HSCs) into myofibroblasts. Myofibroblasts, in turn, lay down connective tissue that leads to fibrosis through the effect of growth factors such as transforming growth factor β (TGF-β) released by the injured hepatocytes and macrophages.[2,3] There is a dose-dependent increase in TGF-β in irradiated liver[4] and inhibition of this growth factor can help prevent fibrosis. Modulating radiation technique has also been shown to decrease the expression of TGF-β

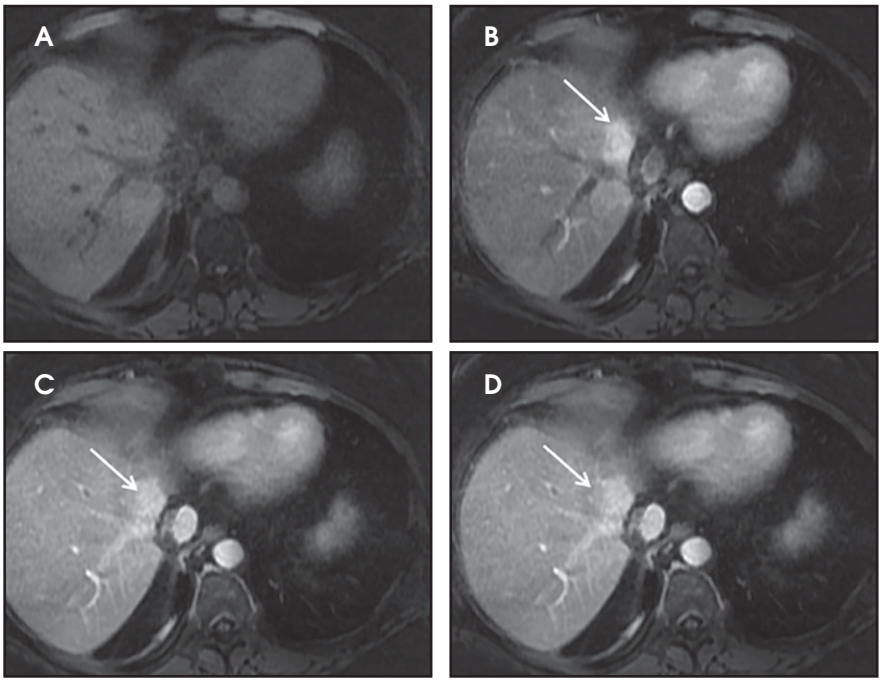

FIGURE 2. *MRI tumor imaging post-SBRT. Noncontrast (A), late hepatic arterial (B), portal venous (C), and 5-minute delayed (D) phase MRI images obtained 6 months following completion of therapy demonstrate a small amount of residual enhancement (arrow), suspicious for a small amount of residual disease (2.5 x 1.9 cm).*

