VOLUME 34 · NUMBER 1 · JANUARY 1, 2016

JOURNAL OF CLINICAL ONCOLOGY

REVIEW ARTICLE

Establishing and Delivering Quality Radiation Therapy in Resource-Constrained Settings: The Story of Botswana

Jason A. Efstathiou, Magda Heunis, Talkmore Karumekayi, Remigio Makufa, Memory Bvochora-Nsingo, David P. Gierga, Gita Suneja, Surbhi Grover, Joseph Kasese, Mompati Mmalane, Howard Moffat, Alexander von Paleske, Joseph Makhema, and Scott Dryden-Peterson

Jason A. Efstathiou, David P. Gierga, Massachusetts General Hospital, Harvard Medical School; Scott Dryden-Peterson, Brigham and Women's Hospital, Boston, MA; Magda Heunis, University of Stellenbosch and Tygerberg Hospital, Cape Town, South Africa; Talkmore Karumekayi, Remigio Makufa, and Memory Bvochora-Nsingo, Gaborone Private Hospital; Joseph Kasese, Bokamoso Private Hospital; Mompati Mmalane, Joseph Makhema, and Scott Dryden-Peterson, Botswana Harvard AIDS Institute; Howard Moffat, Botswana Ministry of Health, Gaborone, Botswana; Gita Suneja, University of Utah School of Medicine, Huntsman Cancer Hospital, Salt Lake City, UT; Surbhi Grover, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA; and Alexander von Paleske, Mpilo-Hospital, University of Zimbabwe, Bulawayo, Zimbabwe.

Published online ahead of print at www.jco.org on November 16, 2015.

Authors' disclosures of potential conflicts of interest are found in the article online at www.jco.org. Author contributions are found at the end of this article.

Corresponding author: Jason A. Efstathiou, MD, DPhil, Department of Radiation Oncology, Massachusetts General Hospital, Harvard Medical School, 100 Blossom St, Cox 3, Boston, MA 02114; e-mail: jefstathiou@partners.org.

0732-183X/16/3401w-27w/$20.00

DOI: 10.1200/JCO.2015.62.8412

ABSTRACT

There is a global cancer crisis, and it is disproportionately affecting resource-constrained settings, especially in low- and middle-income countries (LMICs). Radiotherapy is a critical and cost-effective component of a comprehensive cancer control plan that offers the potential for cure, control, and palliation of disease in greater than 50% of patients with cancer. Globally, LMICs do not have adequate access to quality radiation therapy and this gap is particularly pronounced in sub-Saharan Africa. Although there are numerous challenges in implementing a radiation therapy program in a low-resource setting, providing more equitable global access to radiotherapy is a responsibility and investment worth prioritizing. We outline a systems approach and a series of key questions to direct strategy toward establishing quality radiation services in LMICs, and highlight the story of private-public investment in Botswana from the late 1990s to the present. After assessing the need and defining the value of radiation, we explore core investments required, barriers that need to be overcome, and assets that can be leveraged to establish a radiation program. Considerations addressed include infrastructure; machine choice; quality assurance and patient safety; acquisition, development, and retention of human capital; governmental engagement; public–private partnerships; international collaborations; and the need to critically evaluate the program to foster further growth and sustainability.

J Clin Oncol 34:27-35. © 2015 by American Society of Clinical Oncology

INTRODUCTION

The global burden of cancer is enormous and growing. The greatest increase in incidence is found in low- and middle-income countries (LMICs) where cancer is a major cause of morbidity and mortality and is anticipated to account for up to 70% of new cancer cases and cancer-related deaths worldwide.[1-4]

Although much emphasis has been appropriately placed on prevention and screening, treatment remains an essential element of a comprehensive cancer control program. Radiation therapy is a critical and cost-effective component of cancer care in the definitive, adjuvant, and palliative settings.[4,5] Curative for many localized cancers, radiation is also particularly effective in controlling and extending survival in locally advanced cancers, as well as in palliating metastatic disease by offering symptom control. Advanced cancers are more common in LMICs, because of late presentation and diagnosis increasing need for radiation.[6]

Globally, access to radiation therapy is linked to a country's wealth. Although 50% to 60% of patients with cancer receive radiation at some point during their course of treatment in high-income countries, many LMICs do not have adequate access to radiotherapy despite increased need.[7,8] Worldwide, only 40% to 50% of required radiation services are being met and 36 countries have no radiation capabilities. In fact, there is an immediate global need for an additional 4,000 to 7,000 radiation machines (depending on estimated number of courses or fractions per year and operating hours per day) and there is an even greater scarcity of trained professional radiation personnel in LMICs.[9] In Africa, this disparity is particularly pronounced, with only approximately 25% of the need being met and 29 of 54 countries having no functioning radiation facility.[4,9,10] The available facilities are also concentrated in the higher-income countries in northern and southern Africa (Fig 1).

Although there are numerous challenges in implementing a radiation therapy program in a low-resource setting, providing more equitable global access to radiotherapy is a responsibility and investment worth prioritizing. Acknowledging that developing a radiation center needs to be

