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SA-CME CREDIT

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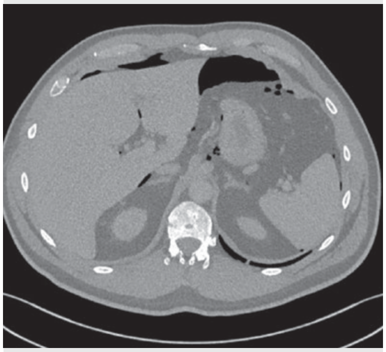

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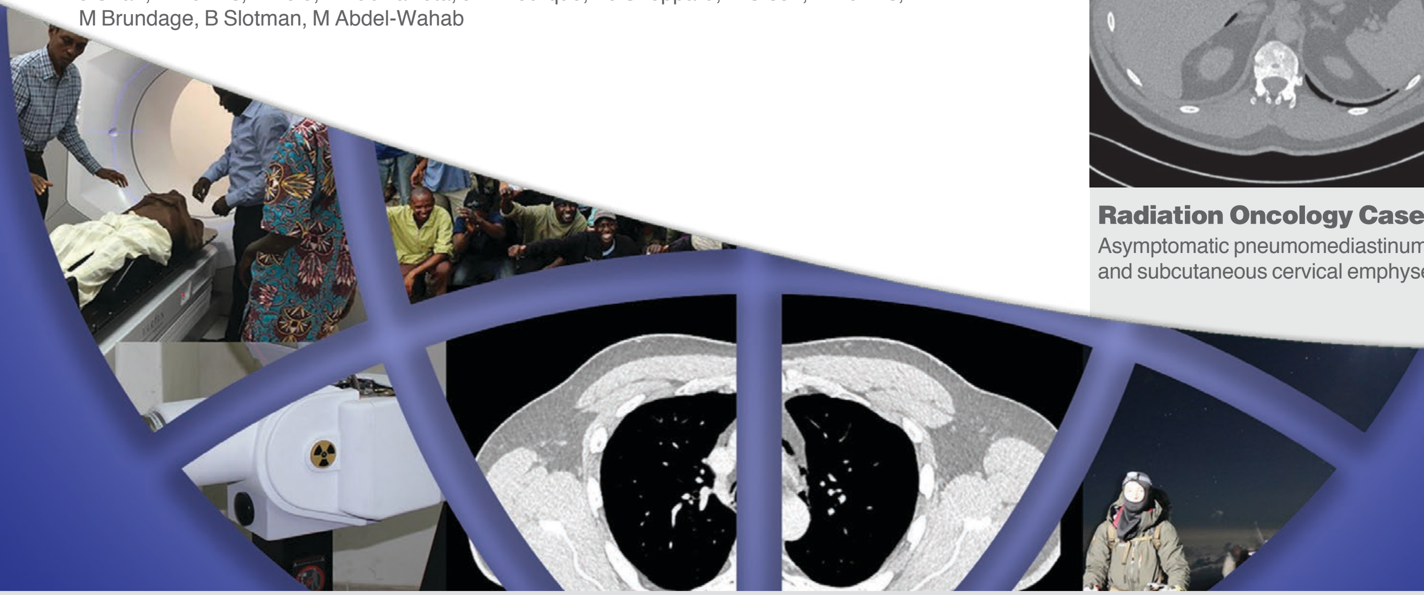

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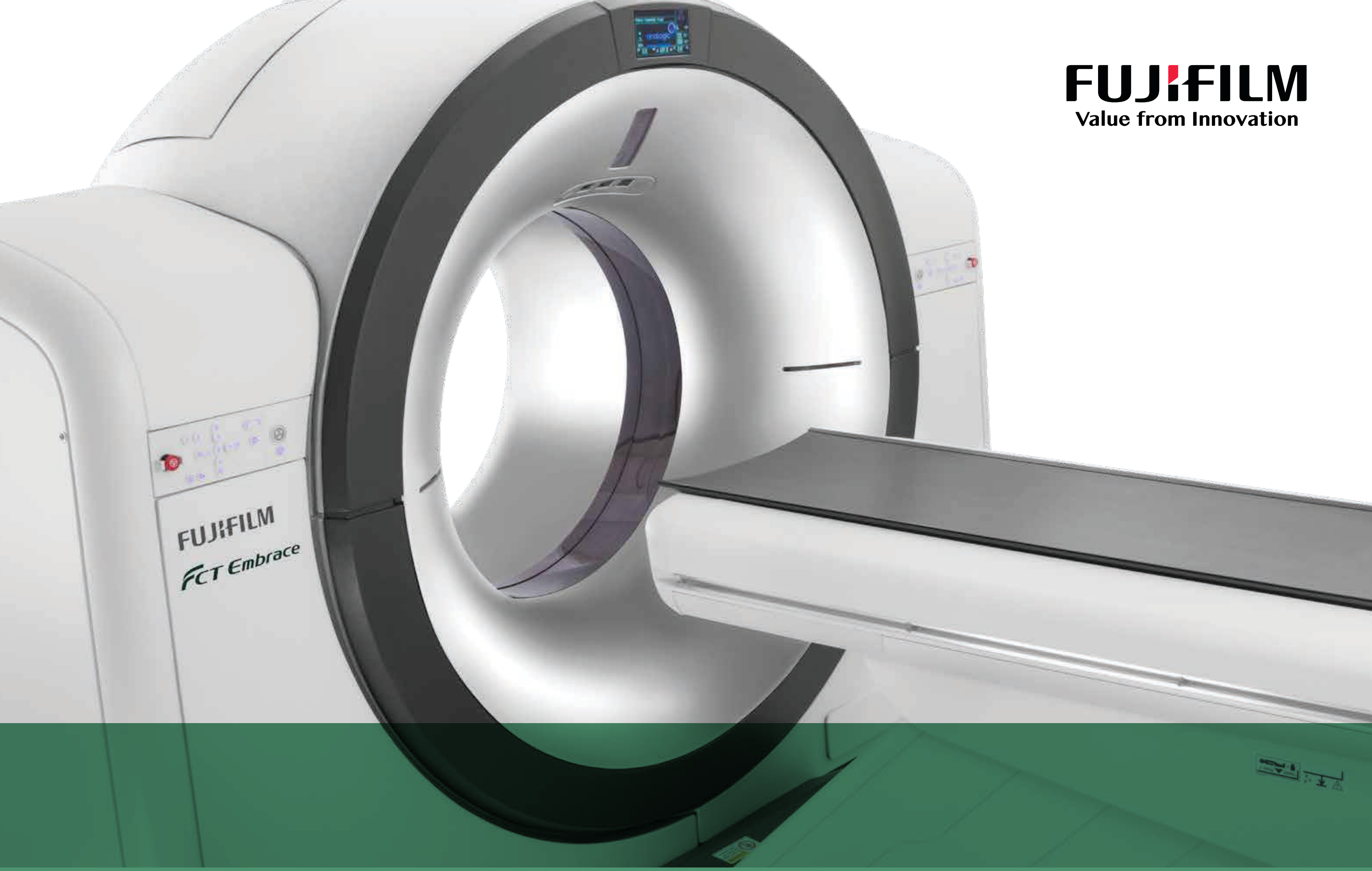

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EDITORIAL

World champions: Improving global access in radiation oncology

John Suh, MD, FASTRO, FACR
Editor-in-Chief

Welcome to the June issue of *ARO*, which focuses on the ever-important topic of global health. We are excited to present three compelling review articles centering on progress and opportunities surrounding global radiation oncology workforce needs by 2030, treatment access in Indonesia, and cancer control in Ghana, all of which offer SA-CME credit. We also feature an excellent research article detailing access and outcomes among indigenous populations in Canada, and several enlightening perspective and profile articles on global accomplishments and challenges in radiation treatment.

Yet, along with our excitement about the issue are several sobering and recurrent themes: limited access to care in low and middle-income countries (LMICs), perpetually scarce education and training in radiation oncology, dated or lack of equipment, and high cancer mortality rates. In low-income countries, for instance, more than 70% of cancer patients are expected to die from their disease compared to about 30% in Western countries.[1] In Indonesia this year, only 93 board-certified radiation oncologists and 65 residents in training are available to serve a nation of 260 million people. And in parts of Tanzania, donated linear accelerators are sitting idle due to the high service costs that preclude their use.

This is where "world champions" come in—those who heed the call to advocate for and improve radiation treatment in developing nations, be it through research efforts, philanthropy, global health residencies or other international partnerships and projects. Our new inaugural column, Global Perspectives chronicles one such example of the eye-opening experiences and accomplishments of a resident in Mwanza, Tanzania, as a Global Health Scholar. We also present a special feature profiling the incredible work of the nonprofit group, RadiatingHope, whose prayer flag and mountain-climbing treks, among other missions, serve to expand the reach of radiation therapy in regions of need. The Technology Trends department highlights the global work of additional advocacy groups, professional societies as well as vendors, and this month's Resident Voice shares key lessons that may inspire others to embrace a global health career, one that truly makes a meaningful difference in the lives of many.

Another common theme in the issue is the underlying impetus for global health initiatives: health equity and universal care. We hope our articles help increase your awareness of this important topic and inspire some of you to consider making a difference.

Please enjoy our global health issue, and thank you, as always, for your continued support!

***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.*

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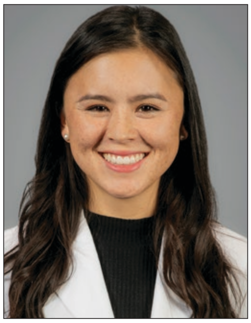
GUEST EDITORIAL

Invested development: Radiation therapy access will shape future cancer care

Madeline Hooper, BA



Madeline Hooper, BA

Radiation therapy (RT) is essential for effective cancer treatment, yet there is a global shortfall of RT infrastructure. Although half of all cancer patients would benefit from RT for curative treatment, palliative care or disease control, most lack access to it because of domestic and international underfunding. Improved RT access will be crucial to preparing for and effectively defending against the growing cancer burden.

Differences in race and socioeconomics strongly correlate with RT access inequities. A 2016 review of 58 studies found that African Americans receive disproportionately less RT treatment than Caucasian patients with the same disease.[1] Variation in patients' education and income levels, treatment center location, and clinician bias likely explain these findings. Moreover, most RT infrastructure is only available at cancer centers in wealthy, developed areas because of RT's high start-up and operational costs. Even in new construction, RT is typically the last resource to be considered.[2] The educational and research efforts associated with the field further contribute to its significant financial and human capital expenses.

Patients' main barriers to RT access are the direct and indirect costs of therapy, namely the burden of travel and time demanded of standard multiple-fraction treatment plans. A 2012 pilot program for hospice patients in Virginia effectively addressed these obstacles and increased palliative RT use by streamlining physician communication, addressing referring physicians' knowledge gaps, and removing the inconvenience of multiple visits through the delivery of single-fraction treatment.[3] While not directly applicable to curative RT therapy, this study demonstrates how effectively lowering the perceived costs of RT increases patient willingness to pursue care. Similar initiatives that debunk the perception that RT is too complex to be standardized and successfully delivered irrespective of socioeconomic context will enhance RT access and use.

Comprehensive cancer care requires RT. Medical students concerned with equitable care have a responsibility to proactively understand the disease landscape we will inherit, and those drawn to oncology must recognize the importance of this niche field. As the WHO estimates the number of cancer-related deaths will increase from 9.6 million in 2018 to 16.4 million by 2040, we should be especially motivated to encourage and prioritize RT development.[4,5]

Fortunately, investment in RT is expected to reap substantial health and economic returns at all income levels worldwide.[2] Wider-reaching and more robust RT access, while costly, will improve our ability to prevent unnecessary death and suffering for all our patients, regardless of where we practice and who we serve.

Ms. Hooper is a first-year medical student at University of South Florida (USF) Morsani College of Medicine, Tampa, FL.

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RESIDENT VOICE

The pursuit of global health during residency: Essential lessons in scholarly inquiry, quality improvement, and health equity

Shekinah Nefreteri Cluff Elmore, MD, MPH

Shekinah Nefreteri Cluff Elmore, MD, MPH

Global health is in the zeitgeist of undergraduate and postgraduate medical education. Medical students and residents from high-income countries (HICs) are more likely to have global health experience and be interested in integrating global health into their current training and future careers.[1,2] Although trainees' motivations to pursue global health differ, they commonly include some combination of an interest in health equity, service, or novel research and clinical experiences.

However, there is seemingly a gap between trainee enthusiasm and training program offerings, particularly in radiation and medical oncology. Program directors, department chairs, and other key leadership in HICs are rightly grappling with how to rigorously and sustainably integrate global health education and research efforts into residency education across specialties.[3] Several challenges exist, including arranging time away from education and service requirements in the primary program, assuring necessary mentorship and supervision, and adequate funding.

The Association of Residents in Radiation Oncology's Global Health Subcommittee (ARRO GHSC) has provided a supportive platform to enhance the pursuit of global health research and clinical innovation during residency for many residents, myself included. ARRO GHSC has monthly calls with committee members to discuss individual and joint projects. Efforts have included global health surveys of residents and program directors, scholarship funding for resident rotations, and a mutual mentorship program that pairs ARRO residents with peer residents abroad to discuss clinical cases and residency experiences.[4]

I am fortunate to be the first resident pursing global health research in the American Board of Radiology's (ABR) B. Leonard Holman Research Pathway. The Holman Pathway is a national track for United States radiology and radiation oncology residents that allows additional research time during training for those with a demonstrated interest in and aptitude for a primarily research-focused career.[5] My work has focused on building a breast cancer research collaboration with the University of Zimbabwe, the Parirenyatwa Hospital, and the Harare Central Hospital to study women with breast cancer and their clinical and quality of life outcomes after mastectomy, with a focus on the role of radiation in this setting. Without the support of my residency program, the ABR, and ARRO GHSC, this would not have been possible.

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***Dr. Elmore** is a resident in the Harvard Radiation Oncology Program in Boston, MA, and the American Board of Radiology B. Leonard Holman Research Pathway. She is the incoming co-chair for ARRO's Global Health Subcommittee.*

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While my experience has been unique, the lessons I have learned may be instructive to other residents who hope to pursue global health and to programs hoping to foster an environment that recognizes the potential benefits of global health experiences for their trainees, namely:

1. **Scholarly Inquiry –** Residents can personally learn a great deal from engaging in global health research, while also strengthening ongoing efforts. In many low- and low middle-income country (LLMIC) settings, talented cancer clinicians with research interests are hoping to develop more experience. Yet, there is only a nascent research infrastructure around oncology. This is the case in Zimbabwe. In collaboration with the institutions in Harare, we have been able to design and implement the foundations of a breast cancer research program, building on the efforts of a young clinical oncologist, Dr. Melinda Mushonga, among others. This has included securing funding, setting up technical infrastructure (eg, WiFi), training a research team, and developing electronic data collection protocols. We can now begin asking questions that will matter very directly in the lives of patients. While every resident will not want to pursue long-term research collaborations in LLMICs, many may benefit from supporting existing efforts in more targeted ways.

2. **Quality Improvement –** In LLMIC settings, the needs often outweigh the human or financial resources to fill them. While solutions from any setting cannot be "dropped" into another without careful consideration, collaboration, and adaptation, there is room for humble, enthusiastic residents to support quality improvement (QI) projects in global settings. LLMIC departments could pose QI issues that need novel solutions that then could be supported by HIC resident/faculty pair partners. These experiences would ideally be longitudinal but could be done remotely in large part with punctuated travel of residents/faculty from both programs. In Zimbabwe, we are developing an electronic data capture system to improve multidisciplinary team care in breast cancer and applying for funding for a full pilot. Initiatives like this may provide residents an additional opportunity to engage in QI projects that fulfill the Accreditation Council for Graduate Medical Education (ACGME) requirement.

3. **Health Equity -** This is the cornerstone of my motivation for global health, and I know the same is true for many others. We have tremendous privilege as residents from HICs. This includes our access to the latest treatment innovations, to well-funded library systems featuring the most recent literature, and to faculty with deep expertise in specialized areas. I have been able to share all of this with my collaborators in Zimbabwe. And they have shared with me a rich clinical expertise and a palpable commitment to patients that is borne from having to serve as general oncologists within a context of resource scarcity. I am thankful to have been embedded in the daily practice of health equity: striving for the best health outcomes for even the poorest, most marginalized patients.

There is a great need to expand radiation oncology capacity in LLMICs.[6] As ARRO GHSC has shown, residents are poised to lead our field in global health scholarship, systems strengthening, and equity. I am hopeful that more medical students and residents in the years to come will find that the field of radiation oncology will support their global aspirations, as it has wholeheartedly supported mine.

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SA–CME Information

THE GLOBAL RADIATION ONCOLOGY WORKFORCE IN 2030: ESTIMATING PHYSICIAN TRAINING NEEDS AND PROPOSING SOLUTIONS TO SCALE UP CAPACITY IN LMICS (PAGE 10)

Description

This review examines the capacity gap in RT through the lens of human resource needs. The authors model radiation oncologist training needs, investigate the disparity between HMICs vs LMICs, and explore solutions for training/licensure and regional collaboration.

Learning Objectives

After completing this activity, participants will be able to:

1. Understand differences in training regulations and durations across the globe.
2. Discuss projected needs for radiation oncologists in LMICs and LICs and how these needs may be met.
3. Identify the need for harmonized training resources for global radiation oncology and the potential role for UMICs and HICs in global training.

Authors

Shekinah Nefreteri Cluff Elmore, MD, MPH*, is at Harvard Medical School, Boston.* ***Gregorius Ben Prajogi, MD; Jose Alfredo Polo Rubio, MD; Eduardo Zubizarreta, MD****, are at the International Atomic Energy Agency, Vienna.*

IMPROVING ACCESS TO RADIATION THERAPY IN INDONESIA (PAGE 17)

Description

To date, the exponential rates of population growth and cancer incidence often outpace the linear rate of radiation therapy services growth, especially in developing countries such as Indonesia. This review article summarizes the challenges and the efforts to overcome them.

Learning Objectives

After completing this activity, participants will be able to:

1. Understand challenges and solutions developing countries such as Indonesia face in providing radiation therapy services.
2. Adopt each solution for all countries that have experienced the issues.

Authors

Soehartati Gondhowiardjo, MD, PhD; Sri Mutya Sekarutami, MD, PhD; Angela Giselvania, MD; Steven Octavianus, MD; *and* ***Mr. Muhamad Iqbal Assegab*** *are with the Universitas Indonesia – Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia.*

AUGMENTING CANCER CONTROL EFFORTS IN A LIMITED RESOURCE SETTING BY LEVERAGING INTERNATIONAL COLLABORATIONS IN RADIATION ONCOLOGY (PAGE 22)

Description

Oncologists may not be familiar with the utilization and operation of radiation therapy facilities in limited-resource settings. This article describes innovative international efforts regarding QA, capacity building, and research/training that address unmet RT needs in Ghana.

Learning Objectives

After completing this activity, participants will be able to:

1. Understand the workflow of RT in low-resource settings.
2. Understand adaptations used to meet challenges in low-resource settings.
3. Provide a roadmap for global health collaborations in radiation oncology using Ghana as a thriving model.

Authors

Joel Yarney, MD; Hannah Ayettey Anie, MD; Verna Vanderpuye, MD; Francis Adumata Asamoah, MD; Baffuor Awuah, MD; Samuel Tagoe, PhD; Samuel Denyo, BTech; Pearl Aba Scott, MD; Francis Doughan, MPhil; Kofi Adesi Kyei, PhD; *and* ***Charles Aidoo, HND,*** *are at the National Radiotherapy Oncology and Nuclear Medicine Center, Korle Bu Teaching Hospital, Ghana.* ***Clement Edusa, MD,*** *is at Sweden Ghana Medical Center.* ***Bismark Dwobeng, MD,*** *is at the National Center for Radiotherapy and Nuclear Medicine, Komfo Anokye Teaching Hospital, Ghana.* ***Rebecca Wong, MD,*** *and* ***Horia Vulpe, MD,*** *are at Princess Margaret Hospital, Toronto, Canada.* ***Shivanshu Awasthi, MPH, PharmD; Angelina Fink, MPH; Stuart Wasserman, PhD; Peter Johnstone, MD; Louis Harrison, MD;*** *and* ***Kosj Yamoah, MD, PhD,*** *are at H. Lee Moffitt Cancer Center & Research Institute, University of South Florida, Tampa, FL.*

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SA-CME (see page 9)

The global radiation oncology workforce in 2030: Estimating physician training needs and proposing solutions to scale up capacity in low- and middle-income countries

Shekinah Nefreteri Cluff Elmore, MD, MPH;* Gregorius Ben Prajogi, MD;*
Jose Alfredo Polo Rubio, MD; Eduardo Zubizarreta, MD

Radiation therapy access is insufficient in low- and middle-income countries.[1] As cancer cases are projected to increase in countries of all economic tiers, the need for radiation therapy will continue to expand.[2] Several analyses have focused on radiation therapy equipment needs as inferred by national cancer burdens.[3,4] However, radiation therapy services depend on factors beyond equipment, with factors such as quality and safety management and human resources playing an important role.[5,6] Human resources, and well-trained radiation and clinical oncologists in particular, are essential to ensuring access, efficacy, quality and safety of radiation therapy. This review will explore the capacity gap in radiation therapy through the lens of human resource needs. We will model the current and projected radiation oncologist training needs and investigate the disparity between high-income countries vs low- and middle-income countries. We will then examine existing and novel solutions to radiation oncologist physician training and licensure. We will focus on the critical nature of regional collaboration between countries in different income strata to meet physician training needs for low-income countries.