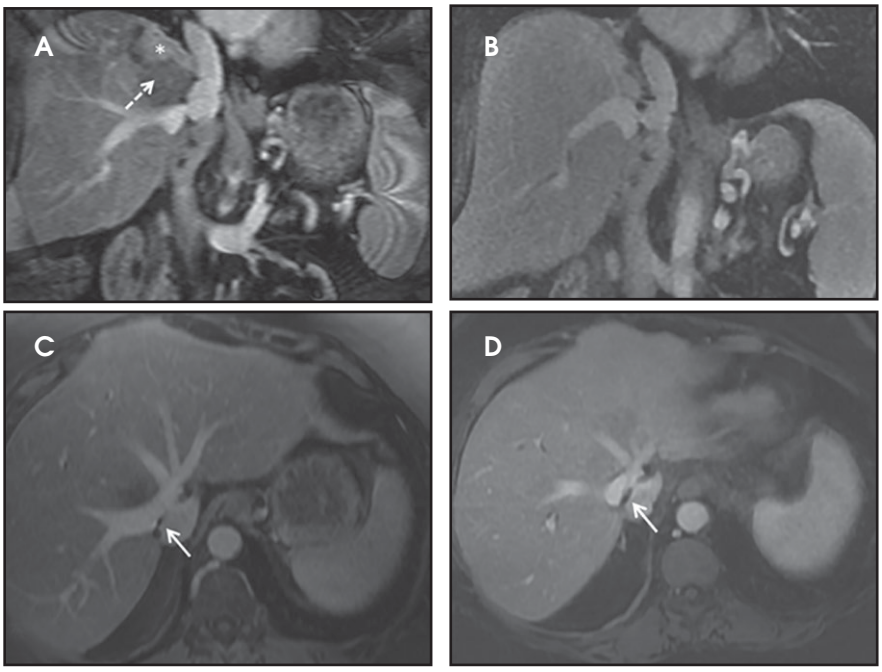

FIGURE 3. *Liver imaging post-SBRT. Demonstration of absence of fibrosis and liver volume loss. Coronal postcontrast images through the mass (*) before (A) treatment and after treatment through a similar plane (B) demonstrate no significant volume loss. The large area of steatosis surrounding the mass is significantly diminished, and not seen on these images. Axial postcontrast images before (C) and after (D) treatment through the level of the caval anastomosis (arrow) also demonstrate no significant volume loss or fibrosis following treatment.*

and improve treatment toxicity in animal models.[5] In the case of our patient, she had a good (76% cross-sectional) response to the treatment of a 5.3-×-3.8-cm tumor to 2.5-×-1.9 cm in a relatively short time, with no new density changes on imaging to show radiation treatment and fibrosis. We speculate that her immunosuppressive drugs, cyclosporine and prednisone, may be protecting her from these changes through their effect on TGF-β expression.

Inflammation regardless of cause (radiation, autoimmune, etc.) promotes fibrosis, and potent anti-inflammatory drugs such as corticosteroids are effective in preventing and treating fibrosis.[4] Corticosteroids have been used to treat liver disease and fibrosis—most commonly in autoimmune fibrosis—with improved outcomes. Hepatic fibrosis improves in up to 57% of patients treated with corticosteroids and prevents fibrosis in up to 79% of patients with autoimmune hepatitis.[6] In animal models, treatment of HSCs with glucocorticoids reduces the secretion of endogenous TGF-β and TGF-β signaling.[7]

Cyclosporine is an immunosuppressive drug used as prophylaxis against organ rejection by forming a complex with cyclophilin A (CypA) to inhibit calcineurin.[8] Cyclophilin A binding leads to several changes in the cell including immunosuppressive, antitumor, and anti-fibrotic effects. Cyclosporine use in the setting of liver fibrosis from autoimmune hepatitis may help stabilize or reverse fibrosis.[9] TGF-β-mediated fibrosis in the liver occurs similarly to idiopathic pulmonary fibrosis (IPF), where it has been studied more extensively. Cyclosporine has been shown to inhibit TGF-β-mediated fibrosis in IPF by degrading TGF-β-induced-hypoxia inducible factor 1-alpha (HIF-1α), which causes dedifferentiation of myofibroblasts, thus reversing fibrosis.[10]