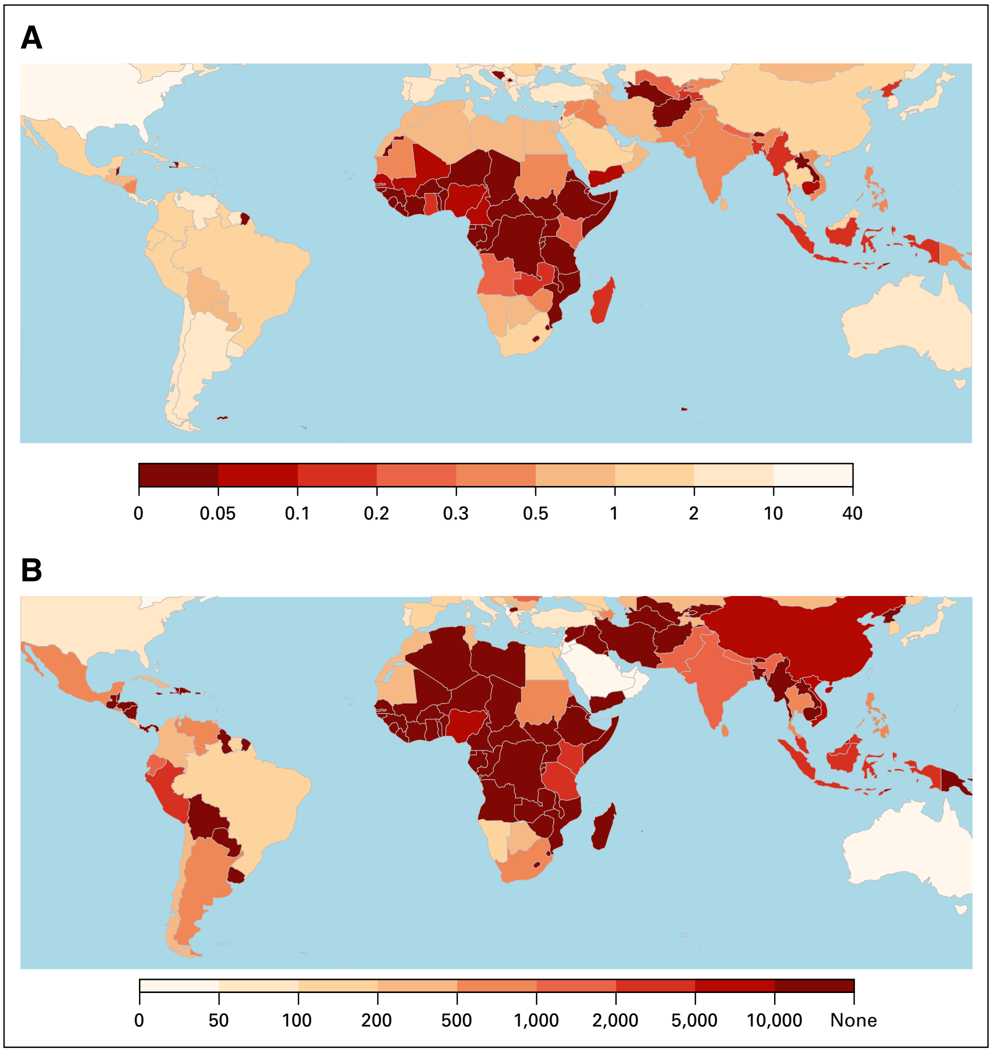

Fig 1. (A) External beam radiation therapy (EBRT): world map of the number of EBRT units (linear accelerator and cobalt-60 units) per million population. (B) High-dose rate (HDR) brachytherapy: world map of annual cervical cancer cases per HDR unit (600 to 800 patients with cervical cancer per HDR unit per year is considered high use, assuming eight to nine procedures per day).[2,10]

approached on an individual country basis given that there is not a single blueprint, and on the basis of the experience in Botswana from the late 1990s to the present, we outline a systems approach and a series of key questions to direct strategy toward establishing quality radiation therapy facilities in LMICs.

Although Botswana has assets of good governance and relative wealth compared with its regional neighbors, it is important to consider that this was not always the case.[11] At the time of its independence in 1966, Botswana was the poorest country in Africa. When advocates initiated efforts to introduce radiation therapy, Botswana's economy in real terms was smaller than nearly all African countries today and its income per capita was only modestly higher than the region today. Consequently, we hope that the story of investment in developing radiation therapy in Botswana can provide a possible example for other LMICs.

WHAT IS THE NEED FOR RADIATION THERAPY?

Determining the need for radiation therapy requires an appreciation of the demographics of the population, cancer incidence and types, and estimates of national disease burden with evidence-based projections for the future. Demand needs to factor in the proportion of the patient population that would benefit from radiation therapy on the basis of cancer site, stage distribution at presentation, and availability of alternative treatment modalities (eg, surgical oncology). Population cancer registries are crucial to estimating need. Further projections regarding anticipated radiotherapy capacity and use (number of radiation courses and fractions per course for each cancer type, as well as the amount of potential retreatment) should also be estimated.[4,8,9]

For most families in Botswana in the late 1990s, life was characterized by an exploding HIV epidemic with weekends spent traveling between multiple funerals for persons with AIDS. Little was known about the burden of cancer, and it was not a priority of the Ministry of Health. Cancer survivors and clinicians joined to form the Cancer Association of Botswana and the Botswana National Cancer Registry.[12] The distribution of registered cases, including those referred to South Africa for radiation treatment, and the recognized growing burden of HIV-associated cervical cancer (risk of invasive cervical cancer increased nearly six-fold in individuals with HIV)[13] and other human papillomavirus-associated cancers[14] provided strong justification for both external beam radiation therapy (EBRT) and brachytherapy.

Table 1. Radiation Usage and Availability in Botswana: Gaborone Private Hospital Oncology Statistics 2001-2014

	Linear Accelerator			Unplanned Downtime (days)	
Year	Patients	Fractions	Brachytherapy Insertions	Equipment	Power
2001	335	5,360	N/A	2	0
2002	469	6,120	N/A	3	0
2003	503	6,895	N/A	4	0
2004	523	7,205	N/A	3	0
2005	566	8,959	N/A	5.5	0
2006	590	9,917	N/A	7.5	0
2007	593	10,088	N/A	6	0
2008	615	9,952	N/A	4.5	0
2009	599	9,966	N/A	8	0
2010	633	9,988	N/A	12	0
2011	735	10,160	N/A	9.5	0
2012	738	10,280	399	17	6
2013	789	10,120	560	19	18.5
2014	890	12,043	689	6	9

NOTE. A general benchmark of between 400 and 500 patients per external beam radiation therapy machine per year was used to measure machine throughput.[9]

Cervical cancer is the leading cause of cancer-related mortality and alone accounts for over 80% of patients receiving radiation in Botswana. Locally advanced cervical cancer requires chemoradiation with both EBRT and brachytherapy for cure. In fact, it has been estimated that more than 70% of cervical cancer cases in LMICs require brachytherapy.[9] Radiation therapy also plays a central role in the management of many other common cancers in Botswana, including breast (such as postmastectomy EBRT for locally advanced disease), head and neck (often human papillomavirus-related for which radiation is effective), lung, esophagus, and prostate; and in the palliation of metastatic disease.[15] Despite rapid expansion of EBRT and, subsequently, brachytherapy in Botswana (Table 1), the continuing growth in annual cases requiring radiation has outpaced capacity (Fig 2).

WHAT IS THE VALUE AND BENEFIT OF ESTABLISHING RADIATION?

Once need has been established, the question arises of whether it is worth the investment. Clearly defining and communicating the value of radiation to a broad range of relevant stakeholders (eg, general public, health-care providers, advocacy groups, policy makers, vendors, international agencies, and other collaborators) is useful to solidify broader support. Radiation has been found cost effective for many cancers in high-income countries[16] and it is expected to be even more cost effective in LMICs,[16a] although further quality studies are urgently needed.

