ACCESS TO EFFECTIVE CANCER CARE IN LOW-MIDDLE INCOME COUNTRIES REQUIRES SOPHISTICATED LINEAR ACCELERATOR BASED RADIOTHERAPY

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Abstract

There are substantial and growing gaps in cancer care for millions of people in Low- Middle- Income countries (LMICs) and for geographically remote settings in High-income countries (HICs), often indigenous populations. Assessing the cancer care shortfall led to understanding the essential gap, that of a radiation therapy machine that can reliably and effectively provide the appropriate first-rate cancer treatments within the challenging environments.

More than 10,000 electron linear accelerators (linacs) are currently used worldwide to treat patients. However only 10% of patients in low-income and 40% in middle-income countries who need radiotherapy have access to it.

The idea to address the need for a novel medical linac for challenging environments has led to the creation of the STELLA project (Smart Technology to Extend Lives with Linear Accelerators) project. STELLA is multidisciplinary international collaborative effort to design and develop an affordable and robust yet technically sophisticated linear accelerator-based radiation therapy treatment (RTT) in LMICs. Here we describe Project STELLA.

INTRODUCTION

The incidence and number of deaths from cancer has been rising for many years in Low-Middle Income Countries (LMICs) [1] as has the gap in available cancer care. Despite a 2011 declaration by the UN General Assembly regarding the importance of addressing the non-communicable diseases (NCDs) as well as the infectious diseases - which are the primary focus of global health - investment in cancer care remains minimal.

There has been a surge in interest addressing the gap in radiation therapy punctuated in 2015 by Atun et al in the report of the Global Task Force for Radiotherapy for Cancer Control (GTFRCC) supported by the Lancet Oncology Commission [2]. Through modelling, this report demonstrated how radiation therapy is not only cost effective but also positive for the economy. A growing interest in global health projects by radiation oncology trainees in the US and Europe raised the exposure of the chronic shortage. Yet, the gap in the number of radiation therapy (RT) machines needed, estimated to be approximately 5,000 by the GTFRCC and possibly twice that by 2035 remained steady. Consequently, a number of experts in global health, cancer care, radiation therapy, accelerator physics & engineers sought a deeper understanding of why this gap persisted and, more importantly, how the gap can be closed.

The need for adequate cancer care for all is obvious yet the chronic lack of improvement perhaps becoming a self-fulfilling expectation of a problem “too hard” to solve. Completely new paradigms are clearly needed. Herein, the various strings of the problem are weaved together: the various channels of technology development, in depth understanding of the on-the-ground problems, health system shortcomings and opportunities, career tracks, concerns of misuse of high activity radiation sources and global agency efforts. These challenges provide the opportunity to investigate potentially disruptive innovative approaches to make a serious impact on the shortage of effective cancer care. Figure 1 shows the variation in RT capacity across Africa [3, 4].

MULTI-LEVEL ANALYSIS OF THE SHORTAGE

Improved Data Sources

The commonly used data sources to address global cancer use a combination of data from surveys and projections of need based on population data. These data are useful for the macroscopic assessment and readily visible demonstrations of shortage as illustrated below. More detailed data are available from the International Atomic Energy Agency (IAEA) [3] that demonstrate the heterogeneity of distribution of resources. However, the essential data for program building and providing the necessary resources and support require detailed site-based data as seen in the ICEC surveys of Africa and Eastern Europe [4, 5, 6]. The act of conducting the survey engages those working on-the-ground who understand the breadth and depth of the issues and can serve as local champions to provide solutions they see as necessary to drive the change.

Engaging Expertise with Commitment to a Solution

The magnitude of the cancer care gap often leads to an overwhelming sense of a problem “to big” to solve. Indeed, it is often suggested by experts in global health that for cancer care only prevention is appropriate in such resource-limited settings. The critical lack of access to cancer care treatment, including radiotherapy, in LMICs and geographically isolated populations in HICs is increasing, and there are few, if any, scalable solutions to address the global cancer crisis. The challenge is so enormous it is perceived as impossible. In 2014, at the ICTR-PHE physics component of the meeting in Geneva, a presentation delivered by Dr. Norm Coleman highlighted

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the critical shortage of LINACs. The size of the challenge had the remarkable opposite impact upon the audience whereupon Professor Ugo Amaldi from CERN stated, "We physicists can help you solve the radiation therapy problem." Thus, the STELLA LINAC Project commenced.