Methods

Cancer Incidence and Income Groups

The International Agency for Research on Cancer (IARC) recently updated the Global Cancer Incidence, Mortality and Prevalence database (GLOBOCAN), providing revised estimates of cancer incidence and mortality in September 2018.[7] Using the accompanying web-based platform, the Global Cancer Observatory (GCO) cancer burden estimates for the 173 countries analyzed by the Global Task Force on Radiotherapy for Cancer Control (GTF RCC) were obtained for 2018 and 2030.[1,2] The individual country datasets were then grouped according to the World Bank income groups classification for 2017 into high-income (50 countries), upper-middle-income (46 countries), lower-middle-income (47 countries), and low-income (30 countries).[8]

Equipment Needs and Costs

The evidence-based estimation (EBEST) method from the Collaboration for Cancer Outcomes Research and Evaluation (CCORE) was used to calculate the number of radiation therapy courses required in 2018 and 2030 based on the cancer incidence for each income group.[9-11] The required number of investment, machines and staff to deliver these courses was then calculated using the activity-based costing model used by the GTF RCC.[1] Because the EBEST method has the potential to overestimate actual needs if radiation therapy utilization rates are not optimized, we also included a "lower estimate" using published Criterion-Based

*Dr. Elmore is a resident in the Harvard Radiation Oncology Program, Harvard Medical School, Boston, MA, and the American Board of Radiology B. Leonard Homan Research Pathway. She is also the incoming co-chair for the Association of Residents in Radiation Oncology Global Health Subcommittee. Dr. Prajogi, Dr. Rubio and Dr. Zuizarreta are with the International Atomic Energy Agency, Vienna, Austria. *These authors contributed equally to this work.* *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.*

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Number of Radiation Therapy Centers and Machines Registered in DIRAC in 2018, by Income Group

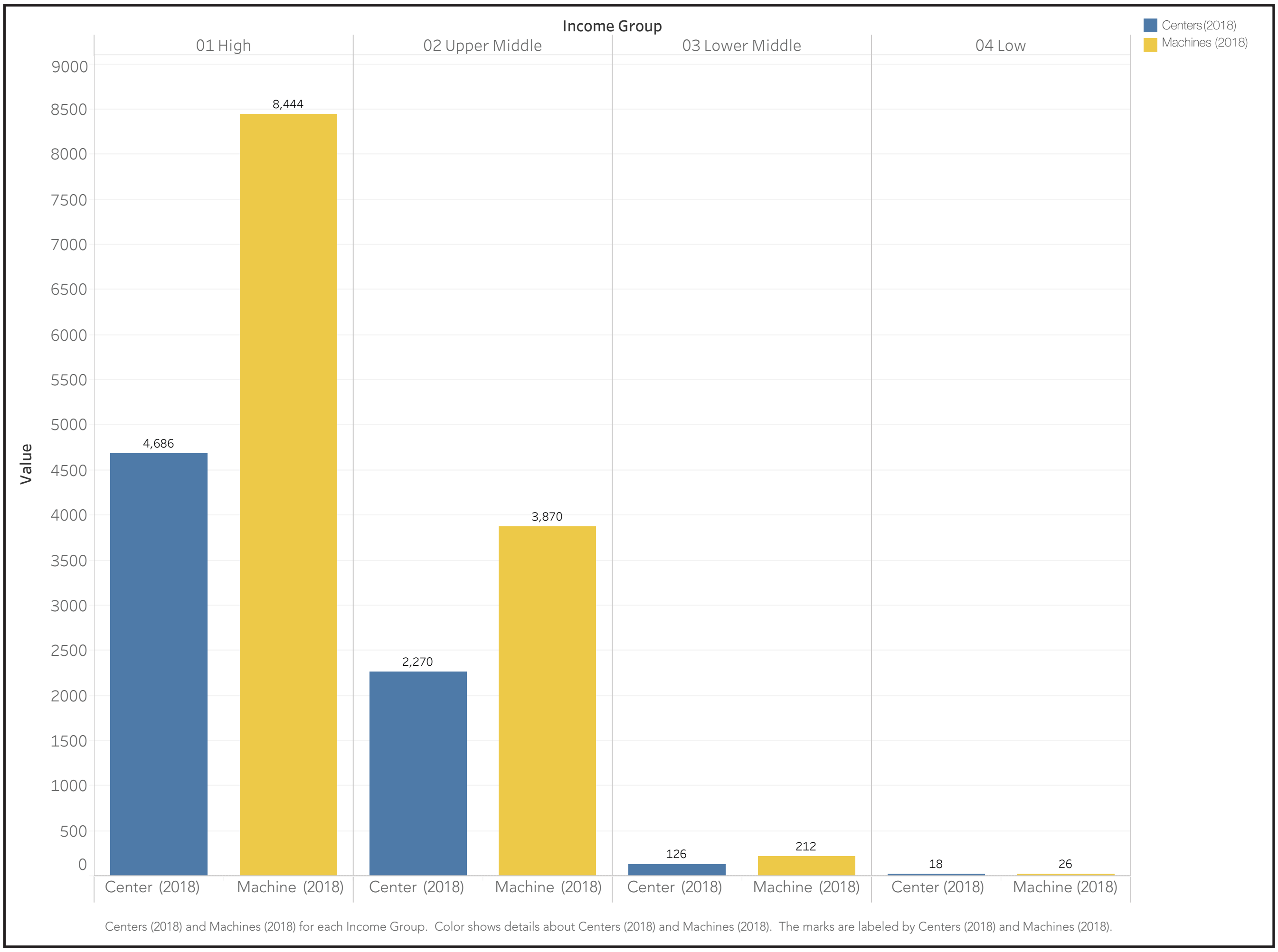

FIGURE 1. *Centers (2018) and machines for each income group. Color shows details about centers (2018) and machines (2018). The marks are labeled by centers (2018) and machines (2018).*

Benchmarking (CBB) estimates of radiation therapy utilization rates within 1 year of diagnosis (RT_{1Y}). We used 26% RT_{1Y} for our "lower estimate" based on recently published Australian data by Barton et al, which was 7% lower than the rate reported by Mackillop et al for Canada.[12,13]

Available Machines, Staffing Level and Training Program Capacity

The number of radiation therapy centers and megavoltage machines in 2018 was obtained from the IAEA Directory of Radiotherapy Centres (DIRAC).[14] Due to the lack of reliable data on the availability of radiation oncologists on a global level, we estimated the number of radiation oncologists needed to deliver optimal radiation therapy services with the number of existing machines for each income group using the approach and assumptions used by the GTF RCC.[1] The number of radiation oncologist full-time equivalents (FTEs) obtained from this calculation was used to represent the current number of practicing radiation oncologist FTEs in 2018. Using the same model, the projected number of radiation therapy courses in 2030 was used to calculate the required number of megavoltage machines and practicing radiation oncologist FTEs for 2030.

Training

There are several recommendations regarding the maximum number of residency positions in a training program. The European Society for Radiation Therapy and Oncology (ESTRO) recommended that the number of residents in a training program should not exceed the number of FTE staff.[15,16] The Accreditation Council for Graduate Medical Education (ACGME) required at least four FTE radiation oncologists at the primary clinical site dedicated to

SA-CME (see page 9)

Estimates of Radiation Oncology Training Capacity by Income Tier and Division of Capacity Sharing

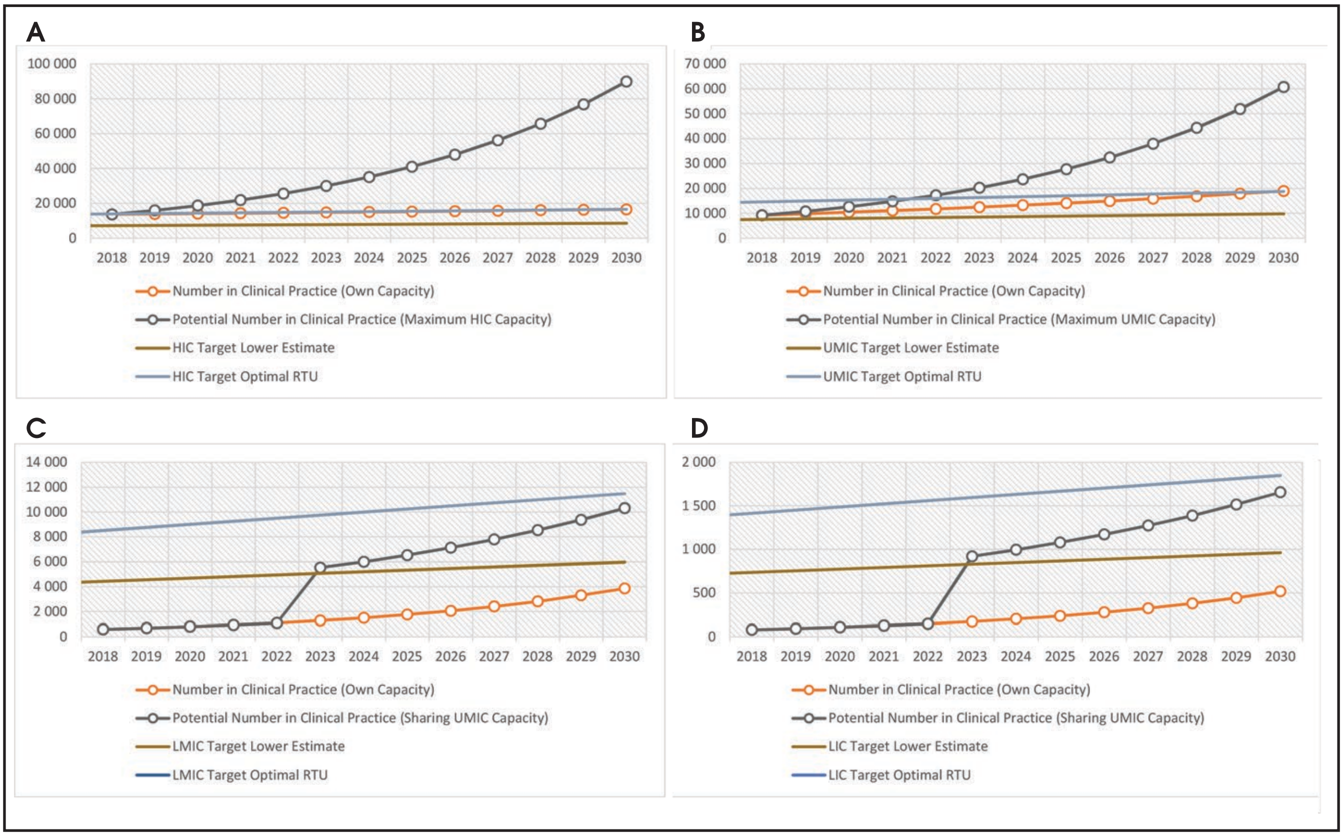

FIGURE 2. *Projected radiation oncologist supply and demand from 2018-2030 for high-income countries (HIC) (A), upper-middle income countries (UMIC) (B), lower-middle-income countries (LMIC) (C), and low-income countries (LIC) (D) under the assumption of 5-year national training programs involving a fixed proportion of practicing radiation oncologists at a ratio of 1 full-time equivalent (FTE) staff per trainee. For high- and upper-middle-income countries, the supply and demand matched when the proportion used ("own capacity") was 23% and 46%, respectively, while for lower-middle- and low-income countries the proportion used ("own capacity") was 100%. Different demand scenarios with "optimal" and "lower estimate" radiation therapy utilization rates (RTUs) were provided.*

teaching activities with at least a 0.67 FTE faculty-to-resident ratio.[17] Both ratios were used to estimate training program capacity based on the number of practicing radiation oncologist FTEs for each income group. The proportion of practicing radiation oncologists involved in training residents was adjusted iteratively until the number available in 2030 matched the projected needs, or 100% involvement was reached (maximum potential capacity).

Most published curricula for radiation oncology residency training required 5 years from entry to certification, with some variation in terms of entry points to the training program following completion of medical school.[18,19] The IAEA Syllabus for the Education and Training of Radiation Oncologists, published in 2009, recommended at least 3 years of residency training.[20] Both scenarios were considered in a sensitivity analysis.

Results

Equipment Needs in 2030

There were 7100 radiation therapy centers worldwide in 2018, 66% of which were in high-income countries (**Figure 1**). The number of megavoltage machines in high-income countries were 8444, and combined with the 3870 megavoltage machines in upper-middle-income countries they constitute 98% of the world's megavoltage machines, leaving the remaining 2% in lower-middle- and low-income countries—212 and 26 machines, respectively.

In 2030, there will be a 21% and 32% increase in the projected cancer incidence in high-income countries and upper-middle-income countries, respectively, compared to 2018. Lower-middle- and low-income countries will see even higher rates of increase of 38% and 34%, respectively. Under the same set of assumptions as in the GTF RCC publication, these increases in cancer incidence will raise the required number of machines in 2030 to 9716 machines in high-income countries, 7872 in upper-middle-income countries, 4134 in low- and middle-income countries, and

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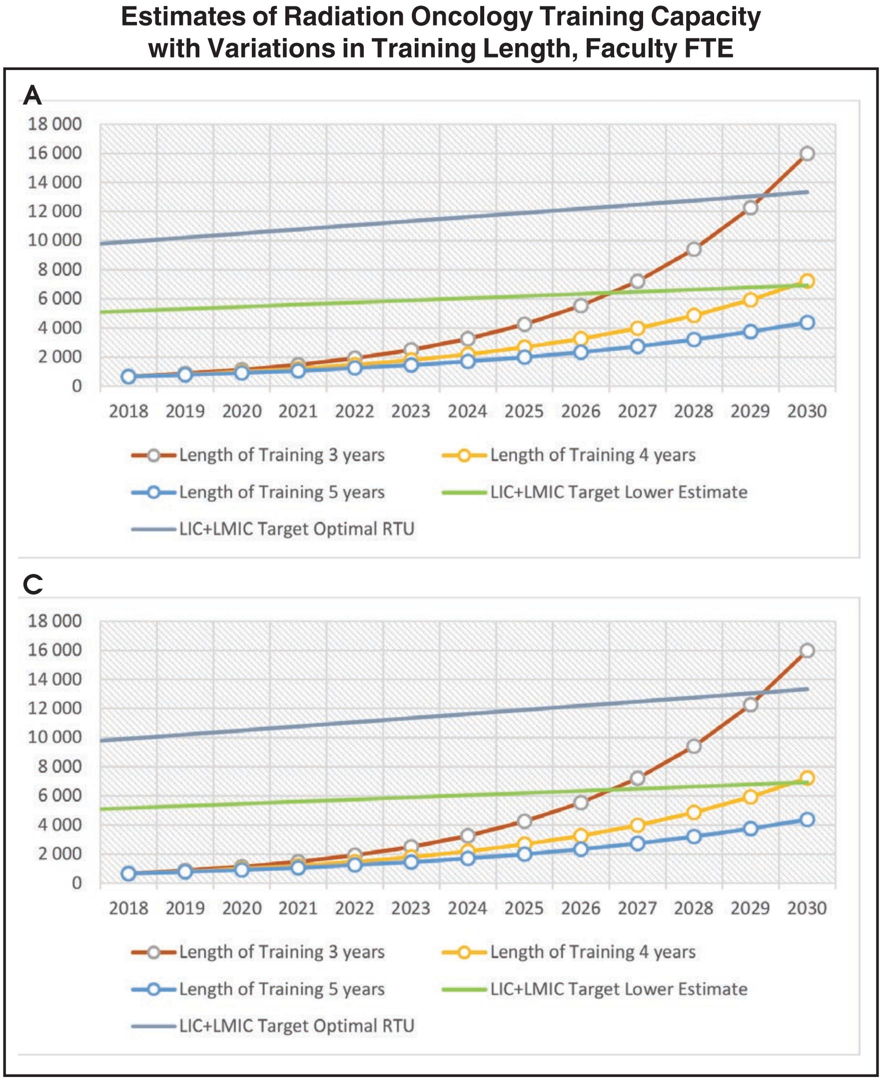

FIGURE 3. *The impact of different durations of training (A) and full-time equivalent (FTE) faculty requirements (B) on projected growth in the supply of radiation oncologists. Different demand scenarios with "optimal" and "lower estimate" radiation therapy utilization rates (RTUs) were provided. Key: LMIC – lower-middle income countries; LIC – low-income countries*

610 in low-income countries, corresponding to a total investment of USD 82.7 billion in capital and USD 31.7 billion in training.

Human Resources Supply and Demand

Assuming there are currently enough radiation oncologists to provide resource-optimized care with the existing number of machines in 2018, we estimated 664 practicing radiation oncologists in lower-middle- and low-income countries. This number needs to grow to 13 322 over the next 12 years to provide optimal radiation therapy access by 2030, assuming enough investment is made in infrastructure. Currently, this would require an increase at the rate of 28% annually without considering any loss from the pool of practicing radiation oncologists including retirement, which, assuming a 30-year interval between training completion and retirement, occurs at a rate of 3% per year.

Even if we assume that every radiation oncology center in low- and low-middle-income countries merge to create one common training program using a 5-year common curriculum, with every practicing radiation oncologist involved as teaching faculty at the recommended ratio of 1 FTE staff per resident (100% involvement), only a net 17% growth could be sustained annually. The deficit of radiation oncologist FTEs remains constant at 8900 despite the increase from 664 in 2018 to 4371 in 2030. (**Figure 2 C,D**)

Reducing the FTE requirement can potentially increase the capacity of training programs to the level required to achieve at least the "lower estimate" of the needs in 2030, and so can reduction in the length of training. Shortening the training duration to 4 years enables the projected number to reach the "lower estimate" number of radiation oncologists, while reducing it further to 3 years or using a staff/resident ratio of 2:3 (0.67 FTE staff per resident) both dramatically boost capacity. (**Figure 3**)

A significant proportion of the radiation oncology workforce FTEs in upper-middle-income countries will need to be involved as teaching faculty to provide enough capacity for training programs to increase practicing radiation oncologists from an estimated 9228 in 2018 to 18 797 in 2030. Assuming the same 5-year curriculum and FTE requirement for residency training, 46% of practicing radiation oncologists in upper-middle-income countries would need to be involved in residency training (**Figure 2B**). Assuming the "excess" capacity of 54% is utilized to train radiation oncologists for low- and low-middle-income countries, it appears possible to reach the "lower estimate" number of radiation oncologists in low- and low-middle-income countries although the total number still falls short of the needs estimated by optimal RTUs (**Figure 2C,D**).

High-income countries, on the other hand, would be more concerned about fine-tuning program requirements to

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prevent oversupply of radiation oncologists, because only a small proportion (23%) of practicing radiation oncologist FTEs need to be involved in a residency program to increase practicing radiation oncologists from 13 665 in 2018 to 16 575 in 2030 (**Figure 2A**).

Cost Considerations

The estimated training costs of such an endeavor at scale are quite significant. The GTF RCC estimated full training costs per trainee of USD 550 000 for high-income countries and USD 100 000 for upper-middle, low-middle, and low-income countries.[1] With the training costs in high-income countries more than 5 times as expensive, there is a strong cost/logistics rationale for prioritizing training support from upper-middle-income countries. However, if only upper-middle income countries were involved in training support, there would still be a shortage of an estimated 1361 radiation oncologists by 2030, assuming optimal utilization rates.

Discussion

Scaling Up Training in Low- and Low-Middle-Income Countries

We found that even when we used optimistic assumptions on a simple model, grossly overestimating the growth of radiation oncologist supply, it was still extremely difficult for low- and low-middle-income countries to train enough professionals to keep up with the optimal infrastructure investment needed by 2030. The training capacity in these countries would limit the potential rate of growth in radiation therapy access to no more than 17% annually, regardless of investments in infrastructure. In reality, the number that could be trained would be much lower because in most countries only practicing radiation oncologists working in the few accredited radiation oncology programs would be involved in training residents. High-income countries, on the other hand, tend to have a higher capacity than expected demand, necessitating in some cases regulation to avoid oversupply.[21] This is not true for all high-income countries, however, with countries such as the UK facing a shortage of clinical oncologists that is expected to worsen in the next 5 years unless training capacity doubles and work conditions improve.[22] Canada has also noted an incremental increase in supply of radiation oncologists with rising caseloads, potentially suggesting an increased training need.[23]

Unless drastic changes are implemented, it is likely that the radiation oncologist deficit will continue to widen if lower-middle- and low-income countries are tasked with training their own radiation oncologists. Compromises in length of training or FTE requirements could potentially accelerate the growth, but these will have to be carefully planned to avoid a negative impact on quality and safety. High- and upper-middle-income countries can potentially help offset the low supply in lower-middle- and low-income countries, and such efforts are ongoing on a small scale, with residency programs hosting a few international trainees per year. However, mobilizing and financing the residency training at scale would be a significant undertaking. Besides the costs and logistics involved, there is a potential risk of migration that could further exacerbate the capacity mismatch between lower- and higher-income nations. Regional collaborations would need to be established so that excess capacity from upper-middle- and high-income countries can be optimally utilized by their neighboring low- and low-middle-income countries to the maximum possible extent while keeping the risk of loss due to migration to a minimum.

Harmonization

For the collaboration to succeed, mutual understanding and shared vision will be necessary. Many components of the residency training curriculum will need to be harmonized to establish the degree of expertise required for a concerted regional or global effort in training future radiation oncologists.

The IAEA recognized the need for harmonization and prepared a syllabus to guide managers and directors of radiation oncology training programs in establishing or upgrading a training program for radiation oncologists.[20] The syllabus, published in 2010 and endorsed by major professional societies, was designed to be implementable within the various limitations in available resources while maintaining a high educational standard. Considering that more than 10 years have passed since it was drafted, however, the syllabus will need to be updated to keep up with recent developments and best practices in the field of radiation oncology, incorporating best practices in postgraduate medical education while remaining resource-aware and system-neutral. Of particular interest would be the potential for a modular, flexible-length training program incorporating a competency-based curriculum, which would enable training duration to be adjusted to the level of needs. The ACGME has begun to pilot such a system in several residency training programs, although radiation oncology is not among these.[24]

The existence of a harmonized curriculum can potentially facilitate the mobility of trainees and teaching staff, allowing expertise to flow freely within the region but at the same time increasing the possibility of permanent emigration. In a recent survey conducted by ESTRO, 77% of trainees expressed some interest in working in a different country than where they were trained.[15] Similarly, in 2016, the World Bank recognized that higher education was an important avenue for facilitating the emigration of high-skilled workers.[25]

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Left to the market mechanism of supply and demand, emigration can worsen the disparity between low- and high-income countries in access to trained radiation oncologists. A control and incentive mechanisms would be needed to prevent outflow of skills and expertise from lower-middle- and low-income countries. In other specialty training programs, this has included a minimum service commitment to the physician's country or region of origin.[26,27] Alternatively, incentives have been provided in areas that may be less sought after to recruit and retain qualified health practitioners.[28] However, despite the disadvantages of migration, accreditation standards must be shared or mutually recognized across training regions or partnerships.

International Collaborations

When properly coordinated and maintained, shared learning resources will allow efficient use of available resources by reducing the teaching workload of faculty in training programs, allowing more time for clinical supervision. These resources, when mutually recognized and standardized, will also help establish a common baseline prerequisite for training programs across the region, accommodating resident training in different countries as discussed above.

The IAEA has developed a distance learning course to supplement the education and training in programs with limited access to expertise. The Applied Sciences of Oncology distance learning course currently covers 80 modules and has been updated several times since its first release in downloadable CD-ROM format in 2004.[29] The modules covered include a wide range of topics from functional anatomy to burnout and coping with patient death and dying. The modules have been downloaded more than 1100 times in the first year after they were launched and are now available as courses in the IAEA's open e-learning platform.[30]

When more such resources are available, officially recognized, and continuously maintained, they will be valuable resources to support curriculum harmonization. Such resources will provide a common basic standard for the prior learning done by a foreign candidate. This allows training programs to use such distance learning resources as prerequisites before accepting foreign trainees. This could potentially shorten training time away from the country of origin and reduce overall training cost.