Radiation therapy needs to be recognized as critical to the development of the health sector. The health benefits that can be expected by appropriate use of radiation (ie, value to patients regardless of curative or palliative treatment intent) and the economic benefits to the region that might arise from improving the health of the population with cancer need to be considered. Value to the economy is real, because it can be an opportunity to keep the population in the workforce longer and potentially decrease cost of care by avoiding outsourcing of care. Furthermore, there is the altruistic, moral, ethical, and humanitarian appeal of providing value to society. Few would argue against the notion that increased emphasis is needed on establishing access to and affordability of better-value radiation and cancer therapies. This makes not only economic sense but is an opportunity to take national pride in improving the stature of one's country and provide a regional example of success.

In Botswana, it was the private sector that identified the oncology market and developed a successful business model for radiation therapy. In the late 1990s, Gaborone Private Hospital (GPH), then owned by South Africa-based AFROX, hired a motivated clinical oncologist (M.H.) to lead development of oncology services. After construction of a radiation bunker and installation of a linear accelerator (LINAC; Elekta, Stockholm, Sweden), the first patients were treated in 2000. The center at GPH has grown and employs a professional staff of more than 30 employees, fostering further economic benefits to Botswana beyond health benefits.

The success of the private sector in radiation therapy is tied to the strong commitment to quality care by the Botswana Ministry of Health. Shortly after the implementation of radiotherapy, the government began fully supporting the costs of radiation at GPH for its citizens. Recognizing the improved access and coordination afforded by in-country treatment and decreased cost relative to referrals to South Africa, the government achieved best value through support of care at GPH. Public-sector patients now compose greater than 90% of the radiation-treated patient population in Botswana, and it is unlikely that the private-sector investment would have been realized without the development of the public–private partnership.

WHAT IS NEEDED TO ESTABLISH A RADIATION PROGRAM?

Implementation of a radiation program requires thinking critically about the core investments that are needed within the local context. Paul Farmer, who, through Partners in Health, has pioneered treatment of complicated diseases in under-resourced regions, has said that one needs to think about "the staff, stuff, space, and systems."[17]

A clear understanding of issues related to the available local infrastructure should be developed[18-21] through an assessment of the existing health-care system, including hospital and community referral clinics already in place and the proportion of the population accessing those systems. What is the geography and population distribution? To address accessibility, the proximity of the population to centers where treatment may be centralized and to available transportation systems to facilitate such access needs to be evaluated. What is the space availability and optimal location for construction of the facility? Considerations also include available pathology, laboratory, medical, surgical, imaging, palliative, and auxiliary services, including information technology. Ultimately, delivery of good cancer care requires multidisciplinary input and coordination of care. Diseases such as cervical, rectal, and head and neck cancers are often best treated with concurrent chemotherapy and surgery, highlighting the need for a functional medical oncology unit as well as surgical expertise. Sometimes, prioritization of patients and cancers treated (radical v palliative) may be needed. In addition,

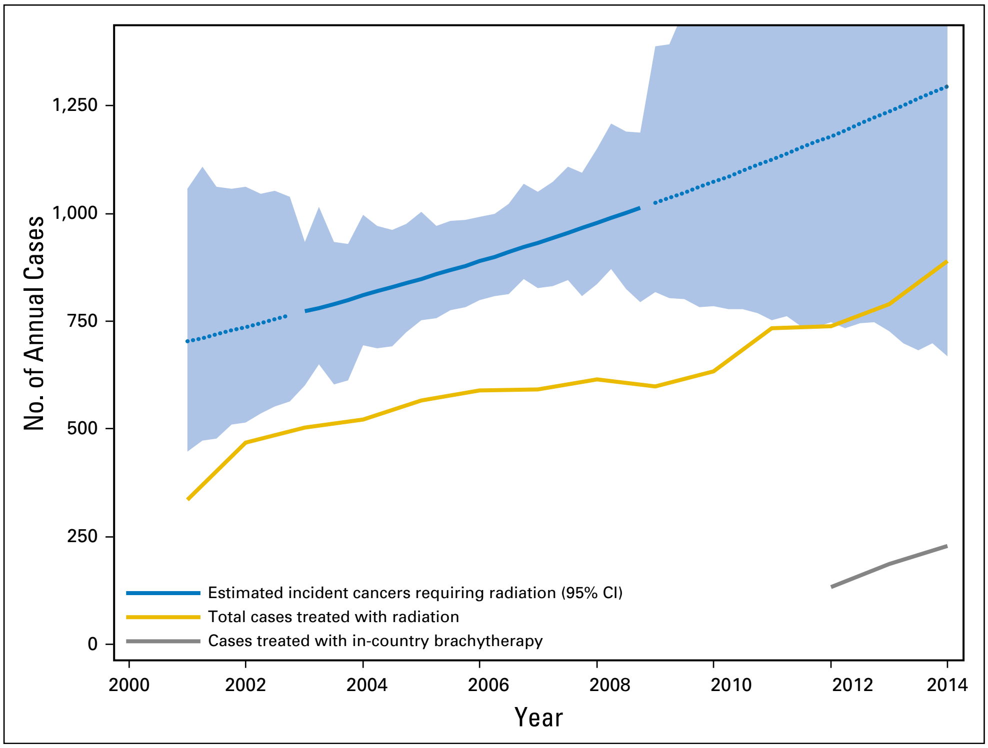

Fig 2. Gap in demand and supply for radiation therapy in Botswana. Data are available from the Botswana National Cancer Registry between 2003 and 2009; the dotted line is a projection beyond data frame (projected from the inverse probability weighted Poisson model with bootstrap CI). For this chart, cancer requiring radiation included cervical, breast, head and neck, lung, esophageal, anal, brain, lymphoma, vulvar, vaginal, penile, conjunctival, and sarcoma.

considerations must be given to the reliability of the electrical grid and power supply and the ability to ensure security of radiation sources and expensive equipment. Successful and sustainable models of financing and funding are paramount and typically involve synchronizing efforts in the public and private sectors.

Beyond the bunker and the machine, development or acquisition of human capital, including clinical oncologists, medical physicists, dosimetrists, therapists, nurses, and engineers, is one of the most important investments and can be challenging.[9,18-21] The government of Botswana, recognizing this need, delayed development of a public radiation facility until citizens could be trained. The government of Botswana was presented an opportunity by the International Atomic Energy Agency (IAEA) to receive a cobalt unit; however, without skilled in-country staff to operate the machine, the government opted to decline this offer. Demonstrating an alternative, GPH recruited expatriate professionals to guide and staff its developing radiation facility. The GPH unit provides ongoing exposure to radiation skills to Botswana nationals returning from IAEA-supported training.

