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Global radiation therapy

Changing the global radiation therapy paradigm

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Filling the gap in cancer care in underserved regions worldwide requires global collaboration and concerted effort to share creative ideas, pool talents and develop sustainable support from governments, industry, academia and non-governmental organizations. Comprehensive cancer care, which fits within and strengthens the broader healthcare system, ranges from prevention to screening, to curative treatment, to palliative care and to long-term follow-up. Radiation therapy is an essential component for curative and palliative cancer care and can serve as a stable focal point physically and for personnel around which regional cancer and health care programs can be established. To build capacity with high quality capability and with the credibility to conduct research to understand specific diseases and treatment outcomes requires a complex systems approach toward both expertise and technology.

To move forward in the aspirational goal of substantially reducing the global burden of cancer as part of the Sustainable Development Goals of the United Nations [1], a workshop was convened on November 7–8, 2016 by the International Cancer Expert Corps (ICEC) [2] and hosted by CERN [3]. Entitled "Design Characteristics and Implementation of a Novel Linear Accelerator for Challenging Environments" a major focus was on innovative radiation oncology technology opportunities. Cobalt-60 units are still in use but, while newer units are increasingly sophisticated, they do not provide the full treatment capability of modern linacs and require ongoing security and ever-increasing costs for disposal of radioactive materials.

While there has been substantial progress in radiation oncology technology development, significant opportunity remains for improvement and innovation in the combination of technology and processes used to deliver basic and advanced radiation therapy in low- and middle-income countries. Most specifically, the adoption of a collaborative approach that ties together broad expertise and perspectives by connecting global need, oncology expertise, and deep capacity in technology innovation was reinforced by this workshop and subsequent efforts and has resulted in a framework for collaboration to address the unacceptable gap in global cancer care.

The magnitude of the problem

It is estimated that the annual global cancer incidence will rise from 15 million cases in 2015 to as many as 25 million cases in 2035, 65–70% of which will occur in low- and middle-income countries (LMICs) [4] where there is a severe shortfall in radiation

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treatment capacity. Cancer care is multi-modal, including pathology, imaging, the range of oncology expertise, nursing and support staff, with at least 50% of cancer patients benefiting from radiotherapy regardless of their geographic location [5]. Radiotherapy is an effective curative and palliative modality for a very broad range of tumors. Yap, et al. have estimated that, if the demand for radiotherapy is met in LMICs by 2035, each year an additional 1.3 million people would experience local disease control and over 615,000 patients would derive a survival benefit [6] with other estimates closer to 1 million per year [7–9]. For the advanced stages of cancer for which surgery is not feasible, radiotherapy can still be curative. Without radiotherapy, effective palliative care is often absent and particularly so in countries that limit the use of narcotics. When considering investment in overall global healthcare, the relationship between the etiology and management of the non-communicable diseases – cardiovascular, metabolic, respiratory, and oncologic – and the communicable diseases, particularly those for which screening and prevention are available (e.g., HPV related illness and hepatitis), gives cancer care an opportunity to be the focal point for coordination, collaboration and strengthening health systems networks.

A Lancet Oncology Commission, the Global Task Force on Radiotherapy for Cancer Control (GTFRCC) of the Union for International Cancer Control (UICC) [7], supported by additional recent data [10], documented the global demand for radiotherapy, the resources required and the economic and societal benefits that would be reaped by additional investment in providing such coverage. It was estimated that as many as 12,600 megavoltage treatment machines will be needed to meet the radiotherapy demands in LMICs by 2035. Using current staffing models, there will be an estimated need by that time for an additional 30,000 radiation oncologists, more than 22,000 medical physicists and almost 80,000 radiation technologists. The financial investment needed in LMICs is approaching $200B USD and the economic benefits demonstrate significant returns to those countries that choose to invest.