To further improve harmonization and reduce the need for trainees to train abroad, an online learning environment can be developed. This online platform will allow trainees, staffs and programs from different countries in the region to interact, share expertise and collaborate, forming a virtual "regional training program." One example is the e-learning platform for Advanced Medical Physics Learning Environment (AMPLE), which was designed and piloted under a Regional Technical Cooperation project in Asia Pacific to support training programs in implementing the IAEA syllabus and guidance documents for the education and training of medical physicists. The platform, based on Moodle and hosted on the IAEA e-learning site, provided a centralized electronic record of training and assessment, linked sub-modules with learning resources, and promoted communication and collaboration through online communication tools. A particularly encouraging observation from the pilot project was that AMPLE enabled medical physicists from one country to assist in the supervision of trainees in neighboring countries, allowing a regional sharing of teaching workload and expertise.[31] Work is now underway to develop similar online platforms for the education and training of radiation oncologists (Advanced Radiation Oncology Learning Environment, AROLE) and Radiation Therapy Technologists (Advanced Radiation therapy Technology Learning Environment, ARTTLE). Additional tools such as discussion forums, online journal clubs, and shared repositories would further encourage collaboration.

Limitations

The EBEST method we used in this analysis allowed us to estimate the future needs in radiation therapy equipment and radiation oncologists. However, this method has the potential to overestimate the actual demands, risking excess capacity.[12] Unfortunately, it is currently the best method we have to estimate the need in lower-middle- and low-income countries where data is limited and access to radiation therapy is inadequate. The "lower estimate" based on 26% RTUs that we used in this analysis is included to provide a safety margin to avoid gross overestimation. The number is also very close to the median actual radiation therapy utilization rate (aRTU) of 28% in a recently published survey of nine middle-income countries.[32] Most of the strategies we describe in this article assume that although the optimal number is beyond reach, this "lower estimate" is reasonably achievable.

Conclusions

While the cost and complexity of radiation therapy machine infrastructure has been well-documented, our analysis shows that radiation oncologist training will be equally important to ensuring access to radiation therapy. A significant deficit in trained radiation oncologists in lower-middle- and low-income countries will likely persist and widen in 2030 unless alternative strategies are pursued. Upper-middle and high-income countries may have a substantial role in training the global radiation oncology workforce. Systematic, scalable, and mutually supported training and accreditation strategies are needed. Collaborative, e-learning platforms in combination with traditional, apprenticeship-based, in-person training are required to maximize

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learning efficiency and minimize costs. Additionally, strategies to optimize migration and incentivize trainees to practice in lower-middle- and low-income countries are needed. Finally, while this analysis focused on radiation oncologists, multidisciplinary training for medical physicists, radiation therapy technologists, and radiation oncology nurses will be essential to realize global access to radiation therapy.

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Improving access to radiation therapy in Indonesia

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Cancer burden is steadily rising globally. For countries in the developing world where most of the global population lives and where most new cancer cases are expected to be diagnosed every year, this is particularly worrying as the exponential rates of population growth and cancer incidence often outpace the linear growth rate of radiation therapy services. The annual cancer incidence in low- and middle-income countries (LMIC) in 2030 is estimated to exceed 14 million new cases per year,[1] a 34% increase over the incidence in 2018.[2]

In Indonesia, 206 megavoltage (MV) machines would have been needed to achieve a 1 MV machine per million population for its 206 million population in 2008, or 176 new machines on top of the 30 machines operational at that time.[3] However, the Indonesian population grew by an additional 60 million by 2018,[4] raising the target goal to 266. Despite nearly doubling the ratio of MV machines per million population from 0.14 to 0.25 through a net increase of 36 machines in 10 years, the deficit of machines barely changed compared to what Indonesia had in 2004. In fact, had the recent burst of radiation therapy investments not occurred between 2012 and 2018, Indonesia would have been in a worse state than it was in 2004 (**Figure 1**).

When evidence-based estimates of optimal radiation therapy utilization rate (RTU) are used to calculate radiation therapy needs for Indonesia, the situation appears even less hopeful. With 348 809 new cancer cases in 2018 and an optimal RTU of 54.3%, 379 MV machines would have been needed, assuming a workload of 500 new patients per machine annually.[2,5] This number would need to grow to 517 to provide optimal access to the 475 502 new cancer patients expected to be diagnosed annually by 2030.[1]

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Whether it is possible or even necessary to achieve this target is up for discussion. However, it has been reported that optimal utilization depends on factors beyond equipment availability and that optimal RTU might even overestimate actual radition therapy need.[6] Consequently, the Indonesian Radiation Oncology Society (IROS) has opted for a progressive target in its advocacy efforts, aiming for 150 MV machines by 2030 (0.5 MV machines per million population) to account for the growth of public awareness and cancer control in general.

Investing in Radiation Therapy

Just like other major economies in Southeast Asia, Indonesia has enjoyed a stable political climate and high rate of economic growth from 1980-1995.[7] In 1982, ahead of other countries in Southeast Asia, Indonesia installed its first linear accelerators and, in the decade that followed, opened several new radiation therapy centers including a national cancer hospital. However, in the absence of a cancer control plan, Indonesia was unable to sustain its growth in radiation therapy access in the decade that followed due to the increasingly low priority given to cancer control. By

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the time a major economic crisis hit the region in 1998, Indonesia had less than 20 radiation therapy centers serving its population of 200 million, and radiation therapy was already low on the list of priorities for healthcare investment.

In 2004, to end an extended period of zero growth in radiation therapy services, IROS began directing its main advocacy efforts on increasing public and government awareness of the important role of radiation therapy in cancer care. These efforts started to gain significant traction several years later, after the Indonesian Ministry of Health adopted the 25-year roadmap prepared by the society. The resulting steady investment commitment from the government enabled Indonesia to not only increase the number of machines but also provide radiation therapy services in more provinces. The development came in parallel with improved cancer control in general, following the recommendations from the integrated mission of the Programme of Action for Cancer Therapy (imPACT) in 2010. The mission, coordinated by the International Atomic Energy Agency (IAEA) and conducted with the World Health Organization (WHO) and International Agency for Research on Cancer (IARC), provided the government with a baseline situation analysis and recommendations to prepare and implement a National Cancer Control Plan (NCCP). At the same time, most radiation therapy centers in the country started undergoing a transition from 2-dimensional (2D) to 3-dimensional (3D) conformal radiation therapy techniques. It was also then that the increased number of linear accelerators began outpacing telecobalt machines.

In 2012, the society expanded its advocacy efforts to begin three major initiatives. The first advocacy effort was aimed at the National Public Procurement Agency for the inclusion of radiation therapy equipment in the government e-procurement system with the hope that the more efficient and transparent nature of e-procurement would encourage hospital administrators and policymakers to consider investing in radiation therapy. This effort proved especially helpful, as evidenced by e-procurement constituting 58.3% of new radiation therapy machines in the government sector during the past 4 years.

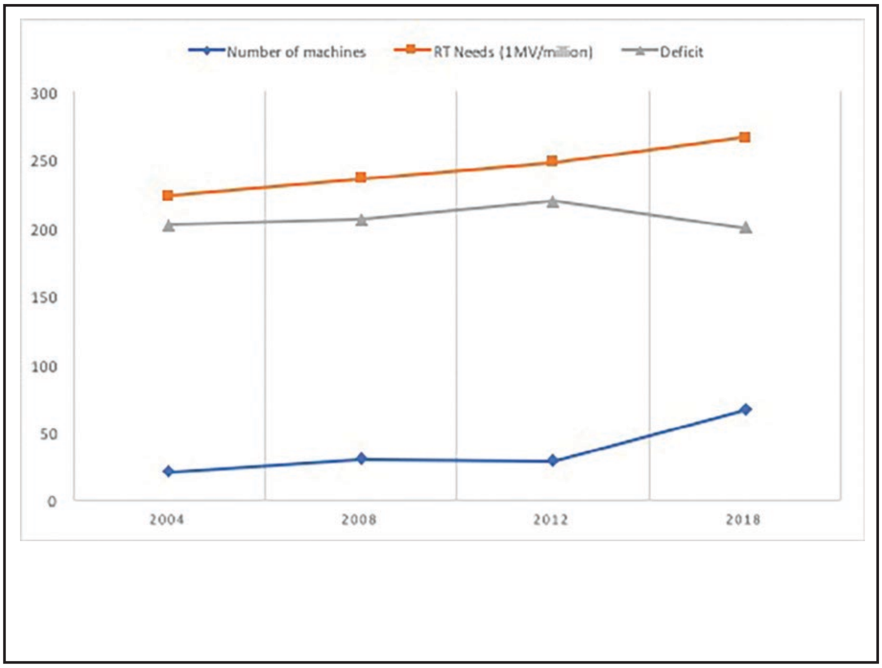

FIGURE 1. Radiation therapy supply and demand, taking population growth into consideration (data from Indonesian Society of Radiation Oncology annual surveys).

A second set of advocacy efforts was aimed at the private sector. In contrast to several countries in the region where private sector providers played a major role in the provision of radiation therapy services, all but two radiation therapy centers in Indonesia were government owned in 2012. To assist new centers, the IROS provided consultancy services at no cost to help in needs assessment, planning, commissioning and training. Public-private partnerships were also initiated and have been gaining interest ever since. The society further supported these efforts by developing tools for implementing a public-private partnership program. In 2019, the number of private hospitals providing radiation therapy services or setting up a radiation therapy program increased to 23, providing 40% of the total national radiation therapy capacity.

The third set of advocacy efforts was on ensuring the inclusion of radiation therapy in the Indonesian Universal Health Coverage scheme. This effort brought about a major increase in radiation therapy utilization, but at the same time caused significant prolongation in radiation therapy waiting time all over the country in 2014. The resulting media coverage caught the attention of provincial governments and hospital administrators, prompting them to establish new radiation therapy services. By 2019, the proportion of radiation therapy centers with more than 1 month of waiting time decreased from 66.67% in 2017 to 30% in 2019 through the addition of 27 new MV machines nationwide.

To ensure sustainable growth in radiation therapy services, a business model must account for capital and operational expenditure, including depreciation. Even for state-owned institutions willing to operate at costs exceeding their revenues, government subsidies are

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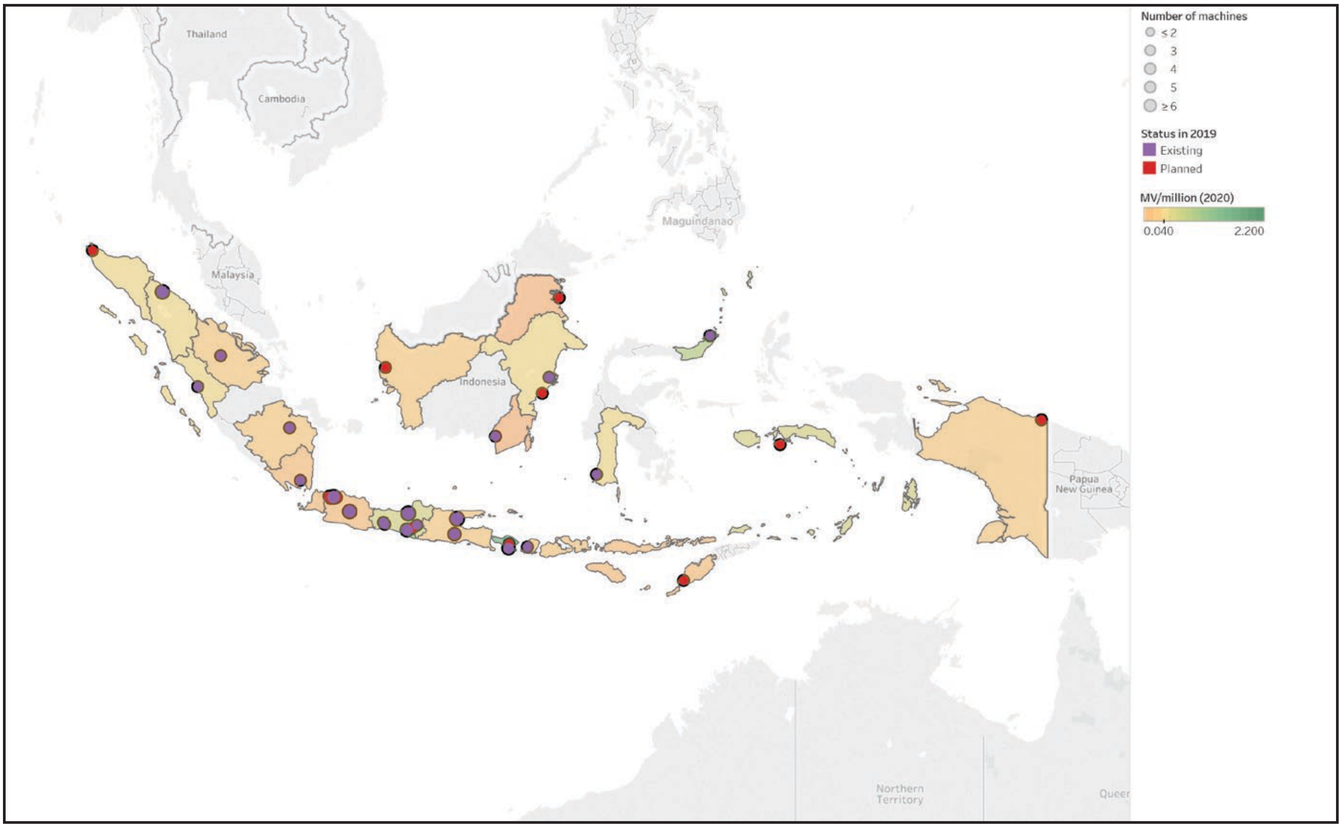

FIGURE 2. *Current radiation therapy status in Indonesia*

not unlimited. In fact, the Indonesian Universal Health Coverage System has encountered several cashflow problems over the past few years and has been continuously trying to optimize expenditures by tightening reimbursement policies for various medical procedures. As a consequence, radiation therapy services in Indonesia are continuously straddling a thin line between affordability and sustainability.

Reducing capital expenditure goes a long way toward accelerating the growth of radiation therapy services, and can be achieved through bulk purchasing. In a recent report, Moraes et al[8] described the experience with the Brazilian RT Expansion Project (EXPANDE), notably how it included the bulk procurement of 140 linear accelerators supporting 15 national federations at a significantly lower total cost than expected from individual procurements. This approach is under consideration by the Indonesian Ministry of Health but will require extensive planning and risk management considering the substantial investment required. The current expansion plan is still focused on ensuring availability of radiation therapy in all provinces (**Figure 2**).

Education and Training

A safe and effective radiation therapy program requires qualified, trained professionals. Therefore, it is important to align the growth of human resources and equipment to ensure enough qualified radiation therapy professionals are available to provide services once machines are installed and commissioned. Unfortunately for Indonesia, this was much harder than it sounded. Achieving a proportional rate of growth between human resources and equipment has required consideration of various factors and often necessitated compromises.

Until 2004, the slow rate of human resources growth had been another factor in addition to lack of government awareness in halting growth in radiation therapy services. This was substantiated by findings during a Quality Assurance Team in Radiation Oncology (QUATRO) audit by the IAEA in 2006. Several factors contributed to the slow rate of human resources growth, including long training periods, a short interval between starting practice and entering retirement, lack of interest in the specialty, and lack of recognition. Most of these factors were related to radiation oncology training being a 2- to 3-year fellowship program for consultant radiologists. Trainees entered the program after 10-15 years of clinical practice in diagnostic radiology at a rate of 1 new trainee per year, and held dual certifications of radiology and radiation oncology upon completion. This format resulted in slow growth of new radiation oncologists,

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barely keeping pace with those exiting clinical practice.

In 2008, a radiation oncology residency program was launched at the University of Indonesia. The entry point for radiation oncology training was shifted to an earlier point, and a curriculum revision was based on an IAEA syllabus.[9] The Indonesian College of Radiation Oncology was founded, and radiation oncology training transitioned from a consultant fellowship to residency training, doubling expected retention by allowing new radiation oncology trainees to enter the profession at a maximum age of 35 years vs 45 years with the previous plan.

Collaborations of the South East Asian Radiation Oncology Group (SEAROG) with the European Society for Therapeutic Radiology and Oncology (ESTRO) started at this time with the first of the SEAROG/ESTRO course series organized in 2009 in Manila, Philippines, providing access to affordable, high-quality educational events for trainees. Compromises, however, were needed. The shift from being a subspecialty discipline to a primary specialty affected the recognition and career path of existing radiation oncologists. Existing IROS members had to choose between letting go of either their radiology or radiation oncology practice as it was not feasible to practice multiple specialty disciplines under the Indonesian Medical Council regulations. Between 2008-2010, IROS membership declined as several members chose their radiology practice instead of radiation oncology. However, this brief drop was soon offset by the increased number of new radiation oncologists entering clinical practice, at a rate of 6-8 per year.

Another compromise was in programmatic standards compliance. To support a rapid growth of radiation therapy services along with technological transition from 2D to 3D conformal and intensity-modulated radiation therapy, the capacity of the only training program in Indonesia needed adjusting several times over the last decade. Instead of the ratio of 1-2 staff members per resident as is common in affluent countries,[10,11] the Indonesian College of Radiation Oncology had to allow the program to train 3-4 residents per staff members instead. Tutorials and lectures outside of office hours as well as distance- and blended-learning initiatives were needed to compensate for this. The IAEA's Distance Learning Course on Applied Sciences of Oncology (ASO)[12] had been helpful in ensuring trainees receive a good foundation for their training within the limited availability of resources. Despite all that, the residency program was barely able to meet the needs of new and expanding radiation oncology centers all over the country even with the expanded capacity. In 2019, Indonesia had only 93 board-certified radiation oncologists and 65 residents in training. Indeed, it was impossible for a single center to train radiation oncologists for the whole country with a 260 million population, but the way residency education was structured as a master's program within the national public education system made it challenging to develop additional residency training programs despite calls from several medical specialty colleges to shift toward hospital-based residency training. This is worrying considering that just to cover the 2018 deficit of 200 machines by 2030, 300 new radiation oncologists would need to be trained in that period.

As a stopgap solution around this limitation, elective rotations to affiliate hospitals have been introduced, allowing residents to gain more experience with a wider variety of clinical cases and practice settings while allowing staffs in affiliate hospitals to gain experience in organizing training for residents. The hope with this plan is that more practicing radiation oncologists could contribute toward education and training, and more residency programs would open in the future. IROS believes that an exponential growth in the number of radiation oncologists is only possible when a fixed proportion vs a fixed number of practicing radiation oncologists are involved in residency education. This means having as many good quality residency training centers as possible.

At a similar pace with radiation oncology, medical physics education and training also underwent a rapid transformation. Within the last decade, Indonesia saw the recognition of the medical physics profession in 2014 and the establishment of the first medical physics residency training program with the support of the IAEA.[13] In 2019, two radiation therapy centers were part of an integrated national medical physics program with an additional three centers in the pipeline.

Unfortunately, the education and training of radiation therapy technologists (RTTs) had been lagging compared with the other two professions. The lack of career development and professional/academic recognition means that it is not uncommon for RTTs to switch careers to medical physics despite the availability of a graduate diploma program. Even in 2019, most RTTs working in radiation therapy centers entered the profession after completing a basic diploma program in radiography followed by brief on-the-job programs organized by the centers where they work.

While the possibility of novel technology in the future such as artificial intelligence will not completely replace the function of professional medical staff, it may help reduce human resource workloads. In particular, it may benefit the radiation oncologist to have more time with patients and help MPs reduce treatment planning time, hence increasing patient throughput.[14] However, it remains to be seen whether this would impact staff requirements.

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Discussion

At several points in the past, Indonesia encountered opportunities to improve radiation therapy access, but was unable to translate them into a sustainable growth due to the lack of a well-defined target. It was only after defining indicators that the IROS maintained proper advocacy efforts supported by clear action plans. However, due to the continuously rising cancer incidence, it is important to periodically evaluate the projections of needs to make adjustments accordingly.

In the case of Indonesia, significant investment would be necessary just to maintain the current level of access to radiation therapy, which becomes even more substantial when considering machine lifetime. In fact, machine lifetime silently but progressively threatens the sustainability of radiation therapy services, as machines (or sources) installed today need replacing in 10-15 years, with budgets determined in advance. Failure to account for these factors can seriously threaten the sustainability of national radiation therapy services, especially in developing countries such as Indonesia where various developmental goals compete for priority in the government budget. Close collaboration between national professional societies, health authorities and private healthcare providers is very important as it provides opportunities to develop and utilize innovative and out-of-the-box strategies to promote and sustain investment in cancer care.

In addition to capital investments, education of radiation therapy professionals is a key area that determines the growth rate of radiation therapy access. Planning for future staffing should take into account the expected growth in radiation therapy utilization to tightly maintain a balance between supply and demand. Experiences in developed countries have shown us that maintaining this balance is challenging even with proper planning.[15,16]

Conclusion

The Indonesian experience of expanding its radiation therapy services has demonstrated the challenges in achieving sustainable access to radiation therapy services. Learning from experience and adapting to challenges has enabled Indonesia to stay on its path toward better access to radiation therapy.

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Augmenting cancer control efforts in a limited resource setting by leveraging international collaborations in radiation oncology

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Cancer remains an important cause of morbidity and mortality globally with incidences projected to rise in the coming decade. Nearly two-thirds of these new cases are anticipated to be recorded in low- and middle-income countries (LMICs) such as Ghana, where infectious diseases remain a major public health challenge.[1,2] More than 70% of cancer patients in low-income countries are expected to die from their disease compared to about 30% in Western countries.[3]

It is estimated that about half of cancer patients would require radiation therapy (RT) as part of their care.[4] In under-resourced environments where screening and early detection programs are almost nonexistent and a large proportion of patients present with advanced disease, optimum RT utilization to improve local disease control and to palliate cancer-related distressing symptoms is estimated to be high.[5] However, the availability of these services is far less than desirable in these LMICs.[5,6] RT is estimated to contribute about 40% toward the curative treatment of cancer,[7] and accounts for only 5% of the total cost of care in Sweden.[8] The unavailability of radiation treatment, therefore, becomes a universal health coverage issue of equity, quality and financial risk for most LMICs.

In this review, we describe the current status of RT in Ghana, West Africa, and explore innovative international collaborative efforts aimed at addressing unmet needs and improving radiation treatment for patients.