The IAEA serves a vital role in human resource capacity building in LMICs.[22] In Botswana and throughout the region, the IAEA has supported the training overseas of a full team. The IAEA has also provided assistance in many LMICs through the provision of requisite equipment (eg, radiation machine, imaging system, treatment planning system, software, record and verify system, immobilization and fixation devices, dosimetry and quality assurance equipment).[22] In practice, it is likely that the acquisition of equipment and the training of personnel (which will likely be abroad initially) need to happen simultaneously.

Recruitment and retention of a trained team requires a functional and well-supported radiation facility. In particular, there is a strong global demand for trained radiation personnel, because providers and supporting professionals will migrate to locations where their expertise can be practiced. Consequently, the development of physical facilities needs to be developed in concert with development of human capital. In Botswana, retention of trained public-sector radiation oncologists has depended on the public–private partnership with GPH to provide a fulfilling role as a public facility is developed.

WHAT ARE THE LOCAL ASSETS AND BARRIERS TO THE IMPLEMENTATION OF A RADIATION PROGRAM?

When assessing local capabilities for radiation services, it is important to ask what assets can be leveraged and what barriers need to be overcome?

As has been detailed,[11,23] Botswana has substantial infrastructure in place to build upon, including a stable democratic government and a growing strong economy with little corruption. Accordingly, it has invested in health care provided by the government for free, including radiation therapy, and there is a network of hundreds of community health clinics (just about every village has a clinic) and dozens of regional hospitals, including three referral centers. The success of its public HIV antiretroviral treatment program (greater than 90% of its citizens who require treatment receive therapy) is laudable and provides precedence in tackling other emerging public health challenges.

Yet there remain many challenges to the implementation of radiation therapy. Botswana is a large and relatively sparsely populated country, with the bulk of patients with cancer residing in rural communities. The distance poses many transportation challenges, given that the centralized radiation services are located in the capital of Gaborone, where urbanization has been more of a

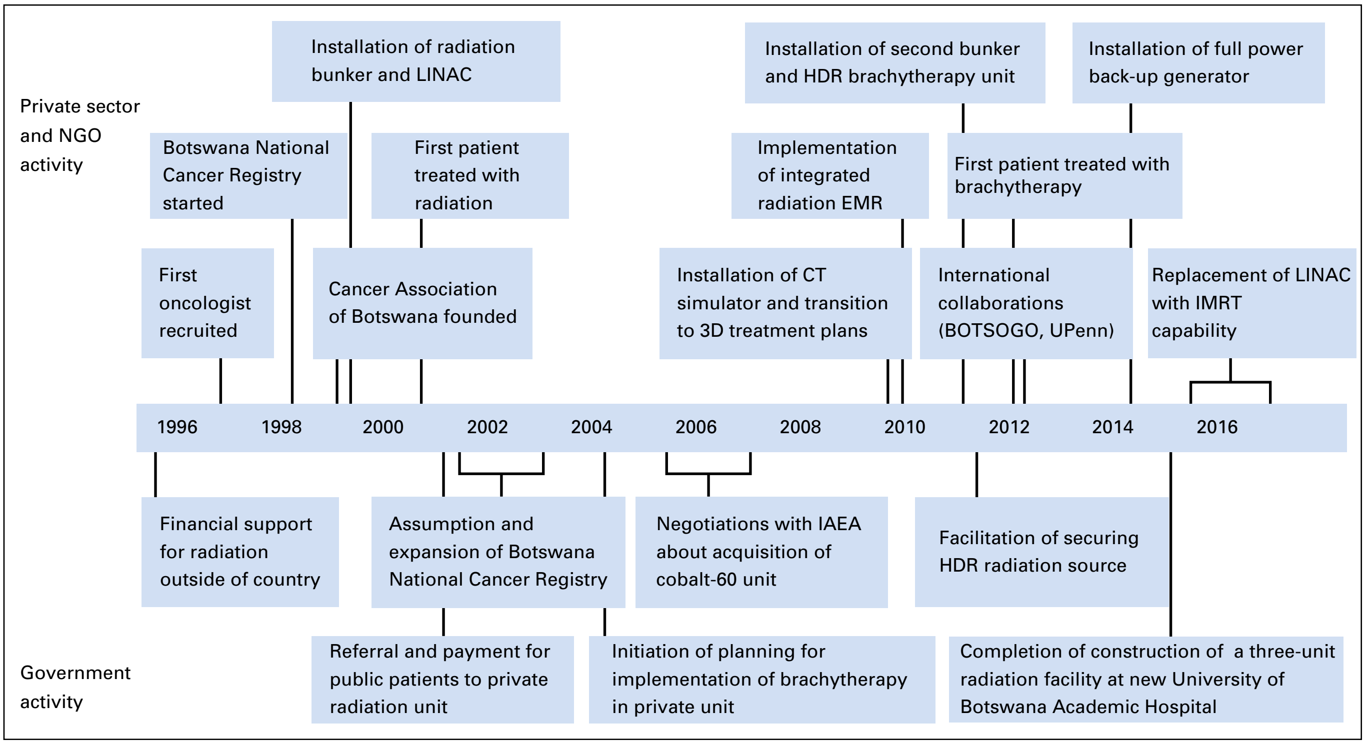

Fig 3. Timeline of key milestones in the development of radiation therapy in Botswana. 3D, three dimensional; BOTSOGO, Botswana Oncology Global Outreach program; CT, computed tomography; EMR, electronic medical record; HDR, high-dose rate; IAEA, International Atomic Energy Agency; IMRT, intensity-modulated radiation therapy; LINAC, linear accelerator; NGO, nongovernmental organization; UPenn, University of Pennsylvania.

trend of the young, wealthy, and educated. Although the Cancer Association of Botswana provides much-needed interim housing for patients relocating from great distances during their multiweek course of radiation, this housing is always at capacity, leading to hospital admissions solely for accommodation purposes and further contributing to overcrowding at such public facilities.

In addition, there remain many cultural barriers to care, including the stigma of cancer and the practice of seeking alternative care in the form of traditional healers. Indeed, public education and literacy rates among patients with cancer need improvement. A number of these challenges contribute to late referral and more advanced cancers at presentation. Many patients referred for radiation actually never keep their appointments. Furthermore, for those who do receive radiation, there is poor follow-up care, especially for patients who are discharged back to the public sector where there is limited expertise in managing radiation toxicities and monitoring for signs of recurrence.