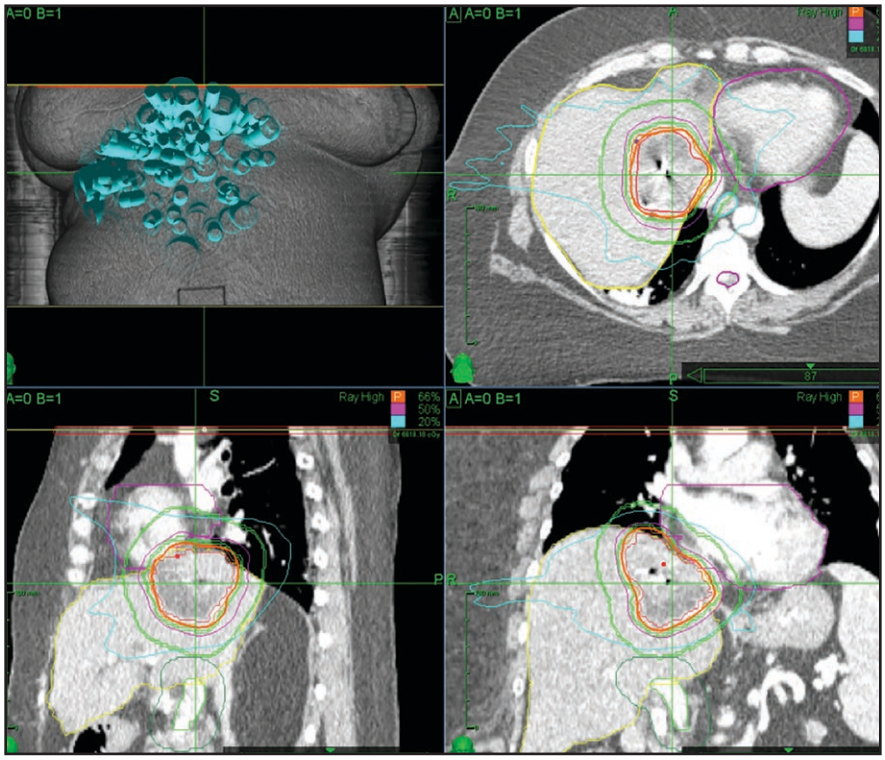

FIGURE 4. *Three-dimensional (3D) figure of isodose distribution.*

CONCLUSION

This is an interesting case of how immunosuppressive drugs—cyclosporine and prednisone—may affect the response of tumor and fibrosis after radiation treatment. Our observation and our research of current literature point to the potential benefits of glucocorticoids and possibly cyclosporine as anti-fibrotic agents.

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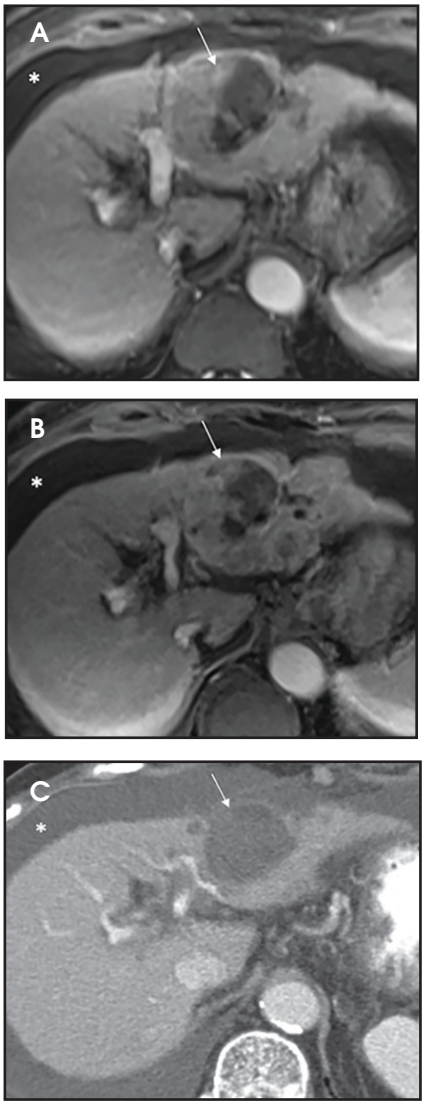

FIGURE 5. *Expected post-treatment fibrosis in an immunocompetent patient. (A) Pre-treatment MRI demonstrates a necrotic mass with solid enhancing components in segments 2/3 (arrow) with ascites (*). (B) Post-treatment MRI obtained 2.5 months following therapy shows no significant change in size or enhancing components within treated lesion, but a subtle decrease in the size of the lateral left hepatic lobe. (C) A post-treatment CT scan obtained 5.5 months following therapy shows a reduced tumor size and resolution of the enhancing components indicative of treatment response. There is further volume loss of lateral left hepatic lobe, an expected finding following radiation therapy.*