Patients

Approximately 3500 new adult and pediatric patients are seen annually at the 3 RT centers in Ghana.[9] The Radiotherapy Centre at Korle Bu Teaching Hospital (KBTH), for instance, sees approximately 1600 patients per year, and the 5 most common cancers seen are breast (27.7%), prostate (11.9%), cervix (8.3%), bone marrow (4.3%), sarcoma (38%) and lung (3.5%), according to current institutional records. Optimum and actual RT utilization for Ghana are 51% and 9%, respectively.[9] Several reasons may attribute to this low patronage, including paradigm-to-disease causation, complementary and alternative medicine use,[10]

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FIGURE 1. *Distribution of radiation therapy centers in Ghana.*

Table1. Installed Radiation Therapy Capacity in Ghana

	Pre 2012			Post 2012		
	KBTH	KATH	SGMC	KBTH	KATH	SGMC
External Beam Teletherapy Unit	1	1	-	2	2	1
Linear accelerator	-	-	-	1	1	1
Cobalt-60	1	1	-	1	1	-
Operational units	1	1	-	2	1	1
Brachytherapy Unit	1	1	-	1	1	1
Low dose rate unit	1	1	-	-	1	-
High dose rate unit	-	-	-	1	-	1
Operational units	1	1	-	1	1	1

number of megavoltage machines per million people and their distribution (**Figure 1**), health literacy and financing.

Equipment/Services

Ghana has made modest gains in improving access to RT services in recent years (**Table 1**). The nation has 3 RT centers, 2 of which are public, and the third private (a joint Sweden-Ghana partnership). Two of the facilities are in Accra—the KBTH and Sweden Ghana Medical Center (SGMC)—and the third is in the Komfo Anokye Teaching Hospital (KATH), Kumasi. The establishment of SGMC has been an excellent addition to the repertoire of treatment options. There are currently 3 modern cobalt-60 teletherapy machines at the 2 government-owned centers (KATH and KBTH), and 3 linacs in the country (5 megavoltage units in total). These consist of a 6-MV and 15-MV linac with electron therapy at SGMC, a newly commissioned 6-MV linac with intensity-modulated radiation therapy (IMRT) and volumetric-modulated arc therapy (VMAT) in Korle Bu, and a dual-photon energy linac (6 and 15 MV with electrons) in Kumasi yet to be commissioned. By international standards, Ghana requires 22 MV machines for its 30 million inhabitants for full access, 12 hours a day.[11]

Cobalt-60 is utilized for cervical high dose rate (HDR) brachytherapy since it is more cost effective, requiring a less frequent source change. The 2 cobalt external-beam radiation therapy machines have proven useful in the past 20 years—indeed several patients have been cured on the cobalt.[12,13] It is a relatively simple machine compared to the linear accelerator and, therefore, has simple quality control and assurance protocols, and by extension requires less sophisticated expertise to keep running. It is also relatively cheap. Source change protocols may, however, be challenging, as is the dosimetry for deep-seated tumors and very superficial tumors in the absence of VMAT and electrons.

Radioiodine treatment for thyroid cancer is available at the National Radiotherapy Oncology and Nuclear Medicine Center (NCRONM). NCRONM also performs prostate brachytherapy using iodine-125 low dose rate (LDR) brachytherapy. The isotopes are ordered as required. The LDR prostate brachytherapy program has been made possible through collaborative work between KBTH and Bard Medical (Covington, Georgia).[14]

Radiotherapy Workforce in Ghana

Ghana has training programs for all cadre of staff required for radiation therapy delivery including oncologists, medical physicists, radiation therapy technologists (RTTs) and biomedical engineers. Currently, there are 12 oncologists and 10 residents in training, 13 physicists, 27 RTTs, 7 engineers, and 59 nurses. These mainline staff work together to serve patients referred to the oncology centers.

Oncologists. Doctors specializing in oncology in most African countries function as both radiation and medical oncologists (clinical oncologists) and, therefore, receive appropriate training for this. In Ghana, oncologists are trained at the Ghana College of Physicians and Surgeons. The training program is in 2 phases—the initial membership phase is a 4-year program followed by a 2-year fellowship, culminating in the award of fellow of the college. To maximize efficiency in patient care as well as personnel expertise, clinics are run based on disease sites on specific days of the week. The NRONMC often experiences heavy clinical workload, which includes extended consulting hours, brachytherapy procedures, patient simulation, tumor volume delineation and treatment planning. More recently, the introduction of a patient appointment system has streamlined patient scheduling.

Medical physicists. Medical physicists play a vital role in the entire process of planning and execution of

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radiation treatment within a radiation facility. Training of medical physicists in Ghana entails a 2-year master of science degree and 2-year internship with the School of Nuclear and Allied Sciences, University of Ghana. A prerequisite for admission into the program is a bachelor of science degree in physics. All of the medical physicists have a master of science degree and 1 recently completed a PhD program. The physicists also function as dosimetrists and execute both roles favorably and are involved in regular quality assurance and quality control procedures. They are actively involved in acceptance testing and commissioning of new RT equipment with acquisition of beam data, as was done when the new linacs were commissioned. The dosimetry was validated by medical physicists from the equipment vendors. Physicists participate in brachytherapy planning (cervical and prostate) in conjunction with physicians, and coordinate and monitor the use of radioiodine therapy. The physicists calibrate suitable scanners outside the hospital to acquire DICOM images for treatment planning, and an in-house computed tomography (CT) scanner is under installation. Of note, another pivotal role of the physicists is collaborating with external manufacturing engineers to report machine malfunctioning and assist in diagnosis and repair of minor faults on the machines.

Radiation Therapy Technologists. RTTs constitute an essential workforce in any RT facility. A 4-year training program with a 1-year internship under the Department of Radiography, School of Biomedical and Allied Health Science, College of Health Sciences at the University of Ghana is available for training RTTs. RTTs treat patients, perform treatment verification, conduct 2-Dimensional (2D) simulation, and provide final simulation after 3-dimensional (3D) treatment planning, as well as molding of custom-made blocks for treatment on the cobalt unit. RTTs also accompany patients who are due for 3D treatment planning to CT facilities outside the hospital to have their scans done according to RT specification with a flat-panel insert into the couch. The newly acquired linear accelerators have multileaf collimators, obviating the use of Cerrobend blocks. RTTs run 2 shifts daily at NCRONM to ensure respectable waiting times.

Biomedical engineers. Biomedical engineers play a significant role in keeping imaging and treatment machines functioning optimally. In NRONMC there are 4 trained engineers: 2 with a 4-year bachelor of engineering degree and the others with a higher national diploma who handle most problems on the RT machines. Equipment manufacturing companies provide backup support for the linear accelerator in conjunction with the on-site engineers and physicists. Warranty issues require engineers from equipment vendors to address certain problems, and there is room for improvement regarding response time.

Nursing. Alongside doctors, specially trained oncology nurses at the NRONMC and the other centers in the country are directly involved in patient management regarding administration of systemic therapy and RT-related nursing services. A significant number of patients receive concurrent or sequential chemotherapy and occasionally targeted therapy. The importance of coordinating chemotherapy administration and RT cannot be overemphasized. Our nurses continually play a vital role in this regard even though they are tasked with the care of large numbers of patients requiring chemotherapy. Furthermore, they take on the additional responsibility of optimally scheduling patients on the treatment machine who are receiving concurrent chemotherapy. Nurse navigation has been introduced over the last few years to ensure the optimal care of patients through treatment and proper handling of any concerns that may arise. With the graduation of the first batch of 3 oncology nurse specialists/practitioners from the Ghana College of Nurses and Midwives last year after a 3-year training program, and ongoing training of more nurses in this specialized capacity, it is believed that patient care will dramatically improve in the ensuing years.

Quality Assurance

These limitations have not impeded progress in ensuring a relatively smooth workflow in the radiation centers in Ghana. The challenges are often mitigated by the excellent coordination between doctors, physicists and RTTs in the process of planning, verification, and treatment. The implementation of departmental clinical quality assurance meetings and weekly multidisciplinary tumor boards in breast, head and neck, and pediatric cancers have markedly improved communication between the staff and enhanced patient care. This process improvement is especially noteworthy considering the tight patient schedules and heavy clinical load. Additionally, doctors and residents engage in clinical didactics, journal club meetings, and continuing professional development programs, and attend national and international conferences throughout the year to learn about pertinent advancements in the field. Another significant activity is the participation by some Ghanaian oncologists (members of the African Cancer Coalition) in the ongoing harmonization of the National Comprehensive Cancer Network guidelines for Sub-Saharan African countries under the American Cancer Society.[15]

Additionally, a radiation safety officer ensures compliance with regulations set out by the country's nuclear regulatory authority. Ghana also participates regularly in International Atomic Energy Agency/World Health Organization (IAEA/WHO) postal dose audits.[16]

Collaboration Efforts in Capacity Building

The radiation centers in Ghana actively partner with several upper-middle income countries to foster cancer

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research and training institution. One example is a thriving collaboration between the Moffitt Cancer Center (MCC), KBTH and SGMC. In 2016, Drs. Yarney and Yamoah mentored a radiation oncology resident from MCC who received the prestigious ARRO-ASTRO Global Health Fellowship award to support a research elective at KBTH to study prostate and cervical cancer. While there are no training collaborations in cancer research between Ghana and MCC, cancer research training and capacity building are under active discussion. This has given birth to the first research fellowship program at MCC, designed to host a Ghanaian radiation oncology fellow for 1 year, which began in the 2018-2019 academic year. The fellow is learning skills to facilitate future collaborations between the radiation oncology program at MCC and Ghana. This fellowship program comes at a crucial time in the development of training and capacity-building programs in Ghana. Through this collaboration, the KBTH and MCC will continue to explore other funding opportunities in cancer research training to allow Ghana to expand its expertise for an independent cancer research infrastructure. Residents also receive an annual compressed didactic course in radiobiology from faculty at MCC.

In addition, mentorship programs with the University of Toronto (Princess Margaret Cancer Center) partner residents with faculty on a 1-year research question as well as a 12-week program using telehealth-facilitated knowledge transfer in clinical decision-making, biostatistics, and quality assurance in RT. Some of these collaborations have resulted in several publications.[13,17–19]

KATH and its oncology directorate have had extensive and continuing engagement with the University of North Norway on a breast health global initiative to revive pathology services. Pathology is central in oncology decision-making, and this collaboration has resulted in tremendous improvement in reporting on breast as well as other cancers. The University of Michigan has also partnered with KATH on breast cancer care and regularly participates in its weekly telemedicine multidisciplinary meeting.[17] The National Cancer Institute, Bethesda, Maryland, has also offered training in cancer epidemiology and advanced epidemiology for a number of participants from Ghana over the past few years.

Furthermore, the IAEA organizes at least 3 training programs a year for member states on common cancers in Africa, occasionally including expert missions and scientific visits as well as training on the management of RT centers. Ghana has taken advantage of these ongoing programs, which have been highly beneficial.

Research and Training in Ghana

To ensure a more sustainable and long-term impact in global health initiatives in Ghana and other LMICs, research and training needs to be integrated into an collaborative partnership by focusing on the following strategic goals: First, training and capacity building should center on conducting research on cancers of common interest to both parties. Second, the cancer research training initiatives must be designed in the context of existing research collaborations within the local oncology centers, thus seamlessly complementing ongoing efforts in Ghana. Currently collaborative activities initiated between MCC and KBTH include 1) providing health professionals with knowledge and tools in research methodologies for the management and use of medical information and abstraction and 2) providing health professionals, staff, oncology residents, fellows, and students with access to MCC's expertise in clinical research methodologies, biostatistics, management of medical information, manuscript writing for publication, and grant writing. Together, these efforts are expected to help fill the gaps and address specific needs outlined in the national cancer research agenda.

Future Directions

Ghana demonstrates that a country with limited resources and obvious challenges is capable of growth and success with the ability to overcome setbacks and harness innovation in the face of limitation. Positive leadership and high-level support cannot be underestimated and has resulted in the acquisition of RT facilities to meet the rising demands of the specialty and gradually bridge the gap with technological advancements. Considering the economic status of the country, coupled with other competing health and socioeconomic interests, this has not been easy to accomplish. The MOH, GAEC and IAEA have been instrumental in supporting and building the public RT centers to their present state of technological advancement. With the recent installment of 2 new linacs and an Eclipse planning system (Varian, Palo Alto, California) with additional contouring stations and an ARIA record and verify system in Accra and Kumasi, Ghana has made great strides. Additionally, the NRONMC has recently acquired a wide-bore CT simulator that is under installation.

The institution and sustenance of training programs to ensure continuing production of high-quality professionals in oncology is empirical evidence of future growth spurts in this field. Upgrading the skill of engineers to handle more sophisticated equipment and training more dosimetrists will be necessary to continue growth and development. These tasks, coupled with the Ministry of Health's commitment to improve healthcare delivery in the country, the roll out of the national cancer control plan and growth of the cancer registry,[18] will ensure that cancer treatment continues to expand and advance in Ghana. In addition, plans to

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start IGRT for prostate cancer treatment with gold fiducial seeds are underway. A new bunker is also being built to accommodate another linac in the near future. Further commitment, however, is required from the government to enhance radiation delivery and cancer treatment as a whole.

With ongoing human resource training and continuous improvement of logistics, equipment, and infrastructure, efforts should focus on: 1) relying on evidence-based data from population-based registries to inform policy on preventable cancers such as liver and cervical cancer; 2) developing health promotion and literacy programs on cancers; 3) promoting screening and early detection programs for prompt diagnosis and optimal treatment in a cost-effective manner; 4) decentralizing newer radiation treatment centers to improve access; and 5) continuing to foster global collaborative partnerships to address cancers of mutual interest in a multidisciplinary and multi-institutional setting.

In the near future, we believe we will put ourselves in a position to participate in research programs undertaken by cooperative oncology research networks that involve multicenter, multi-institutional randomized controlled trials to answer pressing and pertinent questions in oncology, taking advantage of disparity in biology and disease distribution across the world. This can increase accrual rates and answer questions on disease characteristics that are uncommon in high-income countries.

Conclusion

As Ghana has demonstrated, innovative use of basic equipment and gradual building of capacity in a resource-limited LMIC is essential. Acquisition of RT facilities must be considered in the context of available resources with a stepwise approach to increasing capabilities and complexity. This has obviously been an evolutionary process that continues to unfold with time. With general improvements in outcomes of cancer treatment worldwide, patients in LMICs are living longer and quality of life is becoming a real priority. Maximum benefit can only be realized with universal health care.

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RadiatingHope – A decade in global radiation oncology

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RadiatingHope (RH) was founded as a nonprofit organization in 2009, at a time when nongovernmental organizational engagement in global radiation oncology was in its infancy. Co-founders Larry Daugherty, MD, and Brandon Fisher, DO, were radiation oncology residents at the time. As avid mountain climbers, they visited some of the most amazing peaks in the world. On their journeys, they would seek out local hospitals and cancer care facilities, seeing that many of these incredible summits were in underserved low- and middle-income countries (LMICs). Most cancers were diagnosed at advanced stages; cancer care was scarce and access to radiation therapy (RT) was poor or often nonexistent. The number of nations without RT equipment was even greater at that time than the current estimates of 44 nations without RT and a worldwide shortfall of 5000 RT machines in LMICs.[1-4] It was clear to Daugherty and Fisher that the challenges were not limited to equipment alone; radiation oncology personnel were few and training was difficult to access.

FIGURE 1. The 2014 RH Kilimanjaro Climb group at Uhuru Peak. Photo courtesy of Charlie Wittmack.

In this climate, under the mentorship of Dr. Luther Brady, RH forged its mission of improving radiation-oncology-related cancer care globally. Avenues to implement this vision quickly expanded to include advocacy, equipment donation, and education and training. At the heart of RH's vision is to empower local communities and institutions through partnerships with RH, international medical personnel, and members of industry throughout the world.

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SPECIAL FEATURE

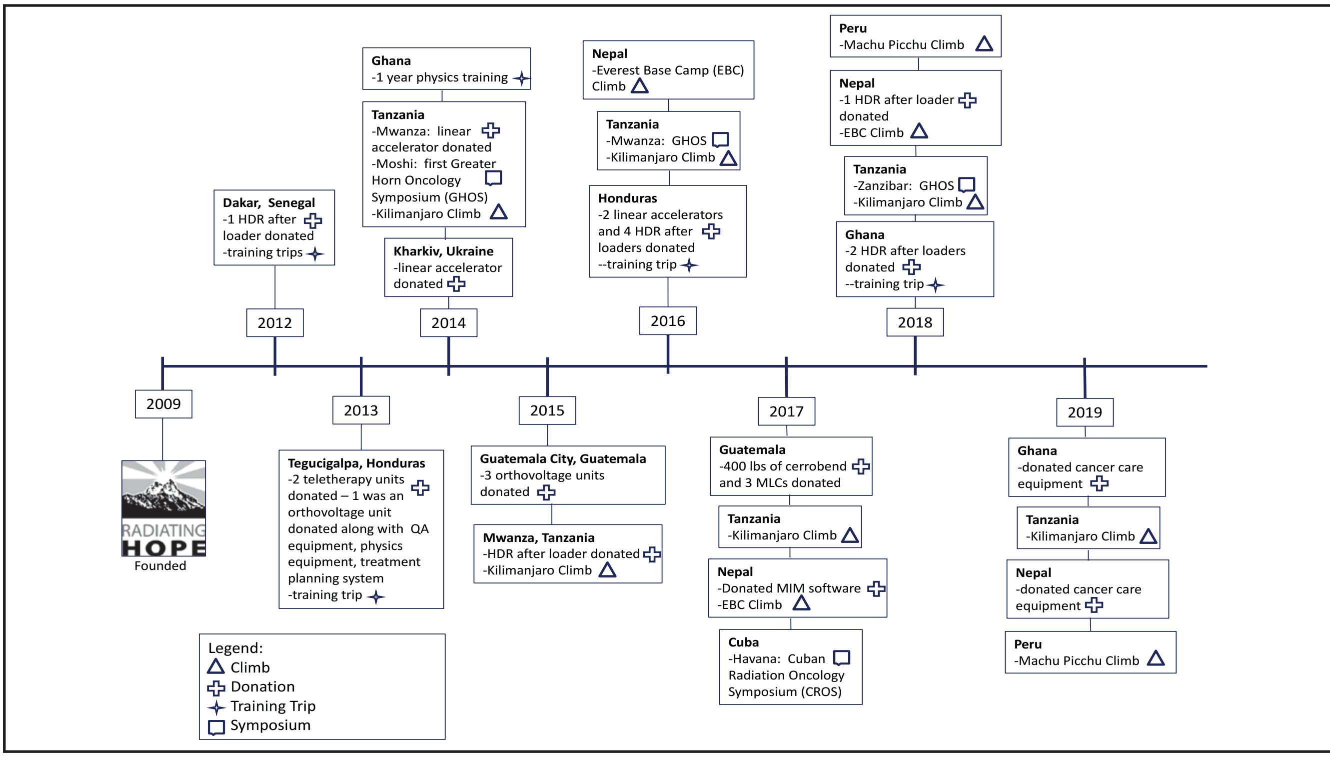

FIGURE 2. *A timeline outlining many of RadiatingHope's projects over the past 10 years*

FIGURE 3. *Participants of the Greater Horn Oncology Symposium (GHOS), June 2018, Zanzibar. Photo courtesy of Rasmus Preston.*

Advocacy

Mountaineering

RH may best be known as the group of radiation oncologists who climb mountains for cancer. These expeditions are a means to increase awareness about the condition of cancer care in LMICs and to further advance radiation oncology services. Each climb has a preset pledge amount; climbers raise tax-deductible funds, which are donated to the mission of advancing cancer care, often in the region of the climb. In the past 4 years, close to 300 climbers – including cancer survivors – have joined RH on the annual Kilimanjaro climb (**Figure 1**), as well as the Everest Base Camp (EBC) and Machu Picchu excursions. The 80 climbers for the 2017 RH EBC trek raised enough funds to purchase a high-dose-rate (HDR) afterloader for the Kathmandu Cancer Center (KCC) in Nepal.

Prayer Flag Project

On their expeditions, designated RH climbers carry Tibetan prayer flags that represent health, hope, strength and well-being. Flags are individually dedicated to cancer patients and are flown at the summit of each peak. So far, these flags have been to Mount Kilimanjaro, Mount Whitney, Mount Aconcagua, Mount Elbrus, Mount Rainier, Mount Washington, the Arctic Circle, Pico De Orizaba, Mount Chukkung Ri, Mount Denali and have now been left flying at EBC.

Equipment Donation, Education and Training

RH realized that its mission of equipment donation was possible when RT machines were donated to Madagascar (cobalt) and Peru (linac) through the

Luther Brady Research Institute. With the project in Dakar, Senegal, RH took its first step into the unknown.

The RH projects in Senegal, Ghana, Honduras, Guatemala and Nepal include equipment donations and training programs to create self-sustainability as well as methods for training others. These endeavors are described in detail in the sidebar to the right; many other projects are listed in **Figure 2**.

Upcoming Projects

RH is working to help build a partnership with Kenyatta Hospital and Stanford University to create a paradigm for sustainable distance-based clinical learning and an HDR distance training program similar to the one in Ghana; in parts of Central and South America, RH is collaborating with Rayos Contra Cancer and Project ECHO to implement a similar program. Uniting with industry and an international builder, RH is working with Hospital Municipal La Portada in La Paz, Bolivia, to build and equip a start-up oncology center.

Symposia

Starting in March 2014, RH hosted its first international meeting – the Greater Horn Oncology Symposium (GHOS), in Moshi, Tanzania, at the Kilimanjaro Christian Medical Centre (KCMC). GHOS serves as a multidisciplinary oncology forum for improving access to cancer care in the Greater Horn of Africa and to create a platform for exchanging ideas among oncology medical professionals around the globe. The second GHOS was held in June 2016 in Mwanza, Tanzania, in collaboration with Bugando Medical Center, and the third in June 2018 in Zanzibar. At the Zanzibar conference, 15 nations were present (Africa - 8, North America - 2, Europe - 4, South Asia -1). Of the 56 attendees, 29 were from Africa, 1 was from Nepal and the remainder were from North America and Europe (**Figure 3**). Ten participants were radiation oncology residents

RadiatingHope past projects

Senegal Project — Lead: Adam Shulman, MS

In 2012, RH identified the Institut Curie at L'Hôpital Aristide Le Dantec in Dakar, Senegal, as a site in need of brachytherapy for the treatment of cervical carcinoma. West Africa has one of the highest rates of cervical cancer in the world.[5] Institut Curie, with more than 500 cases of cervical cancer to treat annually, had a single cobalt teletherapy machine, a fluoroscopic simulator, 2 radiation oncologists (ROs), 3 medical physicists (MPs), 1 nurse (RN) and 2 radiation therapists (RTTs) to serve the RT needs of Senegal and 4 adjacent nations. Unfortunately, the center had no brachytherapy. The treatment paradigm for carcinoma of the cervix was surgery for early stage disease and either palliative hypofractionated radiation and chemotherapy or neoadjuvant chemotherapy/radiation therapy followed by surgery for more advanced disease. Definitive chemoradiotherapy was not an option for curative treatment of the disease.