A significant shortage of trained health-care professionals and lack of local expertise exists. With no postgraduate training or continuing medical education programs for development of personnel in radiation oncology, there has been a reliance on recruiting expatriate clinical radiation oncologists in both the private and public sectors and sending personnel abroad for training. Originally, there was only one clinical radiation oncologist who was trained in South Africa and who championed the growth of the program in Botswana. Personnel have been recruited from Zimbabwe, South Africa, and Zambia. The program has grown to three radiation oncologists, one medical oncologist, one physicist, seven radiation therapists, and two nurses in 2015. Importantly, two current oncologists are Botswana nationals who have returned from training.

Aside from the short supply of human resources, there are also significant barriers to much-needed diagnostic capacity and availability of medications (eg, chemotherapy, antiemetics, analgesics, and antibiotics). Furthermore, local bureaucracy occasionally stunts fluid care delivery and continuity, including the need to replace the radiation source for brachytherapy approximately every 3 months.

Proximity to South Africa has enabled Botswana to benefit from an accessible regional partner with more resources, including more advanced medical capabilities (eg, specialized pathology and treatment) and servicing. In fact, as Botswana was developing its radiation facility, all electrical power came from South Africa. The assumption was that this stable power supply would always be readily available. However, as South Africa began rationing electricity because of its own domestic demand, and Botswana grew more independent in providing electrical power, there has recently been an increase in periodic electrical outages and machine downtime (Table 1).

WHAT IS A REALISTIC AND FEASIBLE TIMELINE FOR ESTABLISHMENT OF RADIATION SERVICES?

Through private initiative and with the local assets detailed in this article, and despite the barriers, radiation therapy has been implemented in Botswana, with equipment currently comprising one linear accelerator and one high-dose rate unit, both housed at GPH. Figure 3 outlines the timeline and the milestones achieved in this effort. Further growth in available radiation capacity in the public sector is expected with a fully constructed, although not yet equipped or staffed, university hospital that will have dedicated oncology facilities.

Table 2. Pros and Cons of Cobalt-60 Versus LINAC

Characteristic	Cobalt-60	LINAC
Power supply	Can operate in suboptimal conditions, reliable	Needs stable electrical supply
Dose distribution	Large penumbra and shallow penetration	Enables more conformal treatment
Safety	Contains a live radioactive source, potential for higher exposure to personnel, simpler maintenance and quality assurance	A more sophisticated device that may require additional attention and resources dedicated to ongoing maintenance and quality assurance
Flexibility	Fixed photon energy, longer treatment times, needs fewer resources	Multiple photon and electron energies, higher dose rate, more versatile
Cost	Lower initial cost but requires periodic source replacement	Higher initial capital cost

Abbreviation: LINAC, linear accelerator.

HOW DO YOU DECIDE BETWEEN A LINAC AND COBALT-60 MACHINE?

Consideration of a number of factors, including cost, infrastructure (electricity source and reliability), human resources, patient population, service contracts, stability of the region, and security of the source, as well as quality assurance needs are paramount to deciding which machine to acquire (Table 2).

For a resource-limited area, the decision to use a cobalt-60 unit or a linear accelerator for radiotherapy depends on the local circumstances.[24,25] The use of LINACs in Africa is increasing; it is estimated that the percentage of LINACs in use has increased from 40% to 68% since 1998.[24,26] With a reliable power supply and adequate access to trained maintenance, a LINAC is preferred, although curative and effective radiation treatments are certainly also possible with a cobalt-60 unit. LINACs can deliver higher-energy photons, which offer improved skin sparing and is better suited to treat deep-seated tumors, such as those in the pelvis (eg, cervical, prostate). Dose distributions from photon beams from LINACs are more conformal because of the larger source size and resulting larger penumbra (lateral falloff) for cobalt. LINACs also have the flexibility to generate electron treatment beams, which can be advantageous for superficial tumors, such as those of the skin. The higher complexity of LINACs does require more frequent quality assurance, ideally performed by a qualified medical physicist. Obtaining a cobalt source may involve more regulatory or safety hurdles than a LINAC because the source is obviously highly radioactive and cannot be turned off. Furthermore, the beam intensity decreases over time (and treatment time increases) because cobalt-60 has a half-life of 5.3 years, and it is recommended that the source be replaced every 5 years.

A cobalt unit, however, has the major advantage of being able to operate in an environment with a poor or unreliable electrical power supply, ensuring that radiation is nearly always available to treat patients. Initial capital costs for a cobalt machine are likely less than for a LINAC. Furthermore, the treatment area may require less shielding because of the lower photon energy from cobalt. The advantage of more advanced radiation delivery of a LINAC must therefore be balanced with the potential disadvantage of increased downtime due to an unreliable power supply or increased machine breakdown. The types of disease also factor into the decision because treating advanced cancers with very large fields reduces the need for more precise dose delivery.

Negotiations with vendors are recommended, as is obtaining multiple bids. Very clear, comprehensive service and maintenance contracts should be prioritized with a cost structure for paying for repairs and with stated expectations regarding timely access to consultants and service providers. At GPH in Botswana, the decision was made to use a LINAC, given familiarity with such units by the involved radiation oncologist and the desire for higher energy and for clinical flexibility. Service for the LINAC is reasonably available from a vendor in neighboring South Africa. Overall, considering the setting and the age of the LINAC, the radiation unit at GPH has had an admirable record with minimizing machine downtime (Table 1). Unit managers attribute this performance to rigorous adherence to monthly and comprehensive annual maintenance schedules and ongoing investment (eg, a back-up electricity generator, components replacement).

HOW DO YOU DELIVER SAFE QUALITY RADIATION?

Having a machine does not necessarily reflect the ability to deliver quality radiation. Despite a relative lack of human resources and equipment, a radiotherapy facility should devote attention to patient safety and ensuring quality delivery of care. At a minimum, a department should have a trained and certified medical physicist to oversee the technical aspects of radiation delivery. Medical dosimetrists are also needed to develop safe and appropriate treatment plans and perform dose calculations. There are a number of published quality assurance guidelines and suggested frameworks for implementation of new radiation technologies and treatment techniques,[19,27-30] but these must be adapted to local circumstances and resources. At a minimum, every patient's treatment plan should be reviewed by the medical physicist (with appropriate software, if available) before treatment. Further, the department should use a minimum of two trained and certified radiation therapists who will be responsible for daily treatment delivery to all patients. A lack of available trained therapists may require hiring of therapy assistants, but treatment should always occur under the direct oversight of trained staff. Radiation therapists should use a simple "time-out" policy to ensure the correct dose is administered to the correct site and to the correct patient. Policies and procedures should be developed for periodic (daily, monthly, annual) quality assurance of radiation delivery units (eg, cobalt-60, LINAC, brachytherapy). It is recognized that resources may not always be available for ongoing routine quality assurance, but special efforts should be made to verify equipment performance before initial use and after any major upgrades. Annual independent output checks for all external-beam treatment energies should also be performed (this can be done via inexpensive mail order services). A system for monitoring dose to personnel should also be in place. The department should also work diligently to foster an environment of peer review (eg, chart rounds and tumor boards, some of which could be done through remote means with international partners) and the appropriate safety culture, and encourage the tracking and reporting of treatment errors and near misses.[11]

HOW DO YOU MEASURE SUCCESS OF YOUR PROGRAM AND IDENTIFY GAPS?