Workshop participants from global health, cancer care, and radiation technology fields addressed: (1) the role of radiotherapy in treating patients with cancer in the challenging environments of many LMICs, (2) the security concerns related to high-activity radiological sources in medical facilities, (3) the design characteristics of linear accelerators and related technologies for use in challenging environments, (4) the education, training and mentoring of the sustainable workforce needed to utilize novel radiation treatment systems and (5) the costs and financing of the implementation of the recommendations from the workshop.

The workshop agenda can be found online [9]. Issues raised there and at subsequent discussions during the International Conference on Advances in Radiation Oncology (ICARO2) [12] in June, 2017 and at a second workshop held at CERN on October 26 and 27, 2017 showed clear evidence that technological opportunities exist to improve global access to radiation treatment.

Focusing on the machine alone will not solve the problem

Numerous national scientific societies and non-governmental organizations (NGOs) provide training globally on a limited scale for radiotherapy professionals and allied health personnel. Radiating Hope, a US-based NGO, provides radiotherapy equipment, often refurbished, on a limited scale to regions that have limited or no capacity [13]. Successful approaches to peer-supported case-based education including pioneering work by Hardenburgh via Chartrounds [14] and the potential for use of highly interactive teleconferencing, such as TELESYNERGY®, developed by the National Institutes of Health for cancer disparities programs [15], are considered critical to education and mentorship. By far, the greatest body of effort and experience in developing radiation treatment capacity in LMICs resides with the International Atomic Energy Agency (IAEA). The aim of IAEA's program on Human Health (NAHU) [16] is to enhance the capabilities in Member States to address needs related to the prevention, diagnosis and treatment of diseases through the application of nuclear techniques. Their Human Health Campus [17] website posts extensive and detailed guidelines for the implementation of radiotherapy programs as well as education and training syllabi and course materials for the diverse professions involved in delivering radiotherapy. Through the IAEA Technical Cooperation Programme, including its Program of Action for Cancer Therapy (PACT) [18], the IAEA addresses the needs of IAEA LMIC Member States by supporting the implementation of radiotherapy programs and by expanding their efforts through cooperation with non-governmental donors.

Successful instances in which an optimal mix of local commitments was available were presented at the workshop [11] as examples of radiotherapy programs that have thrived and are expanding. On the other hand, the lack of secure resources, inadequate planning, the failure of local governments to keep commitments and political instability resulted in weak programs and lack of continuity. Among the current IAEA criteria for project support are: (1) political stability in the country or region, (2) local commitment and (3) political will for sustained ownership and long-term funding of the program. A typical project includes a medium-term plan for the establishment of the first radiotherapy department in a region and a long-term plan that includes adequate staffing and creation of a local training program that will allow the facility to become a nucleus for future regional expansion. Successful regional training centers are stabilizing factors that can mitigate the so-called "brain drain" pressures.

Among the major points of the discussions [11] were:

1. The importance of local champions [19] and local and regional investment in resources. Top-down solutions from upper-income countries contain useful tools and frameworks but the needs, solutions and time-tables should be driven by specialists in local communities and external experts who best understand the issues. Examples of guidelines being developed for LMICs that can be a useful starting point for program building are the National Comprehensive Cancer Network (NCCN) Harmonized Guidelines for Sub-Saharan Africa [20]. Purchase or donation of equipment to countries in which there is inadequate infrastructure and technical capability can result in money wasted or in technology not used appropriately and/or effectively.
2. The treatment capability must not be considered "second-rate" but should be on par with that generally available for cancer care in developed nations. (The highly innovative and expensive technologies, such as particle therapy, should be considered on a regional level, with appropriateness for treatment based on carefully defined criteria.)
3. Research is a key part of this overall enterprise including: (a) population studies to define the cancer problem locally or regionally, (b) biology and epidemiology investigations to understand how genes, environment, the microbiome and infectious agents impact cancer, (c) cancer treatment outcomes studies, (d) policy projects for access to healthcare including access to multiple specialists and supportive care and (e) economic analyses for balancing cost and resources and guiding future investment.
4. Technical programs that might bear on the development of a novel linear accelerator and treatment system are ongoing [11]. Subsequent meetings have addressed specifics of the linear accelerator design and implementation, including a "BOXCare" concept proposed by Jaffray [21].