RH facilitated the donation of a refurbished HDR afterloader to the Institut Curie in December of 2012, when a team from RH (ROs, MPs and RNs) traveled to Senegal for HDR brachytherapy training. The ROs in Dakar were previously trained in placement of low-dose-rate brachytherapy applicators. The trip focused on developing fractionation schedules and a treatment planning process that would be feasible with the limited resources; the afterloader would be housed in the cobalt bunker limiting treatment time, and no CT simulator was available. To optimize resources, while trying to minimize toxicity, a hypofractionated regimen of 3 fractions of 7.5 Gy was chosen. The treatment planning process has been described previously and consisted of using fixed-geometry tandem and ring applicators with a library of plans corresponding to each geometry.[6] After insertion, patients underwent conventional simulation with orthogonal radiographs and isodose overlay transparencies were used to estimate ICRU (International Commission on Radiation Units) rectal and bladder point doses.

In March 2013 a second RH team (ROs, MPs and RN) assisted in performing the first 10 brachytherapy procedures. The process worked efficiently, was reproducible and was easily adopted by the team in Dakar. Over the next 3 years 62 patients with cervical cancer were treated using this approach with acceptable control and toxicity rates.[7] Further work is being explored including a prospective clinical trial using both hypofractionated external-beam radiation and a hypofractionated brachytherapy schedule to further optimize throughput of cervical cancer patients. The training provided to the Dakar team carries on as this center has new linacs and HDR afterloaders; the medical personnel are engaged in training new ROs and MPs. RH continues to fund these efforts and has supported a training trip for the MPs to spend 1 week at the Karmanos Cancer Institute in Detroit.

Ghana Project — Lead: Adam Shulman, MS

RH began to build a relationship with the Sweden Ghana Medical Centre (SGMC) in Accra when Shulman was working as an MP there from August 2014 to August 2015. He worked alongside hospital administration and staff to ensure the establishment of SGMC as a free regional training center for MPs across Sub-Saharan Africa. SGMC is a comprehensive cancer center with medical and radiation oncology as well as primary care. The radiation oncology department has modern equipment including: a linac with MV imaging, treatment planning software, a record and verify system; a 16-slice CT sim, and a 0.3T MRI sim. Department staffing consists of: 2 ROs (1 completed residency in Canada, and 1 completed residency in Accra at Korle Bu Teaching Hospital); 2 MPs (with MS degrees in medical physics from the School of Nuclear and Allied Sciences, University of Ghana, Legon); 1 physics student (in medical physics MS program at Duke Kunshan University in China as of press time); 1 dosimetrist (an RTT trained on dosimetry), 4 RTTs; and 1 diagnostic radiologist (from the University of Ghana).

Training focused on safety with attention to areas with greatest risk for systematic and/or large errors, in addition to working with staff to develop an in-depth understanding of all aspects of clinical workflow and tasks. Process management was emphasized as an essential element of quality assurance (QA) and treatment planning. With his experience in Africa over the past decade, Shulman believes the most effective way to improve clinical understanding, while simultaneously optimizing safety and efficiency, is by introducing standard procedures, documents, and Excel spreadsheets, and by customizing them during training. In this technique, each document is introduced individually, and modified as necessary line by line accounting for the site's environment, staffing, workload, equipment, etc. Through this process, the trainees not only learn exactly why each line is written, but how it is done, while creating a guideline to follow in the future. An invaluable teaching tool, this method of standardization has the additional benefit of facilitating communication among sites trained by RH and RH trainers, allowing for easier discussion and streamlined troubleshooting. Opening doors for communication among African countries and the world is priceless, as one of the largest difficulties faced by many MPs in Africa is isolation. Ultimately, the SGMC staff was trained in theory, clinical use, safety and efficiency. They learned QA on linacs and imaging devices, treatment planning, secondary checks and monitor unit (MU) calculations. They were also trained on data collection and measurement device selection, and performed multiple sessions of annual QA work on all equipment.

The CEO of SGMC and professional staff had agreed to provide free training to MPs across Africa upon completion of this year-long training. This project passed the self-sustainability test when the SGMC MPs trained an MP from Senegal for 2 weeks, educating her on all of the equipment and procedures they had learned; she reported she learned more in 2 weeks at SGMC than she had in 2 months in France. Similarly, an external audit was performed by MPs from South Africa. They stated that the physics program led by the 2 Ghanaian MPs was as good as any physics program in South Africa. Since 2015, the physics team in Ghana has trained MPs from Ghana, Senegal, Nigeria, and Kenya for up to 3 months at a time; RH has received positive feedback from all MPs who trained at SGMC.

Recently, SGMC acquired a cobalt HDR unit, and the Komfo Anokye Teaching Hospital in Kumasi, Ghana, received 2 HDR afterloaders donated with assistance from RH. Using the same principles outlined above, a distance training program for HDR brachytherapy has been implemented for the Ghanaian MPs; RH has provided template documents on all aspects of HDR brachytherapy, from commissioning to source exchange to EQD2 documents and checklists. In the summer of 2018, a 2-week, in-person, RO and MP training was held in Ghana; distance training continues.

Central America Project – Lead: Peter Sandwall, PhD

Honduras

In 2011 a pair of independent, volunteer physicists traveled to Tegucigalpa, Honduras, to ensure the team at the Centro Oncologico Hondureño could use a donated planning system (Pinnacle [Royal Phillips, Amsterdam, the Netherlands]) with their recently purchased linac – a 600C (Varian, Palo Alto, California), the first in the city and second in the country. The linac's multileaf collimator (MLC) system was destroyed in shipment, necessitating the use of cerrobend blocks for 3-dimensional (3D) treatments.

from Ocean Road Cancer Institute in Dar es Salaam, Tanzania, who had the opportunity to speak directly with international experts in radiation oncology. By bringing together this group of radiation oncologists (ROs), medical physicists (MPs), radiation therapists (RTTs), and members of industry for 3 days, GHOS has sparked collaborations among institutions in North America or Europe and LMICs present at the meeting, and among African nations to help create self-sustaining collaborations in developing local cancer care. Examples include partnerships between physicians in Tanzania and Turkey, as well as ties between institutions in Switzerland and Senegal to advance from 2D to 3D planning. The next GHOS is in June 2020.

A similar meeting – the Cuban Radiation Oncology Symposium (CROS) – was planned for October 2017 in Havana, Cuba. Due to US state department travel recommendations at the time, few US participants attended the meeting; however, more than 20 Cuban ROs were present.

These symposia are largely funded with assistance from industry members, such as Varian (Palo Alto, California) and Elekta (Stockholm, Sweden), covering the travel and lodging expenses of local conference participants; all North American and European participants have managed their own expenses.

Challenges

While undertaking global radiation oncology work, the list of challenges quickly outpaces the list of successes. As is clear from the few projects discussed above, equipment alone is not the only piece of the puzzle missing in advancing global oncology care. The current projected need of these medical personnel in LMICs by 2035 is greater than 10 000 ROs, 9000 MPs and 25 000 RTTs.[8] Training sites for these highly specialized individuals are difficult to access, as evidenced by Ghanaian physicists receiving training in China.

Regarding equipment, several nations will not accept used or refurbished RT equipment (including machines and physics equipment). For countries that do, not all donations have been or can be utilized. An institution may have a bunker to hold the machines, but may not have the infrastructure or resources to deploy the equipment. Prior to donating equipment (including machines, treatment applicators, software, etc.), RH undertakes thorough, in-person research of the receiving site in regard to space/bunker availability and appropriateness for equipment, medical personnel availability, medical personnel knowledge, financial stability, energy source stability, local government support, and maintenance for optimal use of equipment. Additionally, contracts are signed for agreement and sustained communication. However, despite these painstaking efforts, not all projects are completed. The 2 orthovoltage units donated to Central America are in storage due to costs of making the units functional, as is the case of the MLCs waiting to be installed in Guatemala. The linac donated to the Bugando Medical Center in Tanzania still sits in crates due to assembly costs required by the manufacturer and the Ministry of Health's challenges in meeting these demands. Furthermore, governments here are often slower to respond and leadership can change frequently, setting back progress. The donation at the Kharkiv Institute in Ukraine could not be reassembled; however, it was used for parts to update linacs throughout the country.

In Dakar, where the HDR afterloader was successfully installed, used and maintained, several challenges remained with continued operation of the unit, including the cost and logistical difficulty with source changes, limited RO and treatment room time availability for procedures, and equipment downtime, which can be significant. Sustained communication with some sites after donation can also become difficult.

Over the years, RH has been able to facilitate several equipment donations to Honduras, including an orthovoltage machine, a daily QA device, miscellaneous physics equipment, and a newer Pinnacle treatment planning system. In 2017, RH received a large donation (valued at more than $1,000,000); 2 high-energy linacs and 4 HDR afterloaders were shipped via container to Tegucigalpa. Upon receiving this donation, the first project was to transfer one of the linac heads (including MLC) to the 600c in operation at Centro Oncologico Hondureño. The construction of a second vault is being explored to house the other linac. Sandwall is working with San Felipe, a public hospital, to place the HDR units at this location.

FIGURE 4. Physicists and technologists following quality assurance training at Centro Oncologico Hondureño with medical director, Roberto Jerez, MD (in orange). Photo courtesy of Peter Sandwall.

This 2017 donation, along with other physics equipment, has facilitated installation of a Varian 2100EX at Hospital Bendaña in San Pedro Sula in 2018; the process of commissioning served as an educational opportunity for the local physics community. Independent initiatives in Honduras continue for the performance of annual QA and reference dosimetry on the accelerator. The internal efforts to improve medical use of radiation in Honduras are becoming more robust by a new generation of MPs. Several trained outside of their home country (Mexico and Italy) and are creating opportunities for hands-on education and academic training at home (**Figure 4**).

Guatemala

An orthovoltage unit was donated and shipped by RH to Liga Nacional Contra el Cancer/Instituto Nacional de Cancerologia (LIGA/INCAN) in Guatemala City, Guatemala, in 2015. Following this donation, RH and an RO, made a trip to this center for a needs assessment; LIGA/INCAN was equipped with 2 linacs and an aging cobalt unit, both without MLCs, and they were suffering a cerrobend shortage. With the help of RH, 400 lbs of cerrobend and MLCs were shipped to this center. In addition to the above-mentioned equipment, in 2018 an Elekta (Stockholm, Sweden) Monaco treatment planning system was given to RH and sent to LIGA/INCAN. In Guatemala, RH is working closely with Rayos Contra Cancer, another nongovernmental organization focused on advancing global radiation oncology-related cancer care.

Nepal Project — Lead: Brandon Fisher, DO

Nepal, a country of 26 million people in the heart of the Himalayas, and home to the highest mountains in the world including Mt. Everest, faces a similarly enormous feat to climb with access to cancer care. With this population, you could justify well over 100 radiation machines; however, Nepal only has only 4 functioning machines (2 cobalt and 2 linacs). RH began working with Nepal in 2016 in partnership with the Kathmandu Cancer Center (KCC) and Dr. Subhas Pandit, with the goal of implementing brachytherapy to provide definitive and curative treatments for cervical

Last, but by no means least, shipping linacs and HDR afterloaders is no small feat. Disassembling a linac, transporting it to storage, shipping it overseas, and transporting it to a facility, can take months, sometimes longer, to reassemble and make functional. These steps depend on the availability of manufacturers in the region, and their ability to put into motion refurbished/used equipment with local government support.

Conclusions

RH's vision remains clear, and its devotion to increasing access to global radiation oncology care runs deep, strengthened by the incredible individuals engaged in the work and their dedication to help provide cancer care to their family and friends. Since its inception in 2009, RH has learned much along its journey of advancing global cancer care and has encountered seemingly insurmountable difficulties. The importance of collaboration worldwide is obvious during the times of these impossible-appearing summits. As RH climbers have adopted a "climb on" mantra when facing obstacles on a trek, so too has the global oncology world.

cancer – the most common cancer treated at the center. KCC uses state-of-the-art external-beam radiation therapy, pulling off technically demanding plans, using 3D planning and intensity-modulated radiation therapy. Their linac runs around the clock – and is powered by a generator during power shortages. Unfortunately, KCC

FIGURE 5. *Dr. Subhas Pandit (second from left) and the radiation oncology team at the Kathmandu Cancer Center in Nepal with the new high dose rate (HDR) afterloader. Photo courtesy of Subhas Pandit.*

lacked funds to purchase a brachytherapy machine. RH was scheduled to receive 2 donated machines to be shipped and installed at KCC in 2017; however, the government restricted entry of used machines. Committed to providing brachytherapy to KCC, RH partnered with Varian to purchase a new HDR afterloader, which was installed in March 2019 (**Figure 5**); the EBC trekkers in 2017 (**Figure 6**) raised over $100K, which was used to purchase this unit. KCC has received their radioactive source and completed its first 4 brachytherapy treatments for cervical cancer on May 1, 2019. Part of ongoing efforts to support the cancer center include annual medical missions to the center and frequent EBC treks; an RH training trip is scheduled in December with ROs and MPs.

FIGURE 6. *RH Everest Base Camp (EBC) climb group at the Kathmandu Cancer Center April 2017. Photo courtesy of Rasmus Preston.*

Acknowledgements

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Disparities in access to radiation therapy for regions inhabited by a higher proportion of First Nations, Inuit and Métis populations in Canada, and its association with cancer outcomes

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Abstract

Background: First Nations, Inuit and Métis (FNIM) peoples in Canada exhibit high rates of cancer mortality. Little information exists on access to radiation therapy (RT) among these populations. We sought to describe geographic access to RT, and to explore its relationship with cancer outcomes among regions inhabited by a higher proportion of FNIM peoples in Canada.

Methods and Materials: We calculated the linear distance from the centroid of each Canadian health region to the nearest RT center using a geographic analytical techniques, and compared distance between regions with a higher (≥ 23%) vs lower (< 23%) proportion of FNIM peoples (self-identified as Aboriginals through census data from Statistics Canada). We examined relationships between distance and proportion of FNIM peoples on cancer outcomes in an initial exploratory analysis, using age-standardized all-cancer mortality-to-incidence ratios (MIRs) from 2010 to 2012. A prediction model based on recursive partitioning was created, and the resulting groups were compared using one-way analyses of variance and nonparametric tests.

Results: Health regions inhabited by a higher proportion of FNIM peoples were located further from RT centers (799 vs 120 km, $p < .0001$), and had worse cancer outcomes (MIR 0.53 vs 0.42, $p < .0001$). Among a subset of overlapping regions 150-750 km from RT centers, those with a higher proportion of FNIM peoples had worse outcomes (MIR 0.50 vs 0.44, $p = .03$), despite a similar distance ($p = .47$). In our prediction model, distance to an RT center had the largest impact on MIR, followed equally by smoking and proportion of FNIM peoples. Regions closer to RT centers with a higher proportion of FNIM peoples had poor outcomes that did not differ from regions furthest away ($p = .41$), and showed a trend toward worse outcomes compared to regions with a lower proportion of FNIM peoples within the same distance ($p = .07$).

Conclusions: Regions inhabited by a higher proportion of FNIM populations are further away from RT centers and have poorer outcomes. Distance is an important factor but does not completely explain these regions' poorer cancer outcomes.

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Indigenous peoples make up approximately 5% of the total Canadian population. Under the Canadian Constitution, they are recognized as "Aboriginal," although the term indigenous is preferred, and consist of three groups: First Nations (approximate population in 2016: 977,000), Métis (about 587,000) and Inuit (about 65,000).[1]

The cancer burden among First Nations, Inuit and Métis (FNIM) peoples in Canada is significant. Although Canada is a high-income country with a universal healthcare system, a recent national study demonstrated poorer survival among First Nations peoples compared with non-Aboriginals for 14 of 15 of the most common cancers.[2] In the province of British Columbia, poorer survival was observed among First Nations vs non-First Nations peoples in 10 of 15 cancer sites studied in women, and 10 of 12 cancer sites studied in men.[3] Similar findings have been reported for First Nations peoples with head and neck cancers in the province of Alberta,[4] across multiple cancer types in the province of Ontario,[5] and for Métis adults with prostate cancer nationally.[6] In addition, all-cancer age-standardized mortality rates among the Inuit Nunangat ("homelands") have been consistently higher compared to national rates from 1994 to 2013.[7]

One reason underpinning the observed disparities in cancer outcomes between indigenous and non-indigenous populations is the poorer access to, or uptake of, cancer treatments once diagnosed, including radiation therapy (RT).[8-10] The barriers to accessing cancer services among indigenous peoples are multifactorial, and include mistrust of the health system, stigma, and a lack of cultural understanding within the health system,[11] stemming from complex sociohistorical factors.[8]

Among such barriers, distance and the resulting travel burden have repeatedly shown significant impact on access to cancer services in the general population, negatively influencing all aspects of a patient's cancer journey from stage at diagnosis to quality of life.[12] RT is no exception to this and, in fact, a longer distance from place of residence to an RT center has been cited as one of the most important barriers to accessing this treatment.[13] Increasing distance to RT has also been associated with decreased RT utilization,[14,15] but its association with cancer outcomes has not yet been explored among indigenous peoples in Canada. We sought to describe geographic access to RT as measured by distance (health region to the nearest RT center), and to determine the association of distance to RT with cancer outcomes among regions inhabited by a higher proportion of FNIM peoples.

Methods and Materials

Data sources and Definitions

Distance to Radiation Therapy Center

We extracted the geographic locations of each Canadian RT center from The Directory of Radiotherapy Centers, an online international registry maintained by the Division of Human Health at the International Atomic Energy Agency (IAEA).[16] We supplemented this with data from the Canadian Association of Radiation Oncology. For this study, we included only RT centers that were operational in 2012 to most closely match the time period of our cancer outcomes data.

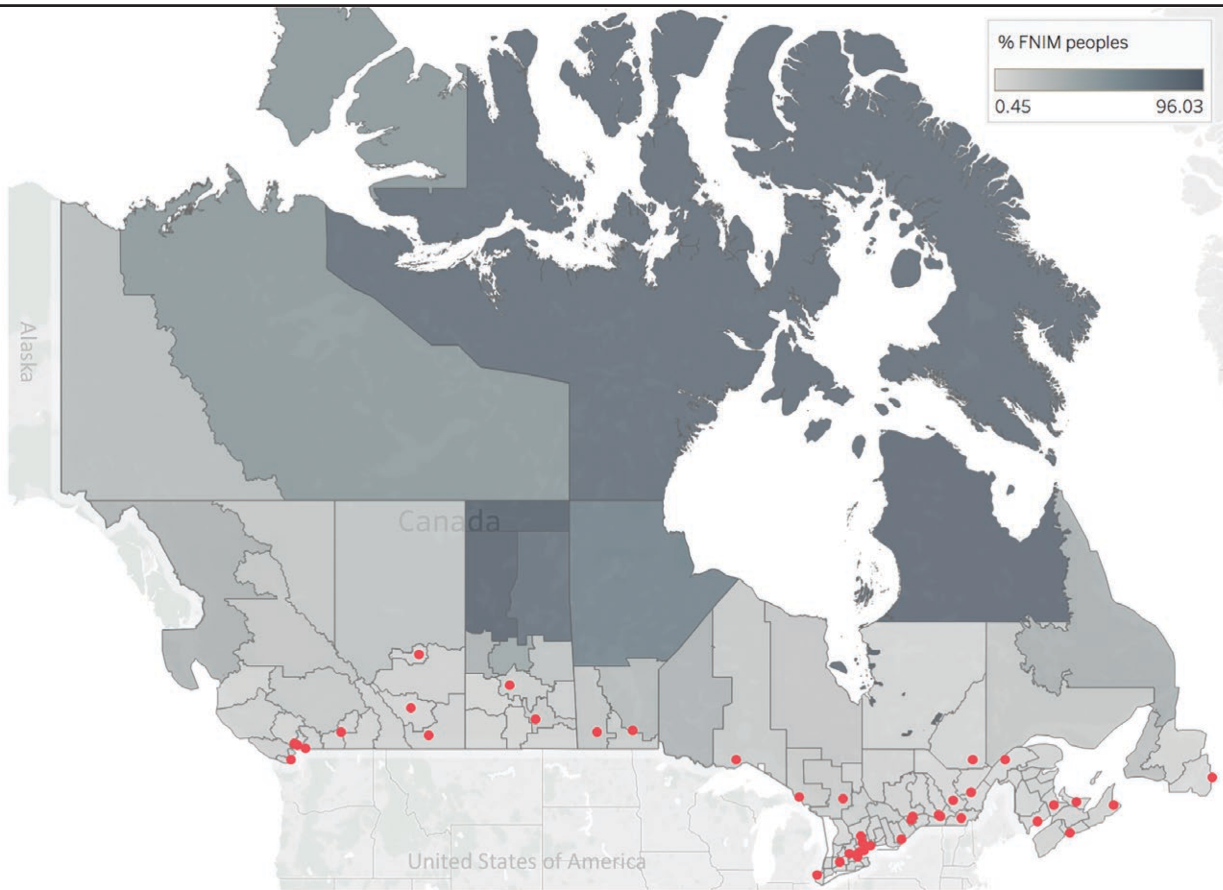
We mapped all health regions in Canada using data from Statistics Canada,[17] and an open-source geographic information systems (GIS) suite (QGIS v.2.18). Health regions are administrative areas based on geographical or operational boundaries, that are one level below provinces in Canada.[18] They provide the most granular level for which cancer data are consistently available across the country. The central geographic point (centroid) of each health region was auto-calculated. The linear distance, in kilometers, from each health region centroid to the nearest RT center was measured irrespective of provincial boundaries, as Canadians can access RT at any center regardless of home province affiliation.