Radiation therapy units in LMICs face unique challenges. Striking differences in the patient population served, the throughput required, and the underlying infrastructure make directly translating established guidelines and procedures from high-income countries tenuous. Consequently, it is even more important for radiation centers in LMICs to regularly assess performance and to share in the published literature successful and unsuccessful strategies. At defined intervals, programs should reflect and measure resource use, process indicators, machine throughput, guideline-based delivery, and outcomes that are both health-related (eg, local control, survival, toxicity, and complications) and economic (eg, cost, quantify value). These data should be analyzed, published, and used to adjust programs to optimize the holistic health value delivered to individual patients and the population served.[31]

Since its initiation, the radiation facility at GPH in Botswana has carefully assessed measures of throughput (patients treated and fractions delivered) and process (machine downtime and missed treatments) to assess returns on its private investment. In addition, clinicians have described the implementation experience with cervical brachytherapy and improvement in time to completion of treatment.[32] However, assessing posttreatment patient outcomes has only begun recently because they are more challenging to measure with rigor. Although the government funds active treatment at GPH, subsequent follow-up is to be obtained in local public clinics. This is a common feature of units in LMICs, where centralized facilities typically cannot provide longitudinal care. Where in-person visits are not possible, quarterly telephone contact to patients or their local clinic has been a low-cost method to ascertain vital status on greater than 95% of recipients. Even this basic follow-up information has identified higher-than-anticipated mortality for cervical[33] and breast cancer,[34] prompting evaluation and reconsideration of treatment protocols. Cancer registries are instrumental in evaluating patterns of care, outcomes, and quality improvement.

HOW DO YOU ALLOW FOR GROWTH AND SUSTAINABILITY OF YOUR PROGRAM?

Once radiation services are available, the demand on them and for them grows rapidly (Table 1). In Botswana, the demand on one linear accelerator for an entire country has been great. Per the IAEA, there should be one megavoltage radiation machine per a population of 250,000 to 500,000 people (as a point of reference, the United States has one machine per 70,000 people).[4,9,27] On the basis of this recommendation, Botswana may need between three and seven additional machines. Furthermore, as screening and earlier diagnosis efforts are implemented, there will be substantial increases in incidence of new cancers and a consequent stage shifting to earlier localized disease that may stress the throughput of the facility and demand more definitive and precise courses of radiation. So what is the ability and scalability of the radiation facility to sustainably treat patients, as well as grow and advance technologically?

To meet the growing demand, there is a need to expand services and update equipment. Relatively simple interventions may include extending work hours to optimize the use of equipment and decrease the number of machines needed. The unit at GPH runs 6 days per week and treats patients into the early evening when needed. In Botswana, the private sector has decided to replace its old LINAC with a new one and upgrade to intensity-modulated radiation therapy with multileaf collimators (instead of blocks) and image guidance. Volumetric modulated arc therapy to enhance throughput is being explored.

With more advanced technologies and improved imaging, the opportunity to use hypofractionated radiation schedules (ie, fewer, larger fractions) arises. Hypofractionation has gained acceptance in common cancers such as prostate, breast, and rectal, as well as in palliative settings (such as single 8-Gy fraction for bone metastases), and has the potential to improve patient throughput and convenience (especially for those with access barriers), allow for better resource use and efficiency (especially given limited treatment capacity), lower treatment costs, and even allow for possible radiobiologic therapeutic gain that may improve disease control.[35] In Botswana, to accommodate more patients and avoid treatment delays, brachytherapy for locally advanced cervical cancer is routinely hypofractionated (three treatments of 7 Gy rather than five or six treatments of 5 to 6 Gy, as is common in the United States).[36] Other means of innovative and remote technology are being looked at to address bottlenecks in contouring and treatment planning.

Further integration of radiation into multidisciplinary care with combined modality therapy, such as more conservative surgery for organ preservation and radiosensitizing chemotherapy (relevant in head and neck, cervical, breast, anorectal, lung, esophageal cancers, and limb sarcomas), may offer patients improved oncologic and functional outcomes. Additional resources are needed to improve referral systems and follow-up care, including management of complications attributable to radiotherapy.

Efforts centered on building human capital and training the next generation, as well as the promotion and retention of trained professional staff, are vital. Early investment in training programs, fostering knowledge transfer, and providing in-country technical expertise are required to ensure sustainability and expansion. Currently, there are only 10 countries in Africa that have training programs in radiation.[8] Without substantial expansion in academic programs in oncology, LMICs cannot meet the growing need for radiation therapy. These programs are vital for training new personnel, retaining existing staff, and providing a fulfilling opportunity to recruit trained personnel living abroad. Through formation of its first medical school and near completion of a comprehensive public cancer center (including two LINACs), Botswana has made important steps in this direction. However, to fulfill this educational promise, Botswana and other LMICs will need continued bidirectional partnerships with academic medical centers, professional societies, and regional centers of excellence.

Fig 4. Memory Bvochora-Nsingo, MBChB, clinical oncologist at Gabarone Private Hospital, reviewing contours and radiation planning with Paul Busse, MD, PhD, visiting radiation oncologist from the Massachusetts General Hospital, in the Botswana Oncology Global Outreach partnership.[11]

Greater engagement and coordination among local governments, regional organizations, international agencies, professional societies, academic hospitals, and volunteers is often helpful in developing cost-effective radiation therapy services and access to them.[4,37] Botswana offers a model of public–private and international partnerships. The IAEA, through its Program of Action for Cancer Therapy and advisory group on increasing access to radiotherapy technology in LMICs; the World Health Organization; and the Union for International Cancer Control Global Task Force on Radiotherapy for Cancer Control are initiatives established to assess the gap in and improve global access to radiation therapy.[16a,20,21,38-43] The IAEA technical cooperation disbursed $289 million for global projects in cancer/radiation therapy between 1980 and 2013.[22] The IAEA is developing standards and providing expertise and investment, though it needs some infrastructure to work with and the will of the local governments. In addition, there are efforts underway by the US National Cancer Institute Center of Global Health to provide collaborative funding opportunities and to develop a mentoring network through an International Cancer Expert Corps.[44] Furthermore, there is a burgeoning academic global radiotherapy movement and a number of successful examples of international academic centers in high-income countries, including the United States, twinning and collaborating to address the gap in radiation access, training, technology transfer, and research that should continue to be encouraged (Fig 4).[11,37,45-47]

Governments ultimately need to place high priority on delivering quality cancer care that includes radiation therapy to their population. Financially feasible models of collaborative decision-making, investment, and cost-sharing need to be promoted, including robust private–public sector partnerships that foster further growth and development.