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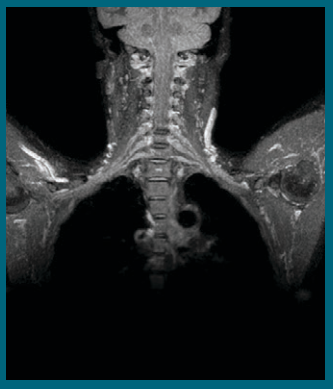

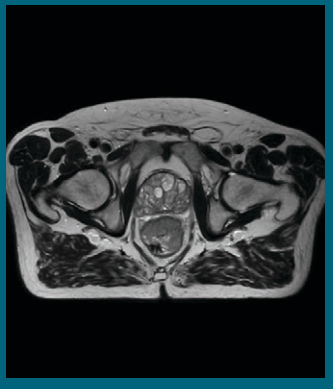

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RADIATION ONCOLOGY CASE

Severe contact dermatitis secondary to metal contaminants in radiation therapy paint pens

Islam Younes, MD; Tzough-Liang Sun, MA; Wendy A. Woodward, MD, PhD

CASE SUMMARY

A 31-year-old woman with a cT1cN0M0 ER-positive, PR-negative, HER-2/neu 1+, grade 3 invasive ductal carcinoma underwent segmental mastectomy, breast reduction and sentinel lymph node biopsy confirming pT1cN0 disease with negative margins. Adjuvant chemotherapy was recommended and she received paclitaxel for 12 cycles and fluorouracil for 4 cycles. Subsequently, she underwent treatment planning for whole-breast radiation therapy, 50 Gy in 25 fractions followed by a 10 Gy boost. Standard setup marks were drawn at simulation using the normal order paint pens (Sharpie Paint, medium point, oil-based, Vietnam), (**Figure 1A**). After 4 weeks of radiation therapy, she developed well-demarcated linear eczematous weeping and erythematous plaques circumferentially around the areola and in linear lines radiating from the right areola corresponding to the paint location (**Figure 1B**). Upon review, it was established that 4 similar cases had occurred in the previous 8 weeks, whereas none had been observed prior to these.

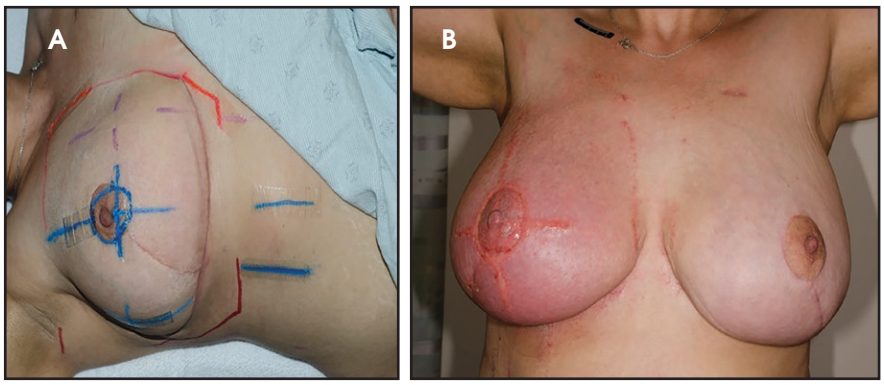

FIGURE 1. *(A) The treatment field is marked by the pen markers at the simulation. (B) The right breast shows well-demarcated persistent erythema; well-demarcated linear eczematous weeping, erythematous plaques circumferentially around the areola and in linear lines radiating from the right areola; and ill-defined eczematous plaque of the central chest.*

DIAGNOSIS

The differential diagnosis included infection, allergic contact dermatitis, or radiation interaction with the paint material. Cases were not confined to a single treatment machine. Infection control was contacted and all pens used for patients were collected and cultured. Cultures were negative. Skin cultures

Dr. Younes *is a visiting research fellow in the Department of Radiation Oncology,* ***Mr. Sun*** *is a senior physicist in the Department of Radiation Physics, and* ***Dr. Woodward*** *is a professor in the Department of Radiation Oncology, University of Texas MD Anderson Cancer Center, Houston TX.* *Disclosure: The authors have no conflicts of interest to disclose. None of the authors received outside funding for the production of this original manuscript and no part of this article has been previously published elsewhere.*