Population of Interest

As a proxy to explore access to RT among FNIM peoples in Canada, we extracted information on the proportion of FNIM peoples per health region. Data were obtained from the 2011 National Household Survey (NHS), a voluntary survey sampling 30% of all private dwellings in Canada that were part of the national census.[19] Populations including FNIM were oversampled to improve response rates.[20] Proportion of FNIM peoples was based on the proportion of self-identified Aboriginals per health region. Aboriginal identity included persons who self-reported being an Aboriginal person, including First Nations (North American Indian), Métis, or Inuk (Inuit) and/or those who reported Registered or Treaty Indian status, and/or those who reported membership in a First Nation or Indian band.[21]

Sociodemographic Variables

To explore the influence of other factors, we extracted data on food security and smoking, which in our previous work, were found to be significantly associated with our cancer outcomes data among the general Canadian population (Chan, submitted). Both variables were obtained from the 2011-2012 Canadian Community Health Survey (CCHS),[22,23] a voluntary survey administered by Statistics Canada that represents more than 97% of the Canadian population ages ≥ 12, but excludes persons living in the Québec health regions of Région du Nunavik and Région des Terres-Cries-de-la-Baie-James, and persons living on reserves



*Data obtained from the 2011 National Household Survey (Statistics Canada). FNIM peoples were self-identified as Aboriginals through census data. Aboriginal identify included persons who self-reported being an Aboriginal person, including First Nations (North American Indian), Métis, or Inuk (Inuit) and/or those who reported Registered or Treaty Indian status, and/or those who reported membership in a First Nation or Indian band

FIGURE 1. *Proportion of self-identified First Nations, Inuit and Métis (FNIM) peoples* by Canadian health region, with radiation therapy (RT) centers in 2012. Dots represent RT centers.*

and other Aboriginal settlements in the provinces.[24] Definitions for food-secure households were based on the CCHS Food Security module, which included questions such as not being able to afford balanced meals, being hungry but not eating, and not eating for the whole day.[25] Smoking was defined as the proportion of daily or occasional daily smokers.[22] Other sociodemographic variables were not included due to high multi-collinearity with the proportion of FNIM variable.

Mortality-to-incidence Ratios

Age-standardized all-cancer incidence and mortality rates were obtained for each health region from Statistics Canada, which were available in three-year aggregates and based on provincial registry data.[26,27] We used the most recent data (2010-2012) for all provinces and territories, except for Québec, where the most recent incidence data was from 2008-2010. Incidence and mortality rates were age-standardized using the 2011 Canadian Census population. All-cancer age-standardized mortality-to-incidence ratios (MIRs) were calculated for each health region as the mortality rate divided by incidence rate.

Statistical Analyses

We conducted two recursive partitioning analyses (RPA) to define cutoffs for our variables and to explore relationships between them. RPA is a method used to classify subjects and variables, and can be useful in identifying synergistic interactions among factors.[28] In the medical context, it has been useful in determining prognostic and risk groups in patients with cancer, and in creating clinical algorithms for patient treatment.[29,30] The order in which independent variables are partitioned indicates its impact on the dependent variable; the earlier it is partitioned, the higher the impact.[31] First, as an initial exploratory analysis, we used RPA to categorize the proportion of FNIM variable into two groups (regions with a high vs low proportion of FNIM peoples). We then conducted

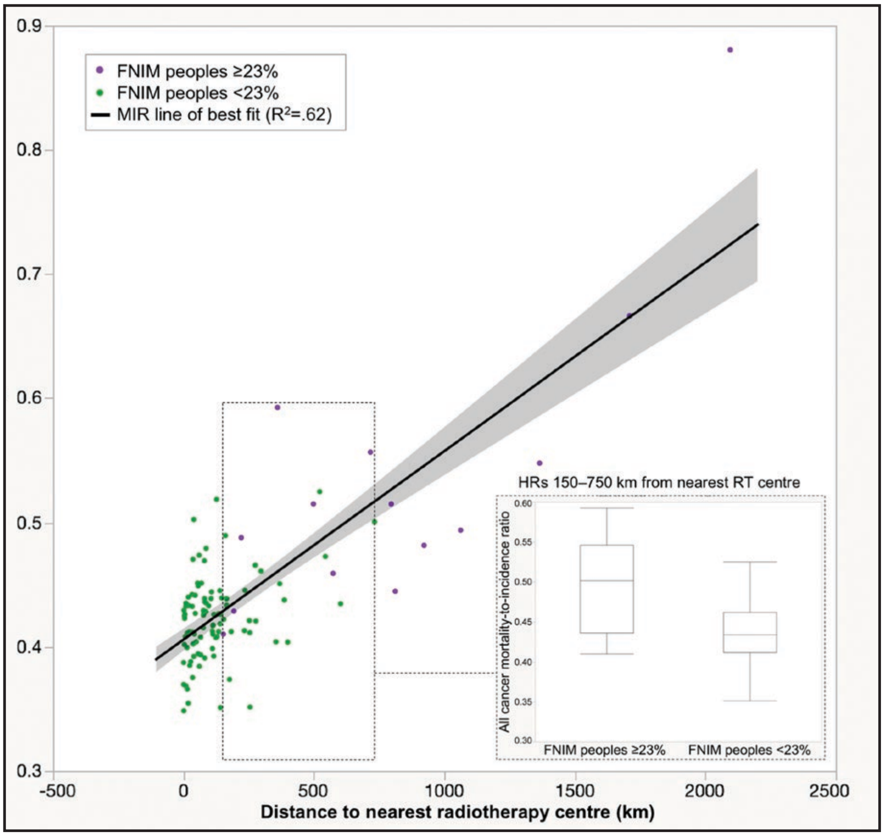


FIGURE 2. *All-cancer mortality-to-incidence ratios (MIR) in 2010-2012 by distance to nearest radiation therapy (RT) center and proportion of self-identified First Nations, Inuit and Métis (FNIM) peoples, per health region in Canada. Regions denoted within the dashed box were within 150 – 750 km from the nearest RT center and did not differ in distance (p = .43), but those with a higher vs lower proportion of FNIM peoples had worse cancer outcomes (p = .03) (outlier box plots with medians shown).*

nonparametric tests to compare distance and MIR between the two groups. Second, we used RPA to create a prediction model, with a proportion of FNIM people, distance, smoking and food security as the independent variables, and MIR as the dependent variable. The RPA algorithm created cut-offs and separated these variables into several groups. These were compared using nonparametric tests (Wilcoxon tests for independent samples) due to small sample sizes. Effect sizes for nonparametric tests were estimated,[32] with r values of 0.1 indicating a small, 0.3 medium and 0.5 large effect.[33]

All statistical tests were conducted with JMP v.12. Choropleth maps were generated using Tableau v.10.4.

Results

Across the 112 health regions in Canada, the median linear distance from health region centroid to nearest RT center was 102 km, with 50% (56/112) of health regions more than 100 km from an RT center. The closest distance was from British Columbia's Vancouver Health Service Delivery Area (1 km), and the largest distance was from Nunavut (2,095 km). Ontario's York Regional Health Unit had the lowest proportion of FNIM peoples at 0.4%, and the highest proportion was in Québec's Région des Terres-Cries-de-la-Baie-James at 96%. Nearly all RT centers were in the south of the country, far from health regions with the highest proportion of FNIM peoples (**Figure 1**). Indeed, 83% of health regions with a FNIM population of 30% or more (the 90th percentile) were 500 km or further from the nearest RT center.

Our first partitioning analysis of the proportion of FNIM variable created two groups: regions with a high (≥ 23%) and low (< 23%) proportion of FNIM peoples. Distance to nearest RT center was significantly further for regions with a high vs low proportion of FNIM peoples (799 vs 120 km, $Z = 5.60$, $p < .0001$). Regions with a high proportion of FNIM peoples also exhibited worse cancer outcomes (MIR 0.53 vs 0.42, $Z = 4.89$, $p < .0001$). Distance explained 62% of the variability in MIR ($r^2 = 0.62$). We also examined a subgroup of health regions that overlapped in distance (those within 150-750 km from nearest RT center); regions with a high proportion of FNIM peoples still had significantly worse outcomes compared to those with a low proportion of FNIM peoples (MIR 0.50 vs 0.44, $p = .03$), despite no difference in distance ($p = .47$) (**Figure 2**).

In our second partitioning analysis to generate a prediction model including smoking and food security, distance to nearest RT center was partitioned first (< 922 vs ≥ 922 km), indicating that it was the most influential variable on MIR (**Figure 3**). This was followed equally by smoking and proportion of FNIM peoples, but not food security. Following the creation of five subgroups in the model, the iteration was terminated, as further partitions were not possible due to small sample sizes within the subgroups, or because further iterations continued to partition the smoking variable into smaller categories, which was felt not to be clinically meaningful.

The resulting five subgroups are shown in **Figure 3**. Regions furthest from RT centers (≥ 922 km) had the poorest outcomes (MIR 0.61) (**Table 1**). However, regions closer to an RT

Table 1. Comparisons of Select All-cancer Mortality-to-incidence Ratios Between the Five Subgroups Created from the Recursive Tree

Subgroup	Description	Mean MIRs	Z-score	p-value	Effect size (r)
5 vs 1	Distance ≥ 922 km vs Distance < 360 km and Smokers < 21%	.61 vs .40	3.57	<.01	.55
5 vs 2	Distance ≥ 922 km vs Distance < 360 km and Smokers ≥ 21%	.61 vs .43	3.51	<.01	.45
5 vs 3	Distance ≥ 922 km vs Distance 360-921 km and FNIM peoples < 30%	.61 vs .46	2.11	.03	.61
5 vs 4	Distance ≥ 922 km vs Distance 360-921 km and FNIM peoples ≥ 30%	.61 vs .51	.82	.41	.24
1 vs 2	Distance < 360 km: Smokers < 21% vs Smokers ≥ 21%	.40 vs .43	- 4.24	<.01	.44
3 vs 4	Distance 360-921 km: FNIM peoples < 30% vs FNIM peoples ≥ 30%	.46 vs .51	- 1.80	.07	.48

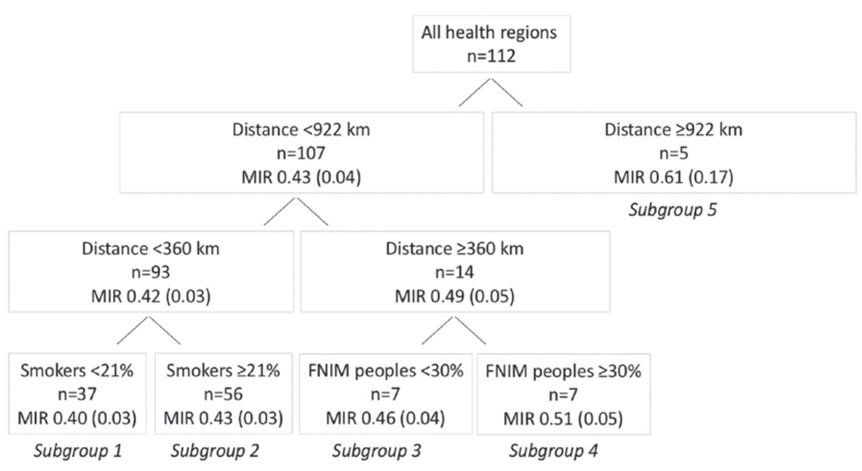


FIGURE 3. *Recursive tree and the resulting five subgroups of Canadian health regions. Each box contains the number of health regions in the subgroup (n) and the all-cancer age-standardized mortality-to-incidence ratio (MIR) (mean and standard deviation).*

center (360-921 km) but with a higher proportion of FNIM peoples had poor outcomes that did not differ from regions furthest away (MIR 0.51; $p = .41$), while also displaying a trend toward worse outcomes compared to regions within the same distance but with a lower proportion of FNIM peoples (MIR 0.46, $p = .07$). The best outcomes were seen among regions closest to an RT center (< 360 km) and with a lower vs higher proportion of smokers (MIRs 0.40 vs 0.43; $p < .01$).

Discussion

Despite living in a high-income country with a universal healthcare system, indigenous peoples in Canada experience significantly higher cancer mortality compared to the general population. As RT has a population benefit on survival when optimally used,[34] we sought to describe geographic access to RT among indigenous peoples in Canada using GIS techniques, and to explore its association with cancer outcomes.

In our study, regions inhabited by a higher proportion of FNIM peoples had significantly poorer geographic access to RT, as measured by distance. This is consistent with the known geographic distribution of FNIM peoples in Canada, where nearly 40% of these populations live in a rural area,[35] far from RT centers, which are typically in large urban centers.

Distance to RT was the most important factor influencing MIRs in our model, and has been similarly associated with poorer cancer outcomes among rectal cancer patients in Australia, where for every 100 km increase in distance to RT, there was a 6% mortality increase.[36] Notably, however, distance did not entirely explain the observed poorer MIRs, as health regions within a similar distance to RT centers still had worse outcomes if inhabited by a larger proportion of FNIM peoples. Similar findings were reported in a national study describing cancer survival between First Nations and non-Aboriginal peoples in Canada, where rurality had little impact on the observed disparities between these two groups,[2] and an international meta-analysis on indigenous mortality by rurality indicated no difference in all-cancer mortality between urban and rural areas.[37] Therefore, FNIM peoples populations may still experience worse cancer outcomes despite being closer to cancer services, including RT.

Other reasons that may contribute to the poorer cancer outcomes observed in our study include smoking, which has a well-established link to cancer mortality with approximately 80% of lung cancer deaths in Canada attributed to cigarette smoking.[38] Conversely, food security was not found to be as influential on MIRs as distance, smoking or the proportion of FNIM peoples per health region. There is a high prevalence of food insecurity among indigenous populations in Canada,[39] which in Ontario has been shown to persist regardless of geography.[40] In addition, the food security variable was obtained from the CCHS, which may not be measuring food insecurity in an indigenous context, and excludes data from on-reserve populations across Canada and two health regions in Québec with a high proportion of indigenous peoples. For these reasons, food security may still be associated with MIR but may not have been measured well enough to produce an effect in our analyses.

Limitations of our study include its ecological design, providing only a high-level description of the current state of RT access, the distribution of FNIM people across Canada, and their associations with cancer outcomes. By grouping large geographic areas that also contain semi-urban centers inhabited by a low proportion of FNIM peoples, we are potentially underestimating the impact of this variable's influence on outcomes. In addition, we were unable to control for other important confounding factors that may influence MIR, including stage distribution and access to cancer surgery. Our sample sizes of health regions were also small in some of the subgroup analyses.

Conclusion

In conclusion, regions inhabited by a higher proportion of indigenous peoples demonstrate poorer geographic access to RT and worse cancer outcomes in Canada. Approaches to improve such disparities in cancer outcomes are required that address the entire spectrum from prevention and diagnosis to treatment, and require further exploration. These may include culturally appropriate health promotion programs, and the hypofractionation of radiation treatments, while incorporating strategies to improve geographic access, including telemedicine and strengthening existing transportation programs. As the lack of indigenous-specific identifiers in many of the country's health data sources continues to be a challenge,[41] our study provides important data in describing access to cancer services and its association with outcomes on a national level, as a first step in striving toward equitable healthcare delivery for FNIM peoples.

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GLOBAL PERSPECTIVES

Mwanza, Tanzania: Challenges and change in RT delivery during global health residency

Adam C. Olson, MD

As a global health resident at Duke University and an Association of Residents in Radiation Oncology (ARRO) Global Health Scholar, I was fortunate to spend 4 months at Bugando Medical Centre (BMC) in Mwanza, Tanzania, during my radiation oncology residency. My initial visits to the oncology clinic at BMC predated their ability to treat patients with radiation therapy (RT), but in my final visit, RT became operational. It was highly gratifying to see patients in need receiving appropriate treatment.

The United Republic of Tanzania is a low-income country of approximately 49 million people in eastern sub-Saharan Africa and an estimated 46% of Tanzanians live below the poverty line of $1.90 per day. BMC is a tertiary care referral hospital in Mwanza, Tanzania, the largest city in the Lake Zone of northwestern Tanzania (**Figure 1**).

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BMC is the only hospital in the Lake Zone with fellowship-trained oncologists for adult oncology, pediatric hematology/oncology and radiation oncology. The Tanzanian government supported BMC's creation of a dedicated oncology clinic in 2012 (**Figure 2**).

RT Services and Staff

RT services at BMC were planned to commence in 2014; however, implementing RT was delayed by technical and human capacity limitations. The BMC RT center contains 4 vaults with sufficient shielding for megavoltage teletherapy, 1 vault for orthovoltage therapy, 2 simulator rooms, and 1 brachytherapy suite suitable for high-dose rate brachytherapy. The BMC RT department began treating patients in August 2017. Current equipment includes a single Bhabhatron-II cobalt-60 teletherapy unit (Panacea Medical Technologies, Bangalore, India) and an IMAGIN simulator (Panacea Medical Technologies, Bangalore, India) capable of fluoroscopy, digital X-ray generation, and cone-beam computed tomography (CT) image acquisition. Two multi-energy linear accelerators have been donated but are currently nonoperational, primarily due to the high cost of a service contract (**Figure 3**).

FIGURE 1. *Map of Tanzania highlighting the 6 regions comprising the Lake Zone (dark blue).*

Current staff at BMC includes 1 radiation oncologist, 1 medical physicist, 2 radiation therapists, and 1 nurse. My clinical experience focused on the oncologic care of cancer patients in both the outpatient and inpatient settings. Before BMC could offer RT services, a typical clinical encounter included a history and physical examination, recommending additional testing for diagnosis or staging, and/or a

FIGURE 2. *Oncology clinic at Bugando Medical Centre*

FIGURE 3. *Donated linear accelerator at Bugando Medical Centre. To the author's knowledge, it remains uninstalled and non-operational.*

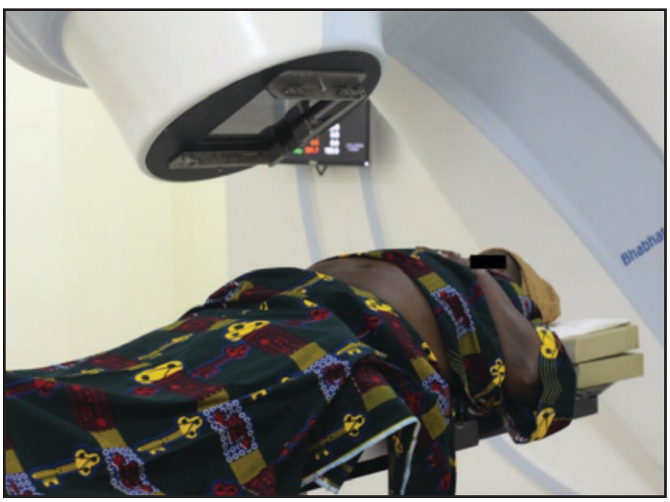

FIGURE 4. *First patient treated with radiation therapy at Bugando Medical Centre*

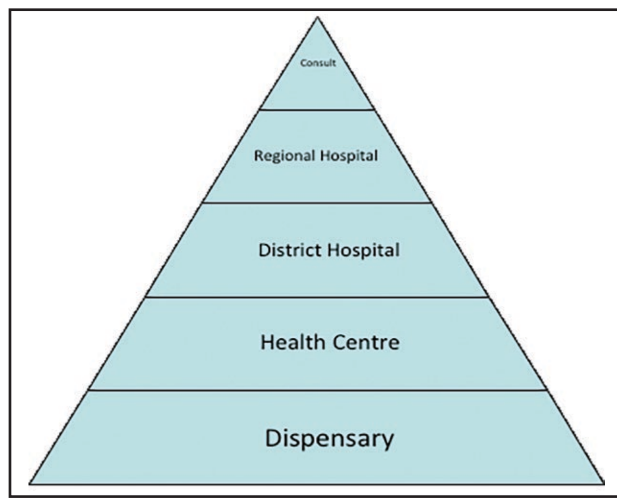

FIGURE 5. *Diagram of healthcare system of the Lake Zone of Tanzania*

prescription for treatment. Staging studies for many malignancies were difficult and expensive to acquire, particularly cross-sectional imaging, so cheaper tests such as x-rays and ultrasounds were often used in lieu of computed tomography (CT). Magnetic resonance imaging (MRI) was not available in that region of Tanzania. In addition to my outpatient responsibilities, I rounded with the clinical team at least twice a week. I rounded with the adult oncology and pediatric oncology services and saw a wide range of patients with cancers.

Cancer Cases

Typically, cancer cases in both the outpatient and inpatient setting were locally advanced and/or metastatic. The reasons for this outcome appear to be multifactorial, but clinical suspicion for cancer at the primary care level appears to be low. As mentioned above, accessing and paying for a workup is out of reach for most Tanzanians. On a cultural and societal level, there is a significant stigma associated with a cancer diagnosis. I suspect many patients choose not to pay for a workup because they believe cancer is a uniformly fatal diagnosis and paying for a staging workup and treatment is a futile endeavor.

BMC treated its first patient with RT in the fall of 2017 (**Figure 4**).

She was a grandmother in her mid-50s who had experienced intermittent vaginal bleeding for several months. She was told by the medical practitioners at her local medical facility that this was of no serious concern. Her bleeding worsened and she then developed pelvic pressure and pain. She was eventually seen by a gynecologist, who performed a vaginal exam and identified a large mass arising from the cervix. A biopsy confirmed squamous cell carcinoma. She had clinical evidence of pelvic sidewall involvement with no evidence of distant metastases by chest x-ray and abdominal ultrasound. She completed a course of definitive external-beam radiation therapy utilizing AP/PA (anteroposterior/posteriorant-erior) fields to 45 Gy with concurrent cisplatin. A brachytherapy boost would only be available at Ocean Road Cancer Institute in Dar es Salaam, the most populous city in Tanzania more than 1,100 km from Mwanza. She was referred there, although I do not know whether she was able to afford the trip.

Research Efforts

In addition to my clinical rotation, I performed some basic epidemiologic research utilizing a hospital-based cancer registry. I validated, assessed, and utilized the BMC cancer registry to guide RT services planning for BMC. I compared the number of cases at BMC to epidemiologic benchmarks used internationally based on the expected number of cases for the Lake Zone population. Because the dataset I used is a hospital-based registry and not population-based, a thorough understanding of the local healthcare delivery environment is important to provide context. BMC is 1 of 3 tertiary consultant hospitals in Tanzania and the only cancer center in the Lake Zone Region of Tanzania. While BMC saw roughly 12% of the expected cancer patients within the Lake Zone region, it is unknown how many are seen in local health care facilities. Entry into the health care system is often initiated at the local dispensary level or health centers, which is attended by medical assistants and nurses, and typically provides preventive services (eg, vaccines, maternal-child health) with limited laboratory or diagnostic testing. There is typically 1 for every 50,000 people. These refer to District Hospitals, then Regional Hospitals, and finally 1 of the 3 consultant hospitals where diagnostic capacity for cancer exists (**Figure 5**).

I validated the cancer registry data by comparing it to the patient charts and determined that the concordance was acceptably high. I then determined the expected RT utilization rate to be approximately 56%, significantly higher than most developed countries and likely due to the high rate of locally advanced cervical cancer. Current RT capacity at BMC, unfortunately, falls far short of the clinical need. Human resources, teletherapy, and brachytherapy are required to meet the RT need for the Lake Zone.

Conclusion

In conclusion, my experience at BMC was a highlight of my residency training. It was informative and compelling. My current practice at UPMC Hillman Cancer Center includes consulting on challenging cancer cases with UPMC's many international collaborative efforts. As radiation therapy is an essential component of cancer care, expanding RT access is a clinical and moral imperative.