In conclusion, the burden of cancer in LMICs now exceeds that of high-income countries and is growing rapidly. The vast majority of cancers in LMICs require radiation for cure or palliation, but patients most frequently die without access to either of these options. Globally, there is a mismatch of radiation treatment resources to need, with nearly 4,000 radiation units in the United States and fewer than 300 in sub-Saharan Africa,[10] a region with more than twice the population. Expansion of radiation therapy in Africa and other LMICs is possible and leads to sustainable health gains, as the story of Botswana illustrates. Introduction of radiation therapy depends on the careful understanding of the local disease burden, infrastructure, and expertise. Led by a small group of committed individuals, the Botswana expansion relied heavily on a newly formed cancer registry, partnerships with institutions in neighboring LMICs and between a private hospital company and the Botswana Ministry of Health, and with academic institutions in high-income countries. Expansion in LMICs with less national wealth than Botswana likely also will require direct financing by high-income countries or international agencies (eg, IAEA). We are optimistic that, together, these institutions can ameliorate the severe shortage of radiation therapy in LMICs and reduce suffering.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at www.jco.org

AUTHOR CONTRIBUTIONS

Conception and design: Jason A. Efstathiou, Magda Heunis, Talkmore Karumekayi, David Gierga, Mompati Mmalane, Howard Moffat, Alexander von Paleske, Joseph Makhema, Scott Dryden-Peterson
Collection and assembly of data: All authors
Data analysis and interpretation: Jason A. Efstathiou, Talkmore Karumekayi, David Gierga, Gita Suneja, Mompati Mmalane, Joseph Makhema, Scott Dryden-Peterson
Manuscript writing: All authors
Final approval of manuscript: All authors

REFERENCES

1. GBD 2013 Mortality and Causes of Death Collaborators: Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: A systematic analysis for the Global Burden of Disease Study 2013. Lancet 385:117-171, 2015

2. GLOBOCAN: 2012 v1.0, Cancer incidence and mortality worldwide: IARC CancerBase No. 11. Lyon, France: International Agency for Research on Cancer. http://globocan.iarc.fr/.

3. Farmer P, Frenk J, Knaul FM, et al: Expansion of cancer care and control in countries of low and middle income: A call to action. Lancet 376:1186-1193, 2010

4. Abdel-Wahab M, Bourque JM, Pynda Y, et al: Status of radiotherapy resources in Africa: An International Atomic Energy Agency analysis. Lancet Oncol 14:e168-e175, 2013

5. Barton MB, Gebski V, Manderson C, Langlands AO: Radiation therapy: Are we getting value for money? Clin Oncol (R Coll Radiol) 7: 287-292, 1995

6. Ramogola-Masire D, Russell AH, Dryden-Peterson S, et al: Case records of the Massachusetts General Hospital. Case 16-2014. A 46-year-old woman in Botswana with postcoital bleeding. N Engl J Med 370:2032-2041, 2014

7. Barton MB, Frommer M, Shafiq J: Role of radiotherapy in cancer control in low-income and middle-income countries. Lancet Oncol 7:584-595, 2006

8. Delaney GP, Barton MB: Evidence-based estimates of the demand for radiotherapy. Clin Oncol (R Coll Radiol) 27:70-76, 2015

9. Zubizarreta EH, Fidarova E, Healy B, Rosenblatt E: Need for radiotherapy in low and middle income countries – the silent crisis continues. Clin Oncol (R Coll Radiol) 27:107-114, 2015

10. International Atomic Energy Agency: DIRAC (Directory of Radiotherapy Centres). http://nucleus.iaea.org/HHW/m/DBStatistics/DIRAC/

11. Efstathiou JA, Bvochora-Nsingo M, Gierga DP, et al: Addressing the growing cancer burden in the wake of the AIDS epidemic in Botswana: The BOTSOGO collaborative partnership. Int J Radiat Oncol Biol Phys 89:468-475, 2014

12. Botswana Ministry of Health: Botswana National Cancer Registry (BNCR) report, 2004. http://afcrn.org/membership/members/118-bncr

13. Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM: Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: A meta-analysis. Lancet 370:59-67, 2007

14. Dryden-Peterson S, Medhin H, Kebabonye-Pusoentsi M, et al: Cancer incidence following expansion of HIV treatment in Botswana. PLoS One 10:e0135602, 2015 [Erratum: PLoS One 10:e0138742, 2015]

15. Botswana Ministry of Health: Botswana National Cancer Registry (BNCR) report, 2010. http://afcrn.org/membership/members/118-bncr

16. Sher DJ: Cost-effectiveness studies in radiation therapy. Expert Rev Pharmacoecon Outcomes Res 10:567-582, 2010

17. Grady D: Better staffing seen as crucial to Ebola treatment in Africa. http://www.nytimes.com/2014/11/01/us/better-staffing-seen-as-crucial-to-ebola-treatment-in-africa.html?_r=0

18. International Atomic Energy Agency. Planning national radiotherapy services: A practical tool. Vienna, Austria, International Atomic Energy Agency, 2010.

19. International Atomic Energy Agency. Setting up a radiotherapy programme: Clinical, medical physics, radiation protection and safety aspects. Vienna, Austria, International Atomic Energy Agency Vienna, 2008.