5. Issues regarding cobalt-60 must be considered. That cobalt-60 therapy has utility and is recognized by its use in LMICs, including the relative roles of linac versus cobalt-60, was recently reviewed (and not a topic of this workshop) [22]. The Office of Radiological Security (ORS) of the United States National Nuclear Security Administration (NNSA) [23] stressed the risk posed by malicious use of high-activity radiological sources, and the potential for linacs to permanently reduce these radiological security risks by providing high-quality treatment without the use of cobalt-60. For hospitals that utilize cobalt-60 teletherapy machines, ORS emphasized the need to protect the radioactive sources from unauthorized access. This theme was expanded by a report from the Center for Nonproliferation Studies (CNS) [24] in the new paradigm "Treatment, not Terror" [25,26].
6. There is novel technology being developed at Stanford and the SLAC National Accelerator Laboratory at Stanford University that is a pluri-directional high energy agile scanning electronic radiotherapy system (PHASER) using advanced RF linac technology that employs 16 independent electron beams. The device is capable of delivering a radiation dose approximately 300× faster than a conventional medical linear accelerator. While an interesting concept, the potential role for this technology in resource-rich and lower-middle income countries will depend on future development and costs of both equipment and power.
7. An ideal radiotherapy treatment system characteristic is modularity in order to make it easy to ship, to assemble in-situ, to repair and to upgrade periodically as local patient treatment expertise develops. Policies and procedures must be developed to minimize the need for local specialized technical staff to maintain the equipment and promptly repair it. In addition, a national or regional supply of standard (modular) spare parts and uncomplicated replacement procedures will be needed in order to make maintenance reliable and easy.

Moving ahead

The medium-term goal for technology development is to 'bury the complexity' [27] of radiotherapy by taking advantage of software to incorporate automation to affect ease of use and, in conjunction with excellent diagnostic imaging, to insure high quality treatment. In addition, examples of the emerging role of software to lower the cost of radiotherapy through new software tools (optimization and automation) demonstrated that software can compensate for machine "weakness" and can eliminate inconsistencies in simulation and treatment planning [28].

That the solution for global cancer care requires attention to expertise and technology and is an opportunity for global leadership by radiation and clinical oncologists is illustrated in Fig. 1. The focus is on patient care based on healthcare systems in LMIC centers. Onsite expertise is essential and robust technology is critical for sustainable programs. The specific expertise and criteria for the technology are noted within the figure. The unique aspects of the implementation model include global mentoring and expert support. These provide mentoring for the onsite experts and the creative global technology partners and collaborators to support and enhance the existing technology and to develop innovative solutions. This is not a theoretical construct since there are ongoing