A world of difference: Addressing the global need for radiation oncology systems

Mary Beth Massat

According to the World Health Organization (WHO), approximately 70% of cancer deaths occur in low- and middle-income countries (LMIC).[1] However, less than 30% of low-income countries have treatment services and only 26% have pathology resources.[1] On top of that, only 20% of LMICs have the data needed to drive cancer policy.[1] This disparity results in late-stage detection of cancer or worse, as well as inaccessible diagnosis and treatment.

"There is a tremendous lack of access to radiation oncology services in developing countries," says Larry Daugherty, MD, a radiation oncologist at Alaska Cancer Treatment Center in Anchorage, Iditarod musher, and co-founder of RadiatingHope, a nonprofit charitable organization dedicated to improving radiation oncology care around the globe (**Figures 1A-B**).

RadiatingHope around the world

RadiatingHope raises funds through donations, mountain climbing and prayer flags—an idea that spawned while Dr. Daugherty and co-founder Brandon Fisher, MD, a radiation oncologist with Gamma West Cancer Services in Ogden, Utah, were medical students. As they were scaling mountains and carrying prayer flags for patients, they realized they could raise money for RT in developing countries through these efforts. Given that 50% to 60% of all cancer patients can benefit from radiation therapy (RT),[2] the impact of securing RT equipment for LMIC residents would be enormous.

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Today, funds from these efforts pay to refurbish and install older RT systems. On a recent climb on Kilimanjaro, for instance, more than $50,000 was raised in a single expedition.

John Einck, MD, president of RadiatingHope and a professor of Radiation Medicine and Applied Sciences at the University of California San Diego School of Medicine and co-chair of its brachytherapy program, says the organization provides high dose rate (HDR) brachytherapy, linear accelerators and other equipment to countries in need.

"There was a realization that in the US, facilities are getting rid of radiation oncology systems that we think are end of life but could be refurbished and repurposed for use in areas of the world where they don't have this equipment," says Dr. Einck.

Tanzania, for example, has two functioning RT systems for its 45 million people. In contrast, the US has on average one system per 100,000 citizens.

Since its inception, RadiatingHope has donated and installed dozens of machines in 13 different countries, including linacs in Honduras and Tanzania, and HDR brachytherapy units in Ghana, Senegal and Nepal (**Figure 2**).

Funding the refurbishment and installation of donated systems is only part of the challenge, however. Sustainability and its many layers of education, training and perseverance is also essential.

"We can't install a machine and be done," says Dr. Einck. "We need to first create a sustainable system, including a partner on the ground that can perform quality assurance for safety and perform the necessary maintenance."

In some cases, equipment has been donated to areas that weren't fully ready. But fortunately, success stories outnumber failed attempts. In one case, already stretched oncologists at a site in Senegal were working long hours and often lacked time to perform brachytherapy procedures. RadiatingHope helped install a linear accelerator and HDR brachytherapy system so they could treat their nation's biggest cancer killer, cervical cancer.

Another success story was in Nepal, where a ground-up approach became the framework for results. "This was a cancer center organically created by an amazing oncologist who believed in and desperately wanted to elevate care," says Dr. Daugherty. "He was ready to accept new technology in a modern cancer center. However, they didn't have reliable electricity or adequately trained staff. So we accomplished one hurdle at a time and

FIGURE 1. *A) Larry Daugherty, MD, co-founder of RadiatingHope, prepares to summit Mt. Kilimanjaro. B) One of six groups from RadiatingHope prepares for its first fundraising climb on Mt. Kilimanjaro in Tanzania in April 2014. Since then, RadiatingHope has organized more than 300 fundraising adventures all over the world. Photo courtesy of RadiatingHope.*

FIGURE 2. *Tom Ladd (right), executive director of RadiatingHope, with an HDR brachytherapy system donated to Kathmandu Cancer Center in early 2019. Dr. Subhas Pandit, head of radiation oncology at the center, is to the immediate left of the HDR system. Photo courtesy of RadiatingHope.*

a developed a model that we can scale to other places."

Most interestingly, he adds, is that the linac is powered by a diesel generator—something engineers said was impossible. This story fuels the optimism that, even with limited resources, RadiatingHope can help revolutionize RT in developing countries and aid local oncologists in saving tens of thousands of lives.

Battling brain drain

Qualified staff and education pose another challenge, due in part to a "brain drain" over the last few decades, whereby the best and brightest leave to pursue education in a developed country only to never come back. To address this problem, RadiatingHope has created centers of excellence in LMICs so physicians and staff can learn—and ideally remain—in their native country. The model has been used successfully in Sweden to keep radiation oncology clinicians in northern rural regions.

"The general consensus is that it is the lack of people with the knowledge on how to use these systems—the radiation oncologist, dosimetrist, physicist, nurse—that is the key challenge we face," says Derek Brown, PhD, director of the UCSD Radiation Oncology Learning Center, Program Director of the Medical Physics Residency Program, and associate professor at UCSD who is involved with RadiatingHope and i.treatsafely.

i.treatsafely provides access to high-quality and practical learning videos to improve quality and safety in radiation therapy. The nonprofit organization initially held one- to two-day workshops in different countries; however, this proved an inefficient means of maximizing outreach. The organization turned to YouTube and now provides free access to 300-plus videos. About half of the users are outside of North America and Europe, notes Dr. Brown.

ASTRO, ARRO address educational needs

To further address education and training, the American Society for Radiation Oncology (ASTRO) and the Association of Residents in Radiation Oncology

FIGURE 3. *A) RadiatingHope donated a cobalt machine with a newly loaded high dose rate (HDR) afterloader at B) the Institut Curie in Senegal. C) Simulator film from one of the first brachytherapy implants performed at Institut Curie in Senegal. Photos courtesy Dr. Einck.*

(ARRO), the resident section of ASTRO, formed a Global Health Initiative that includes a Global Health Scholars program. Samuel Marcrom, MD, a resident at the University of Alabama at Birmingham, is vice chair of ARRO's Executive Committee and co-chair of the Global Health Subcommittee.

"Beyond equipment, we need people who know how to use the equipment and can stay informed of the latest advances," Dr. Marcrom says. "Through our mentorship program (Global Health Mutual Mentorship Program), radiation oncology trainees in other countries can learn from trainees in the US, and vice versa."

While radiation oncology is in its infancy regarding global health compared to some other fields, fortunately it can glean lessons from their experiences.

"We are trying to learn from the history of other disciplines such as infectious disease," Dr. Marcrom explains. "It is possible to think you know the needs of other people and regions and be completely wrong."

He advocates a needs assessment that includes organizations and residents, and evaluates what type of education or changes the local people need and are amenable to. "Then we can intervene and help," he says. "Cookie cutter education materials will not work in every country every time."

The ARRO Global Health Initiative and RadiatingHope have also worked with Rayos Contra Cancer, or Rays Against Cancer, which is committed to expanding access to radiation oncology through education, training, research and collaboration, beginning in Latin America. An official partner of Project ECHO (Extension for Community Healthcare Outcomes) based out of the University of New Mexico School of Medicine, Rayos Contra Cancer uses a hub-and-spoke, knowledge-sharing network model to pair experts around the world with clinics that lack radiation oncology education and training.

By also addressing financial limitations, Serguei Castaneda, MD, a resident at Drexel University College of Medicine, co-chair of ARRO's Global Health subcommittee and vice president of Rayos Contra Cancer, helped bring an HDR brachytherapy system to a cancer center in Nepal.

The case for cobalt

"Many low-income countries don't have a healthcare system that pays for radiation oncology and that is a huge limitation to access," says Dr. Castaneda, who was also an ARRO Global Scholar. In such cases, older cobalt systems (**Figure 3A-C**) can deliver a significant benefit. Consider that a modern linac requires simulation software, advanced MR and positron emission tomography/computed tomography (PET/CT) imaging, plus additional education and training for 3-dimensional (3-D) treatment plans. In contrast, with a cobalt-based therapy unit, simulation is performed on the unit, it can withstand high throughput with limited downtime, and it costs significantly less.

"They can treat more patients at a lower cost with cobalt, so it is the most efficient and cost-effective way to deliver radiation in these areas," says Dr. Castaneda.

Adds Dr. Marcrom, "In areas where radiation access is severely limited, it is possible that treating more people with older, less complex and more reliable technology, such as cobalt, may potentially be better than treating fewer patients with more advanced equipment. It's a tough balance, with no quick or simple solution."

Other key challenges include lack of infrastructure, particularly electrical power. That's why the HDR brachytherapy and cobalt radiation therapy systems are great options for areas without a stable power grid.

"An HDR unit is compact, has fewer moving parts and is less complex than a linac so it is easier to keep it operational," says Dr. Einck. "The main drawback is the unit needs a 10-curie source made of iridium-192 and it may

FIGURE 4. A new Halcyon system installed in February 2019 at the NSIA-LUTH Cancer Treatment Centre in Idi-Araba, Lagos, Nigeria. Also installed were two VitalBeam radiation therapy systems. Photo courtesy of Varian.

FIGURE 5. The CyberKnife System at the Mount Miriam Cancer Hospital in Tanjong Bungah, Penang, Malaysia. Photo courtesy of Accuray.

be hard to obtain this in some regions of the world."

Additionally, consideration must be given to Ministry of Health decisions and goals regarding a country's people and the resources needed to acquire, operate and sustain an advanced radiology oncology system.

Vendors respond to global RT needs

Radiation therapy system manufacturers have also made a global impact, either by collaborating with organizations such as RadiatingHope and ARRO Global Health, or through direct investment in a country.

"We are entering an era that will see the largest demand for global health needs," says Chris Toth, president of Oncology Solutions, Varian Medical Systems, Palo Alto, California. "Communicable diseases are largely under control and people in low- to middle-income countries are living longer. While cancer today is the No. 2 killer globally, by 2030 it will be No. 1."[3]

In China, for example, estimates suggest that by 2030 the country will have more than 8 million new cancer cases each year, representing one-third of the global cancer burden. Yet, only 25 percent of the population has access to radiation oncology, says Toth.

As a sponsor of the Cancer Foundation of China, Varian provides education to hospital presidents, radiation oncologists, and residents in training. Through the foundation and associated programs, Varian hopes to increase access in medium-sized cities of 5 million plus residents so patients can limit or avoid traveling for care. Academic medical centers in China will also have free access to Varian's oncology software solutions to use in education and training.

Additionally, in India Varian recently signed a three-year agreement with Tata Trusts, one of the country's oldest philanthropic organizations, to install RT treatment systems as a preferred supplier. Toth estimates the agreement will reach upward of 200 linacs with a capacity to treat 250 000 patients each year. As with China, he notes that only 25 percent of Indians have access to radiation oncology services.

There may also be an opportunity to harness artificial intelligence (AI) and machine learning (ML) to deliver technology-enabled services such as high-quality treatment plans. In many clinics throughout the developing world, even if a clinician and staff can operate their radiation oncology equipment, they may lack time and expertise to develop a more advanced 3D treatment plan. Whether the solution is cloud-based or software infused with an AI or ML algorithm to guide development of the treatment plan, Toth sees an opportunity to provide planning guidance as a fee-for-service to areas throughout the world.

"We also need to cross the chasm and create more capabilities for delivering care by engineering solutions differently," adds Toth. He points to the company's Rapid Plan knowledge-based treatment planning that uses ML to help generate a baseline treatment plan, and the Halcyon system (**Figure 4**) with an intuitive user interface, standardized workflows, one-step patient setup, and ability to image and treat patients in nine steps.

A Varian RT system recently installed in Tanzania, for instance, was used to treat a 5-year-old girl with retinoblastoma, a curable cancer. Without this system, she would have not had access to treatments that saved her life.

Describing the lack of RT systems in developing countries as "a massive problem," Ioannis Panagiotelis, chief marketing officer at Elekta (Stockholm, Sweden), says that according to the Global Task Force on Radiotherapy for Cancer Control (GTFRCC), there will be a 12 000-plus linac system gap to meet the needs of LMICs by year 2035.[3] More importantly, he adds, is that 30 000 radiation oncologists, 22 000 medical physicists and 80 000 radiation technologists are needed in this same time frame.[4] In fact, data compiled by the IAEA in 2013 reported that, at the time, more than 30 countries had no radiation therapy service at all.[5] Elekta recently installed a system in one of these countries, Nicaragua.

The company also donated a linac to Al Bashir Hospital in Amman, Jordan, in 2018, facilitated through the International Atomic Energy Agency's (IAEA) Programme of Action for Cancer Therapy in response to the influx of Syrian refugees. The five-year survival rate across all cancers is 46% in Jordan, compared to 86% in the US.

Elekta is also investing directly in China and in many regions of Africa, long recognizing the need for education and training in those and many other areas. After a linac sale in Algeria, for example, Elekta worked with the site to send a medical physicist to France for training, and later worked with the Ministry of Health to open an education center hub in Algeria for ongoing training needs.

In addition, Elekta has sponsored fellowship programs for the past decade to train oncologists and medical physicists to operate linear accelerators and plan more complex treatments. And in China, the company launched an RT Academy to train technologists in anticipation of the country's growing need for cancer care.

Elekta is also establishing local offices to further support sales, training and service. "Service is a critical aspect that has been impeding progress in the past," says Panagiotelis. Currently, the company says 80 percent of Elekta systems worldwide are connected to Elekta IntelliMax, providing securely controlled remote access for support and predictive maintenance. Plans are to soon achieve 100% connectivity.

To address power supply problems, Elekta is investigating whether other renewable sources of energy, such as solar energy, could power a linac, says Panagiotelis, noting that a prototype is undergoing testing.

At Accuray, the company has built relationships with distributors and local medical associations to address the need for systems and service in LMICs. Birgit Fleurent, chief marketing officer, says the company has collaborated with the European Society for Radiotherapy and Oncology (ESTRO) Cancer Foundation and the Union for International Cancer Control and its C/Can 2025: City Cancer Challenge, which supports cities that lead the design, planning and implementation of cancer treatment solutions.

Success, however, often relies on the country's healthcare policy, says Fleurent. A 2017 resolution at the 70th World Health Assembly called for member states to adopt a cancer prevention and control policy that includes reducing premature mortality from noncommunicable diseases—including cancer—by one-third. Such a policy is needed for sustainable education, training, service and financing for capital equipment and healthcare funding, she says.

"It is critical that countries have a policy in place that links cancer care and radiation therapy with healthcare coverage," she stresses. "That policy needs to start with prevention, then screening and treatment, including palliative and end-of-life care. Cancer care is a continuum and the WHO resolution for countries to implement cancer care policy is a must-have."

Accuray has seen success in developing countries when multiple stakeholders—public and private—have come together to address the need for cancer care and the funding behind it. While the perception may be that developing countries need a low-cost "value" system, adds Fleurent, that is not necessarily true.

She notes that Accuray's RT systems—the Radixact, TomoTherapy and CyberKnife (**Figure 5**)—were designed to help clinicians deliver precise and accurate radiation therapy to patients for a wide range of cancers, regardless of where they reside. It's important, she adds, that clinicians can effectively control the cancer and minimize side effects that compromise quality of life.

"We believe, along with other vendors, that low- to middle-income countries need systems that are a workhorse and offer state-of-the art treatments for patient safety and quality of life," she says. However, most important is patient access to all forms of cancer treatment.

"Radiation therapy is not generally used as a stand-alone," Fleurent adds, "rather it is complementary to surgery, chemotherapy and immunotherapy. So we need to raise awareness of all viable cancer treatments."

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RADIATION ONCOLOGY CASE

Nasopharyngeal stenosis following curative chemoradiation therapy for oropharyngeal cancer in a patient with active oral lichen planus

Luke Massaro, BA; John Fantasia, DDS; Dev P. Kamdar, MD; Nagashree Seetharamu, MD; Sewit Teckie, MD

BACKGROUND

Lichen planus is an inflammatory disorder of immune dysregulation that affects the skin and mucosa. Oral lichen planus (OLP) is a chronic variant characterized by white mucosal lesions,[1] most commonly with bilateral buccal mucosa involvement and frequently involving the tongue and gingiva as well.[2] Although the underlying cause remains obscure, OLP is thought to have an autoimmune etiology and has been linked with genetic factors, hypertension, diabetes mellitus, hepatitis C virus, and thyroid dysfunction.[3]

OLP onset involves the activation of immune pathways leading to migration and activation of T cells and the destruction of keratinocytes.[4] It is thought that oral mucosal keratinocytes are activated by the expression of unknown antigens, which recruit lymphocytes. This T-cell-mediated response is coupled with the simultaneous nonspecific response of matrix metalloproteases, chemokines and mast cells, together causing apoptosis of the basal keratinocytes by various mechanisms.

OLP can undergo malignant transformation to oral squamous cell carcinoma (OSCC) in a small subset of OLP patients (1%), more commonly in smokers, alcoholics, and hepatitis C patients.[5] It is thus considered an OSCC precursor lesion. Topical steroids are the first-line treatment, but systemic steroids and topical calcineurin inhibitors can be used to manage recalcitrant cases.[6]

Oral and oropharyngeal SCC are commonly treated with surgery and/or radiation and chemotherapy, which cause adverse reactions including mucositis, xerostomia, dysphagia, dysgeusia, and thrush. These toxicities can persist weeks to months following treatment, and severity is correlated with the chemoradiation (CRT) dose.[7] Pharyngoesophageal stenosis, a late effect, can significantly compromise quality of life, often necessitating parenteral nutrition.[8]

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In this report, we present a case of a patient with active OLP for 26 years who was diagnosed with HPV-associated oropharyngeal SCC and treated with CRT. Following treatment, nasopharyngeal stenosis and dysphagia developed.

CASE SUMMARY

A 63-year-old woman presented to her physician with a sore throat, dysphagia and an enlarged left neck lymph node. She had a 26-year history of OLP for which she followed regularly with a dentist. She has a 7.5 pack-year smoking history and quit 25 years before presentation.

After fine-needle aspiration of the lymph node raised suspicion for malignancy, the patient was referred to a head-and-neck surgeon. Examination identified white oral patches consistent with OLP. In addition, an exophytic left base of tongue (BOT) lesion was visible (**Figure 1A**). Nasopharyngoscopy showed no involvement of the tonsils or right BOT.

IMAGING FINDINGS

Computed tomography (CT) of the neck confirmed a left BOT mass with inferior extension to the vallecula, crossing the left glossotonsillar sulcus. A 2.5-cm left level IIA cervical nodal involvement and smaller adenopathy in left level IIB and left level III were

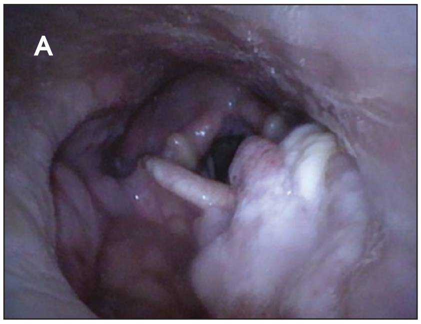

FIGURE 1A. *Laryngoscopy before chemoradiation (CRT) showing patent pharyngeal inlet and exophytic left base of tongue tumor.*

identified. A PET/CT (positron emission tomography/CT) showed hypermetabolic activity in the left BOT and the identified left neck lymph nodes.

DIAGNOSIS

A biopsy of the BOT confirmed a diagnosis of AJCC (American Joint Committee on Cancer) 7th edition stage cT2N2bM0 HPV-positive SCC of the oropharynx (overall stage IVA).

TREATMENT

The patient underwent concurrent CRT to a total dose of 7000 cGy over 33 fractions, with cisplatin 100 mg/m^2 delivered on days 1, 22, and 43 of radiation. The radiation technique was intensity-modulated radiation therapy (IMRT) with volumetric-modulated arc therapy (VMAT) and a simultaneous integrated boost. Target volume coverage was excellent, with planning target volume (PTV) 7000 D 95% = 6800 cGy. Doses to organs at risk were minimized while prioritizing optimal PTV coverage. Dose to nearby superior constrictor muscles were mean 6361 cGy and max dose 7336 cGy, and middle constrictors received mean 6650 cGy and max 7415 cGy. Hot-spot dose closest to the area that developed stenosis was 105%, or 7350 cGy (**Figure 1B**).

Treatment was completed without breaks. She experienced the following expected side effects: grade 3 mucositis (**Figure 2**); grade 2 dysphagia, dermatitis, dysgeusia, constipation; and grade 1 pruritis, neck edema, nausea, xerostomia, and salivary duct inflammation. She was able to tolerate soft and some solid foods during the treatment course. Karnofsky Performance Score was stable at 80% to 90% throughout the course, and oral analgesics were not required. She lost 11.5% of her body weight during CRT.

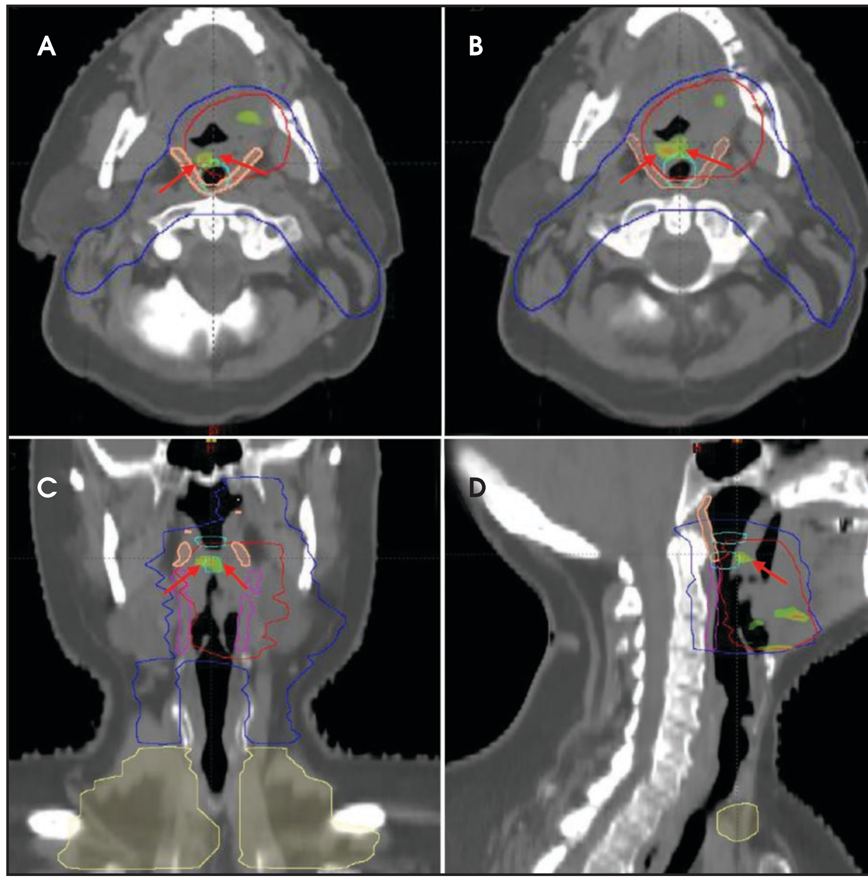

FIGURE 1B. *Computed tomography (CT) simulation images in multiple planes (A/B – axial, C – coronal, D – sagittal) demonstrating the relationship between PTV_7000 (red), PTV_6300 (blue), area that developed nasopharyngeal stenosis (neon blue), superior constrictor muscle (peach), and 105% 7350 cGy hotspot near the nasopharyngeal inlet (red arrows seen on all planes). PTV = planning target volume.*

During follow-up, she had no evidence of disease clinically and radiographically on PET/CT scan, and she experienced improvement in saliva production and gustation. However, she complained of dysphagia at the conclusion of CRT without improvement 8 months later. She could not eat large portions or gain weight, and experienced dyspnea while eating. Nasopharyngoscopy revealed marked stenosis of the pharyngeal inlet at the level of the inferior nasopharynx (**Figure 3**). Specifically, there was moderate narrowing of the inlet to the oropharynx, with an approximately 1 cm opening (normal inlet opening: ≥ 3 cm).