20. Slotman BJ, Cottier B, Bentzen SM, et al: Overview of national guidelines for infrastructure and staffing of radiotherapy. ESTRO-QUARTS: Work package 1. Radiother Oncol 75:349-354, 2005

21. Datta NR, Samiei M, Bodis S: Radiation therapy infrastructure and human resources in low- and middle-income countries: Present status and projections for 2020. Int J Radiat Oncol Biol Phys 89:448-457, 2014

22. Rosenblatt E, Acuña O, Abdel-Wahab M: The challenge of global radiation therapy: An IAEA perspective. Int J Radiat Oncol Biol Phys 91:687-689, 2015

23. Suneja G, Ramogola-Masire D, Medhin HG, et al: Cancer in Botswana: Resources and opportunities. Lancet Oncol 14:e290-e291, 2013

24. Page BR, Hudson AD, Brown DW, et al: Cobalt, linac, or other: What is the best solution for radiation therapy in developing countries. Int J Radiat Oncol Biol Phys 89:476-480, 2014

25. Van Dyk J, Battista JJ: Cobalt-60: An old modality, a renewed challenge. Curr Oncol 3:8-17, 1996

26. Grover S, Xu MJ, Yeager A, et al: A systematic review of radiotherapy capacity in low- and middle-income countries. Front Oncol 4:380, 2014

27. Kutcher GJ, Coia L, Gillin M, et al: Comprehensive QA for radiation oncology: Report of AAPM Radiation Therapy Committee Task Group 40. Med Phys 21:581-618, 1994

28. Klein EE, Hanley J, Bayouth J, et al: Task Group 142, American Association of Physicists in Medicine: Task Group 142 report: Quality assurance of medical accelerators. Med Phys 36:4197-4212, 2009

29. Zietman AL, Palta JR, Steinberg ML, et al: Safety is no accident. American Society for Radiation Oncology (ASTRO). https://www.astro.org/uploadedFiles/Main_Site/Clinical_Practice/Patient_Safety/Blue_Book/SafetyisnoAccident.pdf

30. Brown DW, Shulman A, Hudson A, et al: A framework for the implementation of new radiation therapy technologies and treatment techniques in low-income countries. Phys Med 30:791-798, 2014

31. Kim JY, Farmer P, Porter ME: Redefining global health-care delivery. Lancet 382:1060-1069, 2013

32. Bvochora-Nsingo M, Gwangwava E, Makufa R, et al: Introduction and implementation of brachytherapy for cancer of the cervix in Botswana. National Cancer Institute Symposium on Global Cancer Research, Boston, MA, March 2015

33. Dryden-Peterson S, Bvochora-Nsingo M, Medhin H, et al: HIV infection and survival among women with cervical cancer in Botswana. Conference on Retroviruses and Opportunistic Infections, Seattle, WA, 2015

34. Mak K, Hodgeman R, Bvochora-Nsingo M, et al: Breast cancer in a prospective cohort of HIV-infected and HIV-uninfected patients in Botswana. National Cancer Institute Symposium on Global Cancer Research, Boston, MA, March 2015

35. Ritter M, Forman J, Kupelian P, et al: Hypofractionation for prostate cancer. Cancer J 15:1-6, 2009

36. Viswanathan AN, Beriwal S, De Los Santos JF, et al: American Brachytherapy Society: American Brachytherapy Society consensus guidelines for locally advanced carcinoma of the cervix. Part II: High-dose-rate brachytherapy. Brachytherapy 11:47-52, 2012

37. Zietman A: Bringing radiation therapy to underserved nations: An increasingly global responsibility in an ever-shrinking world. Int J Radiat Oncol Biol Phys 89:440-442, 2014

38. Jaffray DA, Gospodarowicz M: Bringing global access to radiation therapy: Time for a change in approach. Int J Radiat Oncol Biol Phys 89:446-447, 2014

39. Rodin D, Jaffray D, Atun R, et al: Global Task Force on Radiotherapy for Cancer Control and the Union for International Cancer Control: The need to expand global access to radiotherapy. Lancet Oncol 15:378-380, 2014

40. Jaffray DA, Atun R, Barton M, et al: Union for International Cancer Control's Global Task Force on Radiotherapy for Cancer Control: Radiation therapy and the global health agenda. Clin Oncol (R Coll Radiol) 27:67-69, 2015

41. Porter A, Aref A, Chodounsky Z, et al: A global strategy for radiotherapy: A WHO consultation. Clin Oncol (R Coll Radiol) 11:368-370, 1999

42. Rosenblatt E, Zubizarreta E, Wondergem J, et al: The International Atomic Energy Agency (IAEA): An active role in the global fight against cancer. Radiother Oncol 104:269-271, 2012

43. Abdel-Wahab M, Rosenblatt E, Holmberg O, Meghzifene A: Safety in radiation oncology: The role of international initiatives by the International Atomic Energy Agency. J Am Coll Radiol 8:789-794, 2011

44. Coleman CN; many others: Bringing cancer care to the underserved globally: A challenging problem for which radiation oncology can pioneer novel solutions. Int J Radiat Oncol Biol Phys 89:443-445, 2014

45. Einck JP, Hudson A, Shulman AC, et al: Implementation of a high-dose-rate brachytherapy program for carcinoma of the cervix in Senegal: A pragmatic model for the developing world. Int J Radiat Oncol Biol Phys 89:462-467, 2014

46. Chabner BA, Efstathiou J, Dryden-Peterson S; visiting team from the Massachusetts General Hospital Cancer Center and our partners at the Medical School of the University of Botswana, the Princess Marina Hospital, the Gaborone Private Hospital, and the Botswana Ministry of Health: Cancer in Botswana: The second wave of AIDS in Sub-Saharan Africa. Oncologist 18:777-778, 2013

47. Bvochara-Nsingo M, Grover S, Gierga DP, et al: Cervical brachytherapy exchange: Steps toward oncology capacity building in Botswana. Oncologist 19:e1-e2, 2014

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Establishing and Delivering Quality Radiation Therapy in Resource-Constrained Settings: The Story of Botswana

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or jco.ascopubs.org/site/ifc.

Jason A. Efstathiou
Consulting or Advisory Role: Medivation/Astellas, Bayer Healthcare

Magda Heunis
No relationship to disclose

Talkmore Karumekayi
No relationship to disclose

Remigio Makufa
Employment: Life Gaborone
Travel, Accommodations, Expenses: Elekta

Memory Bvochora-Nsingo
Employment: Gaborone Private Hospital
Leadership: Gaborone Private Hospital
Stock or Other Ownership: Gaborone Private Hospital
Speakers' Bureau: AstraZeneca
Travel, Accommodations, Expenses: Genentech, Novartis, Bauer

David P. Gierga
Travel, Accommodations, Expenses: VisionRT

Gita Suneja
No relationship to disclose

Surbhi Grover
No relationship to disclose

Joseph Kasese
No relationship to disclose

Mompati Mmalane
No relationship to disclose

Howard Moffat
No relationship to disclose

Alexander von Paleske
No relationship to disclose

Joseph Makhema
No relationship to disclose

Scott Dryden-Peterson
Honoraria: UpToDate