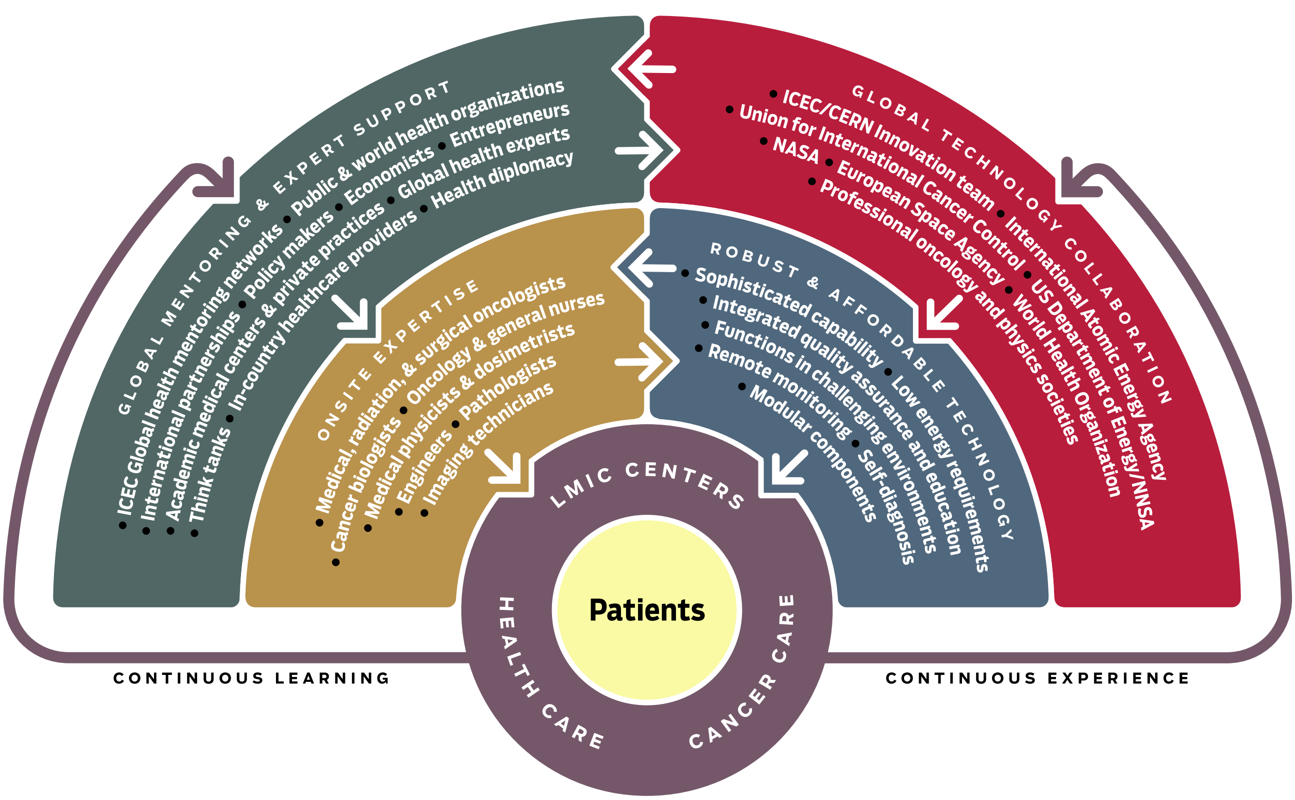

Fig. 1. Building global cancer care: capacity, capability, credibility and continuity. See text for details. *Abbreviations:* ICEC – International Cancer Expert Corps: CERN – Conseil Européen pour la Recherche Nucléaire, or European Organization for Nuclear Research; IAEA – International Atomic Energy Agency; WHO – World Health Organization; UICC – Union Internationale Contre le Cancer or Union for International Cancer Control; NASA – National Aeronautics and Space Administration; NNSA – Department of Energy, National Nuclear Security Administration. Graphic by David Herbick.

efforts in all of these areas, some of which are detailed in this paper and as part of recent issues on global health [29–31].

A presentation on entrepreneurial strategies highlighted how disruptive innovation [32] requires cooperation across disciplines. ICEC's unique strategy is to establish a sustainable team of mentors to guide local cancer care providers throughout the various phases of training and implementing guideline- or protocol- based cancer control and treatment programs [33,34]. In this way, each cancer disparities region radiation treatment center would be aligned with mentors based in a university cancer center or private practice radiotherapy center in a resource-rich country. After centers in low-resource regions develop sufficient expertise and meet global guideline- and/or protocol-based standards for cancer care, they can become regional resource centers for less developed local groups that are motivated to undertake a similar path. Professionals in medical oncology, radiation oncology, surgery, medical physics as well as nurses and ancillary staff will be recruited in order to ensure mentoring of all of the members of the treatment teams in LMICs. Implementing these programs will require sustainable support, a career path for mentors [35], multi-sector involvement to take advantage of the broad favorable impact cancer care will have [36] and visionary leadership from NGOs, industry, government and international health and global security-related agencies.