FIGURE 2. *Confluent oropharyngeal mucositis noted 6 weeks after chemoradiation (CRT).*

RADIATION ONCOLOGY CASE

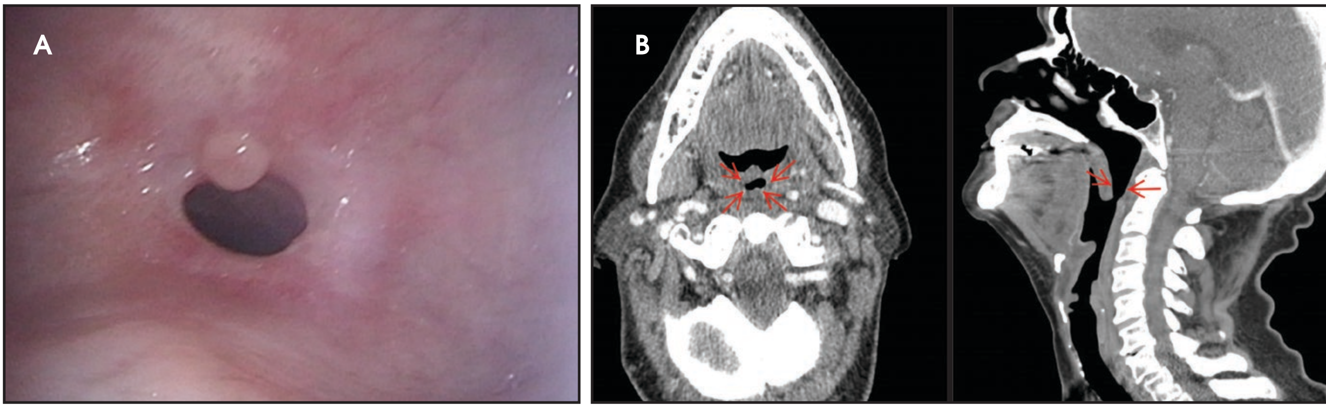

FIGURE 3. *(A) Nasopharyngoscopy demonstrating nasopharyngeal stenosis 9 months after chemoradiation (CRT). (B) Nasopharyngeal stenosis on axial and sagittal neck CT with contrast 10 months after CRT, 1.25-mm scan slice thickness.*

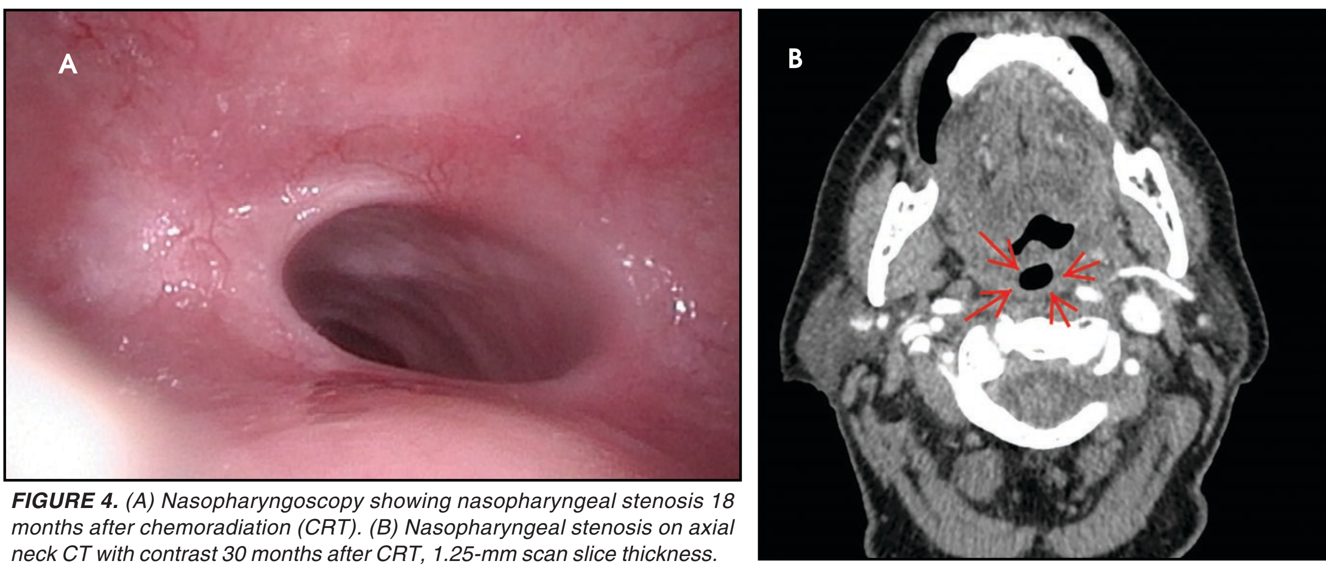

FIGURE 4. *(A) Nasopharyngoscopy showing nasopharyngeal stenosis 18 months after chemoradiation (CRT). (B) Nasopharyngeal stenosis on axial neck CT with contrast 30 months after CRT, 1.25-mm scan slice thickness.*

Mucosal surfaces were notable for telangiectasias and post-RT fibrosis. True vocal cords, supraglottis, and hypopharynx appeared normal.

The patient's surgical oncologist initiated a conservative regimen of intranasal inhaled steroids twice a day and nasal saline 4 times a day, which led to gradual improvement. A percutaneous endoscopic gastrostomy tube was not inserted. A year later, she reported subjective swallowing improvement for the first time. Eighteen months after initiating this regimen, she tolerates soft foods without difficulty and repeat nasopharyngoscopy demonstrates a wider nasopharyngeal opening with less circumferential stenosis (**Figure 4**).

DISCUSSION

Long-term dysphagia as a result of radiation-related stenosis is an uncommon complication of CRT typically observed in patients with hypopharyngeal malignancies. Nasopharyngeal stenosis is rarer, although it has been reported in cases of RT for nasopharyngeal carcinoma.[9] It is unclear why mucosal injury from CRT resolves spontaneously in some patients while it progresses to stenosis/stricture in others.[10] Nonradiation risk factors for stricture include chemotherapeutic agents, tumor characteristics, age, sex, and patient co-morbidities. We believe that OLP was a risk factor for this patient's stenosis. Radiation-related factors shown to contribute to pharyngoesophageal stricture, a similar post-CRT complication, include dose, fractionation, target, and technique.[11] The structures at risk during radiation that can lead to long-term dysphagia are the constrictor muscles, the BOT, the larynx, the upper esophageal sphincter, and esophagus.[12] Efforts should be made during planning to reduce the dose to these structures, particularly the constrictor muscles.[13] Different CRT delivery may have prevented this complication; for example, radiation fraction size (212 cGy) should be limited to ≤ 200 cGy. In addition, weekly cisplatin dosing is less likely to cause severe mucositis[14] and therefore may lead to less permanent dysphagia. In this particular patient, hotspots were not excessively high (105%). We did not prioritize constrictor muscle dose constraints over PTV coverage. As a result, the constrictors received a high mean and maximum dose. These doses may have contributed to the development of the localized stenosis in this region. However, we have never at our institution observed a similar complication in any of the dozens of oropharyngeal and nasopharyngeal cancer patients who receive similarly high doses to this region; therefore, this case exhibits a rare complication. We hypothesize that the chronic inflammatory state of oral lichen planus is related to this unusual complication. It is unclear if reducing constrictor dose would have made a difference in the setting of the chronic inflammatory state.

In this case, our patient had active OLP during CRT. The patient had known disease in the oral cavity, but additional inflammatory involvement of the pharynx is possible. Although less common than oral involvement, lichen planus can involve any mucosal surface and there are reports of LP affecting laryngeal and esophageal mucosa.[15,16] Esophageal lichen planus is becoming increasingly recognized and is reportedly seen in a quarter of patients with OLP, often with patients complaining of dysphagia.[17] The presence of this disease process close to the radiation field could have created subclinical pharyngeal mucosal disease or an inflammatory milieu that contributed to severe mucosal injury, ultimately leading to nasopharyngeal stenosis. In the setting of an autoimmune process such as OLP, the radiation-induced inflammation of the oral/pharyngeal mucosa may lead to hyperactive immune response, resulting in fibrosis and stricture formation during recovery. To our knowledge, this mechanism has not yet been reported. It is unclear if the HPV association of this tumor plays any role in the aforementioned inflammatory response.

Treatment of pharyngeal stenosis requires knowledge of its cause and severity. Nasal steroids were used in this case because the stenosed area was accessible to inhaled medication and because the patient experienced sinonasal symptoms secondary to the stenosis. Conservative treatment here was effective and durable. Strictures refractory to medical therapy are amenable to serial dilation. Deeper tissue injury and scarring can also occur following aggressive CRT,[18] and treatment options available for these cases include balloon dilation and reconstructive surgery.

CONCLUSION

We report a case of long-term nasopharyngeal stenosis and dysphagia post-CRT for HPV-related OPSCC in a patient with a long history of active OLP. Her inflammatory state combined with radiation-induced fibrosis likely led to stenosis, which lasted almost 2 years before conservative treatment eventually improved symptoms. We advise that OLP patients who will receive RT/CRT undergo pre-treatment multidisciplinary consultation with their oncologists and dentist to select an ideal treatment paradigm for their unique conditions. This proactive approach may prevent pharyngeal stenosis and dysphagia post-CRT in the setting of chronic inflammatory conditions such as OLP.

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RADIATION ONCOLOGY CASE

Asymptomatic pneumomediastinum and subcutaneous cervical emphysema without esophageal tear following gastrostomy-associated pneumoperitoneum in oropharyngeal cancer

Nirav V. Patel MD; Nagy Elsayyad, MD; Charif Sidani, MD

CASE SUMMARY

More than 500 000 cases of head and neck cancer are diagnosed worldwide each year.[1] Placement of a gastrostomy tube (G-tube) is often needed during definitive radiation therapy (+/- chemotherapy) for cancers of the head and neck. Although this procedure is usually uncomplicated, it is reportedly associated with a complication rate of 13.7% and mortality rate of 0.3%.[2] Pneumoperitoneum is common after such procedures, and is self-limited when no findings indicate organ perforation.[3] Pneumomediastinum, on the other hand, is a rare complication after G-tube placement.[4] In general, pneumomediastinum may occur due to a complete tear of the esophagus (secondary to direct trauma or violent vomiting with retching), spontaneous pneumothorax, or gangrenous (gas-forming) infections.[5,6] We present a rare case of a patient who was incidentally found to have asymptomatic pneumomediastinum and subcutaneous emphysema of the neck approximately two weeks after G-tube placement without evidence of an esophageal tear.

Dr. Patel is a resident and Dr. Elsayyad is an assistant professor in the Department of Radiation Oncology, and Dr. Sidani is an associate professor in the Department of Radiology, all at the University of Miami Sylvester Comprehensive Cancer Center, Miami, FL.
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.

A 48-year-old man was diagnosed with p16 positive squamous cell carcinoma of the base of the tongue with bilateral cervical lymphadenopathy (stage II, cT2N2M0, American Joint Committee on Cancer [AJCC] 8th edition). He was treated definitively with intensity-modulated radiation therapy (IMRT) with concurrent weekly cisplatin 40 mg/m^2. Reactive placement of a gastrostomy tube became necessary when oral intake decreased substantially. This tube placement was advised prophylactically but at the outset was refused. The patient had a violent gag reflex initially, rendering routine oral examination difficult. Starting on day 2 of radiation therapy and chemotherapy, he developed vomiting that became intractable. On day 28 of the radiation therapy course after 34 Gy / 17 fractions over 23 days, percutaneous endoscopic gastrostomy (PEG) tube placement was attempted but failed due to an inability to find a clear window with transillumination. The patient subsequently underwent G-tube placement under fluoroscopic guidance by the interventional radiologist and was discharged in stable condition. Over the following two weeks of treatment, he continued to experience persistent nausea, vomiting, and retching despite the use of various anti-emetics and benzodiazepines (prescribed for extreme anxiety). At fraction #27 of radiation therapy, daily cone-beam computed tomography (CBCT) that was obtained as part of intensity-guided radiation therapy (IGRT) showed subcutaneous emphysema (**Figure 1**) not present on prior imaging. At the time, the patient had no chest pain, dyspnea or fever, and there was no evidence of respiratory or hemodynamic instability. On examination, the chest and precordium were unremarkable, vital signs were normal, and a crepitus of subcutaneous emphysema could be elicited in the left side of the neck from the left angle of the mandible down to the supraclavicular region. A CT of neck/chest/abdomen with IV contrast revealed pneumoperitoneum (**Figure 2**), pneumomediastinum (**Figure 3**), and subcutaneous

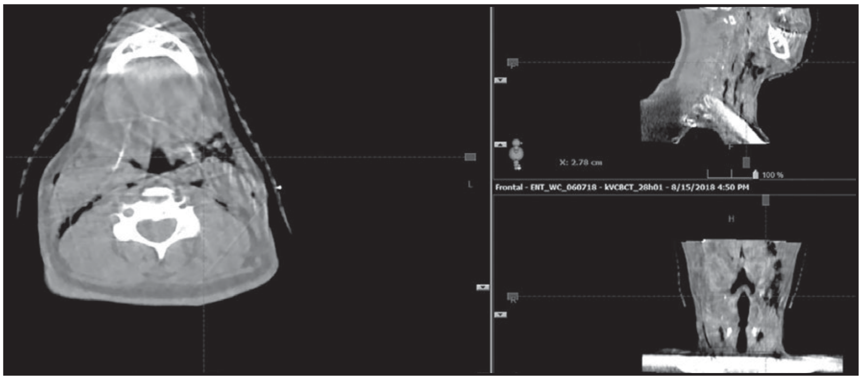

FIGURE 1. *Subcutaneous emphysema in the neck incidentally detected on daily cone-beam computed tomography (CBCT).*

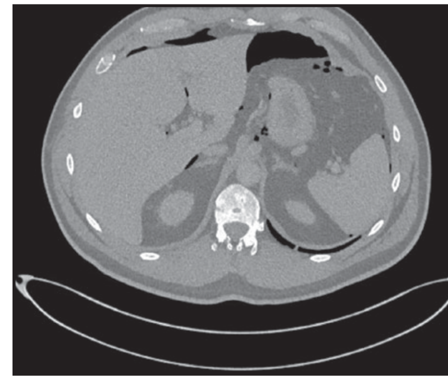

FIGURE 2*. Pneumoperitoneum noted on diagnostic abdominal computed tomography (CT)*

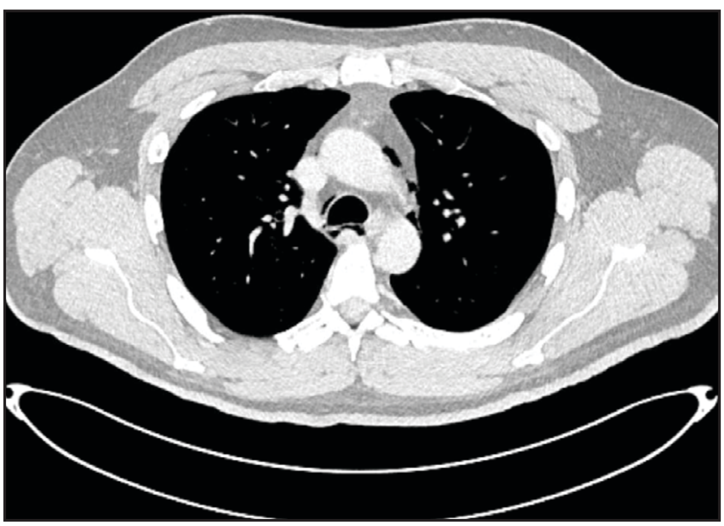

FIGURE 3. *Pneumomediastinum noted on diagnostic chest computed tomography (CT).*

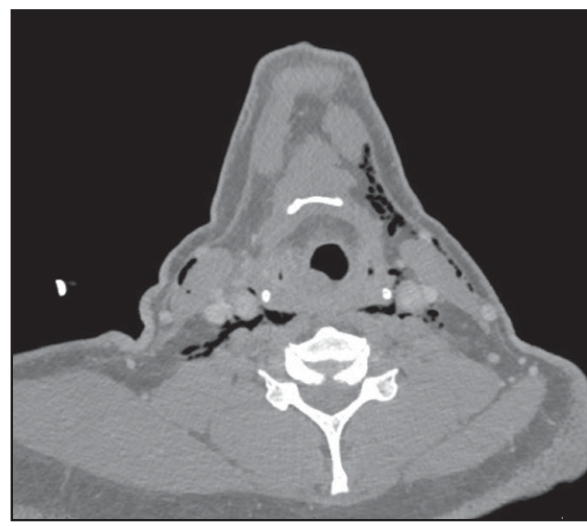

FIGURE 4. *Subcutaneous emphysema noted on diagnostic neck computed tomography (CT).*

emphysema in the neck (**Figure 4**). An oral Gastrografin (Bracco Diagnostics Inc., Monroe Township, New Jersey) study was attempted but his odynophagia and retching rendered it impossible to perform. An esophagogastroduodenoscopy (EGD) was carefully performed with caution (minimizing air insufflation). There was no esophageal tear and the esophageal mucosa appeared entirely normal with no evidence of mucositis. A fluoroscopic upper GI series with small bowel follow-through was obtained by introducing Gastrografin through the G-tube and did not show extraluminal contrast extravasation. He was observed as an inpatient for one week and remained hemodynamically stable and free of clinical evidence of mediastinitis or respiratory distress. Follow-up imaging revealed resolving pneumoperitoneum, pneumomediastinum, and subcutaneous emphysema. The patient was discharged in stable condition and completed his radiation therapy course. At the end of his course, the cervical lymphadenopathy could no longer be palpated and no tumor could be seen at the primary site on examination.

IMAGING FINDINGS AND DISCUSSION

We report on a patient who was incidentally noted to have pneumomediastinum, and subcutaneous neck emphysema approximately two weeks after G-tube placement without attributable symptoms and without evidence of esophageal tears. Yount et al described two patients who developed symptomatic pneumomediastinum without esophageal perforation within 24 hours after PEG.[4] To our knowledge there have been no reports of pneumomediastinum development and subcutaneous emphysema after pneumoperitoneum following G-tube placement with no mediastinal symptoms.

Pneumomediastinum is most concerning for esophageal perforation, particularly in patients with a history of vomiting and retching as was the case with our patient. Patients usually present with retrosternal chest pain, dyspnea, cough, esophageal odynophagia, or dysphagia, and quickly deteriorate into hemodynamic shock.[7] A high level of suspicion is warranted as delayed diagnosis can have a significant prognostic impact with mortality ranging from 20% to 35%.[8] Gastrografin esophagram remains the standard for diagnosing esophageal rupture but may have a false negative rate of up to 10%. Endoscopy is controversial as the endoscope together with the insufflated air may enlarge a perforation and worsen the condition. Treatment of pneumomediastinum may involve surgery or nonoperative management, including nothing by mouth for 24-48 hours, broad spectrum antibiotics for 7-10 days, and total parenteral nutrition.[9]

In our patient, esophageal rupture was ruled out by endoscopy and the source of air may be explained by two potential processes: First, pneumoperitoneum, a fairly common complication of G-tube placement, with an incidence as high as 50% following such procedures, may be a potential source of air tracking back to the mediastinum. The source of pneumoperitoneum, in turn, may be insufficient fixation of the tube into the peritoneal cavity. Alternatively, air may escape into the peritoneal cavity during the procedure when the needle punctures the abdominal wall and stomach.[10] In most cases, pneumoperitoneum following PEG is a benign and self-limited process that does not require additional intervention.[3]

In most patients there is no direct path for air to escape from the peritoneum to the mediastinum, but pneumoperitoneum may result in pneumomediastinum via the diaphragmatic hiatus as a result of congenital anomalies, weak points, defects, or tears near the diaphragmatic hiatus.[11-12] The risk of developing pneumomediastinum in this manner is thought to be associated with high intraperitoneal pressures, which was likely the case in our patient who was persistently retching. From the mediastinum, air can potentially dissect the fascial planes, which ultimately manifests as subcutaneous emphysema in the neck.

An alternative mechanism to explain the pathogenesis of pneumomediastinum in our patient is the development of a "spontaneous pneumomediastinum" as originally described by Louis Hamman in 1939. Caceres et al found Valsalva maneuvers, particularly emesis, and sudden increase of intrathoracic pressure to be the predominant initiation event of spontaneous pneumomediastinum in their retrospective review.[13] In much the same manner as above, air may enter directly into the abdominal cavity through a pleuroperitoneal defect.[12]

Regardless of the source of air, this patient's pneumomediastinum was incidentally noted on daily CBCT, which is otherwise utilized to verify patient alignment.[14] This case highlights the importance of using daily imaging not only for geometric verification purposes, but also for evaluating anatomical changes that may warrant additional workup or a pause in treatment. Moreover, the patient's pneumomediastinum proved to be clinically inconsequential and slowly resolved spontaneously. Despite the absence of sequelae from this process, one must maintain a high level of concern with this radiographic finding as any delay in diagnosis of a possible underlying esophageal tear may result in significant morbidity and mortality. Further studies are warranted to determine the incidence and implications of this rare finding during the treatment of head and neck cancer patients who require G-tube insertion.

CONCLUSIONS

We report on an interesting and rare finding of pneumomediastinum and subcutaneous emphysema of the neck approximately two weeks after G-tube placement incidentally detected on CBCT. The value of the case report is to call attention to identifying this rare problem, to emphasize that in this case it was not associated with a poor outcome contrary to the usual expectation with pneumomediastinum, and to report an additional advantage of frequent CBCT.

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