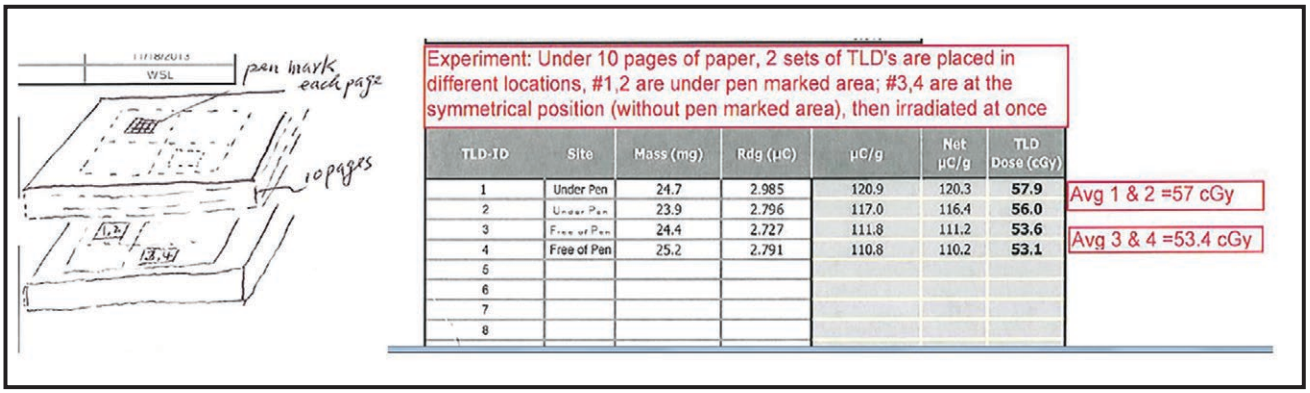

FIGURE 2. *Thermoluminescent dosimeter (TLD) measurements: Radiation dose under the ink vs. control. The results show that the dose is 7% higher under the 10 pages of marked areas (< 1% higher for each layer) and this was consistent with 10 pen-marked pages providing either build-up effect or possible higher Z material in the paint to make the dose higher.*

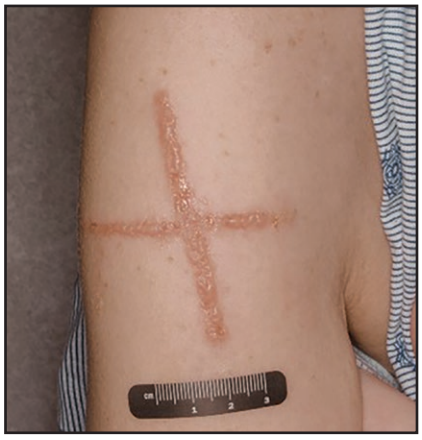

FIGURE 3. Shows well-demarcated vesicles and bullae related to the pen marker lines.

from patients demonstrated normal flora. Referral to dermatology suggested contact dermatitis. All patients were determined to likely have been marked with pens from a single lot. The manufacturer stated there had been no change in materials used in manufacture, noting that the dyes are purchased from external distributors and they could not obtain information on dye lots for specific purchases.

Recognizing that metal is common in tattoo ink, MRI safety screening includes asking about the presence of tattoos. In turn, we hypothesized that metal in the paint pens could lead to contact dermatitis or increased radiation dose received. To test the latter, we applied paint to 10 sheets of paper stacked on top of each other and compared dose through this to a control of unmarked paper using thermoluminescent dosimeters (TLDs). The results interestingly showed that the dose was 7% higher under pen-marked areas, suggesting the pens contribute to a build-up effect or that there is higher Z material in the paint, increasing the dose (**Figure 2**). We considered that this dose difference would also cause the clinical symptoms noted. Also of note, the patient reported to dermatology that she removed a necklace she had worn for years because it was irritating her skin. The patient was treated with topical steroids, and her symptoms improved. We concluded that a metal contaminant in the paint led to contact dermatitis.