Actions

Three tasks forces are at work.

Task Force 1: Technical Task Force

From a systems perspective stimulate innovation in radiotherapy technologies and processes. In the near-term, develop optimal design requirements for a novel high-quality, lower-cost treatment solution that leverages existing linac technologies and incorporates intelligent software designed for robust operation in a range of challenging environments. Such a system would be modular, rugged, easily operated, less reliant on personnel, and easily repaired but sufficiently sophisticated to also bring benefits to radiotherapy in high-income countries. This is an example of reverse innovation with learning passing from low- to high-income countries [37,38].

For the long-term, clearly identify shortfalls in existing critical subsystems (radiation production, power consumption, heat dissipation, automated maintenance, electromechanical collimation, imaging, safety, and training subsystems) and, through engagement of international centers of excellence, stimulate the development of next generation solutions to these important needs.

Task Force 2: Education, Training and Mentoring Task Force

Identify (a) the education and training requirements for current as well as future radiotherapy equipment and treatment systems worldwide, (b) the current extent of education and training program resources and (c) the education and training needed to fill the gaps. In coordination with Task Force 1, develop recommendations for specific training and mentoring, including new education technology, to ensure that the advanced radiotherapy treatment systems will be fully utilized as soon as they are introduced in the near-term as well as in the more distant future. Continuously evaluate the impact of changing patterns of practice and treatment techniques, and changes in cancer incidence and population mix in order to appropriately update content and methodology of education, training and mentoring programs.

Task Force 3: Global Connectivity and Development Task Force

Linked closely with Task Forces 1 and 2, develop and implement a strategy for securing financial support in client countries as well as from governmental, academic and philanthropic organizations and individuals to insure success of the effort to make excellent near-term and long-term radiation treatment systems, including staffing and physical infrastructure, available for the treatment of patients with cancer in LMICs and other geographically underserved regions worldwide. Patient engagement as seen in the cancer survivorship community is critical to optimal design on cancer care systems [39].

Summary and conclusion

The magnitude of the global shortfall in cancer care, especially radiation oncology, is a crisis that cannot be ignored and presents an opportunity for innovative systems solutions to include developments in technology, capacity, expertise, advanced treatment capability and sustainable mentorship and education. Detailed definition and documentation of the problem provides essential metrics upon which to make improvements, but action is required to begin to implement solutions to the urgent need for expertise and enabling technology. This initial workshop and subsequent progress are important steps toward solutions. Indeed, this is an example where reverse innovation and disruptive technology can transform cancer care in the underserved world for the better while reducing costs and bringing innovative science and technology to the better-resourced world. The potential of this effort to have a positive impact on the lives of millions of people presents a great opportunity for global collaboration, sustainable cross-cultural relationships and a leadership role for healthcare to create common bonds among nations.

Disclaimer

The information in this paper and the presentations at the Workshop and subsequent meetings are personal opinions of the individuals and do not represent opinions or policy statements of the institutions or organizations in which they work. Presentations from the CERN workshop are posted on the meeting website with permission of the presenters.

Conflict of interest

AD – ADAM S.A.
MEG – Board of Directors, IBA.
PH – CEO, Chartrounds, LLC.
DAJ – Inventor of cone-beam CT for image-guided radiotherapy; Active-breathing control; Integrated Quality Monitor; Elekta Image-guided Perfexion; AQUA – Co-founder Acumyn Inc.; MORFEUS Deformation System; Pentaguide – Modus Medical; Inventor Cx225 small animal irradiator; Owner – Nanovista Inc.; Board member–CanProbe; Existing or Complete sponsored research/development agreements with Elekta, GE, Varian, Raysearch Labs, Philips Medical Systems, iRT, Merrimack, Waters, Siemens Medical Systems.
SM – ADAM S.A.: Board of Directors, AVO(plc).

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