DISCUSSION

Radiation-induced skin reactions or radiation dermatitis are one of the most reported side effects of radiation therapy in cancer patients. These cutaneous reactions can be divided into the categories of acute, consequential late, and chronic.[1] Cutaneous reactions can vary from erythema to desquamation to ulceration. Sensitivity to radiation differs in different areas of the body. The most sensitive areas are the anterior neck, chest, extremities, chest, abdomen, face, breast and hair follicles of the scalp.[2] Approximately 10% of patients will experience moist desquamation and ulceration, which may result in treatment delays,[3] decreased quality of life, and pain.[4,5] In light of this, we should be on alert for any other contributing factors that can aggravate these reactions.

In our reported case, we noted skin symptoms inconsistent with expected radiation dermatitis and found that pens used for setup marks caused an allergic reaction. However, the dosimetric findings of a 7% increase in dose makes the possibility that the contact dermatitis and the increased skin reaction from the metallic contaminants may have combined effects. This could be checked by marking the same patient within and outside the radiation field. Different metals such as mercury, cadmium, nickel, cobalt, copper, iron and chromium are used in manufacturing variant colors of tattoo pigments, and these metals can cause allergic reactions in some people. Red pigment commonly causes more allergic reactions than other pigments,[6] as it is often made with mercury, to which an estimated 1% to 5% of the general population is allergic.

Additionally, nickel is one of the most common causes of allergic contact dermatitis.[7] Unilateral nickel-induced facial dermatitis elicited by cell phone use has been reported.[8] Likewise, hairdressers have been diagnosed with allergy-related hand eczema from prolonged skin contact with nickel-containing scissors and crochet hooks.[9] Other common causes

of contact dermatitis are poison ivy, fragrances and neomycin.[7]

Contact dermatitis is divided into two categories: irritant contact dermatitis, which is caused by direct cutaneous inflammation or direct skin injury from an irritant; and allergic contact dermatitis, which is caused by type 4 (delayed) hypersensitivity reaction. Allergic contact dermatitis develops after repeated or prolonged exposure to an antigen. When a foreign allergic antigen comes into contact with the skin, it links to skin protein, forming an antigen complex and then activating T cells, leading to sensitization. Upon re-exposure of the skin to the antigen, the activated T cells initiate an inflammatory process, leading to a manifestation associated with contact dermatitis.[10] Contact dermatitis usually manifests with pruritus, erythema, pain, vesicles and bullae with relatively well-demarcated borders.[10] Diagnosis of contact dermatitis is essentially made by patient history, examination and improvement upon avoidance of the allergic substance. If patient symptoms don't improve by avoidance and empiric treatment, or the allergen isn't known, then a patch test may be indicated. All of our patient's symptoms improved after replacing the pen markers and using topical steroids.

Regarding process improvement, all pens were replaced with the Sharpie Permanent Marker, Fine Point, (Atlanta, Georgia), and a new policy required new pens for each patient. One further incident was identified over a year later in a patient simulated in the main hospital for palliation. It was determined that the simulator in this building had not disposed of all prior pens, leading to this additional case (**Figure 3**).

CONCLUSION

Paint pens are routinely used in radiation therapy practices for daily setup. These can promote contact dermatitis, and care should be taken to avoid metallic paint pens.

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Important Safety Information

Most side effects of radiotherapy, including radiotherapy delivered with Accuray systems, are mild and temporary, often involving fatigue, nausea, and skin irritation. Side effects can be severe, however, leading to pain, alterations in normal body functions (for example, urinary or salivary function), deterioration of quality of life, permanent injury, and even death. Side effects can occur during or shortly after radiation treatment or in the months and years following radiation. The nature and severity of side effects depend on many factors, including the size and location of the treated tumor, the treatment technique (for example, the radiation dose), and the patient's general medical condition, to name a few. For more details about the side effects of your radiation therapy, and to see if treatment with an Accuray product is right for you, ask your doctor.

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