Building a Trusted Network

Our experience with outreach programs and building partnerships teaches the critical importance of trusted partnerships. This involves multi-generational mentorship, including capturing wisdom from career-long experience [7], pioneering career paths in global health [8], cross-disciplinary expertise and an interest in research.

MOVING TOWARD THE SOLUTION

As detailed in the CERN Courier, (Dec 2021) by Graeme Burt, Manjit Dosanjh and Deepa Angal-Kalinin the following highlights the technical progress [9]. The estimated demand for linacs for LMICs over the next few decades, will go from the current 5000 RT machines to over 12,000. To put these figures into perspective, Varian, the market leader in RT machines, has a current worldwide installation base of 8496 linacs. [10]. Understanding that many LMICs provide RT using cobalt-60 machines because of their limited need for infrastructure (stable power, cooling, etc) the reasons for moving toward linacs, source security and HIC level care – were a strong impetus to project STELLA. However, the current cost of linac RT machines is significantly higher than cobalt-60 machines, both in terms of initial capital costs and more importantly annual service contracts, linacs are more complex and labour-intensive to operate and maintain. These challenges for LMICs involve macro- and micro-economic conditions the ability of these countries to provide linac-based RT which are addressed by project STELLA.

Stimulated by the discussion with Ugo Amaldi and Steve Myers after Norm Coleman's presentation on the lack of RT globally and the ICEC model at the ICTR-PHE conference, the following progress was rapidly accomplished.

- November 2016, CERN hosted a first-of-its-kind workshop in collaboration and at the request with the International Cancer Expert Corps (ICEC) iceccancer.org, to discuss the design characteristics of RT linacs for the challenging environments of LMICs. Using the broad open-approach of CERN type projects leading experts were invited from international organisations, government agencies, research institutes, universities and hospitals, and companies that produce equipment for conventional X-ray and particle therapy [*CERN Courier*, vol. 57, no. 1, January/February, 2017, p. 31]. Subsequent workshops and progress are described below.
- October 2017, CERN hosted a second workshop titled "Innovative, robust and affordable medical linear accelerators for challenging environments," in collaboration with ICEC and the UK's Science and Technology Facilities Council, STFC who funded the participation of LMIC countries by their Official Development Assistance (ODA) funding [*CERN Courier,* vol. 58, no. 1, January/February, 2018, p. 35].
- March 2018, workshop hosted and funded by STFC in the UK in collaboration with CERN and ICEC.
- March 2019, workshop funded by STFC in Gaborone, Botswana. Acknowledged and identified substantial opportunities for scientific and technical advancements in the design of the linac and the overall RT system for use in LMICs.
- June 2020, STFC funded the Innovative Technologies towards building Affordable and equi5e global Radiotherapy capacity (ITAR) project, a partnership established by Lancaster University, STFC, CERN, ICEC, Oxford University and Swansea University. ITAR's first phase aimed to examine and analyse the persistent shortfalls in basic infrastructure, equipment which act as barriers to effective radiotherapy delivery in LMICs and to develop a Conceptual Design Report (CDR) for addressing the challenges.

STUDIES TO ANALYZE SHORTFALL-ON-THE-GROUND DATA

Recognizing that the linac needs to be low-cost, robust and easy to maintain, it was essential to assess the challenges and difficulties RT facilities face in LMICs and in other challenging environments.

African Radiation Therapy Study [4]

Building on a related 2018 study on the availability of RT services and barriers to providing such services in Botswana and Nigeria [6], the STELLA collaboration carried out a survey of RT facilities in 28 African countries and compared them to Western hospitals to quantitatively and qualitatively assess and compare variables in several domains to define necessary next-generation technologies (Figs. 1 and 2).

The ITAR design development and prototyping process identified the need for information on equipment failures, maintenance and service shortcomings, personnel, training, country-specific challenges. The STELLA collaboration questionnaire obtained relevant information from all African countries that possessed Linac -based RT for defining design parameters and technological choices based on issues. These included well-recognized factors such as ease and reliability of operation (Fig. 3), machine self-diagnosing and a prominent display of the impending or actual faults, ease of maintenance and repair, insensitivity to power interruptions, low power requirement and consequent reduced heat production.

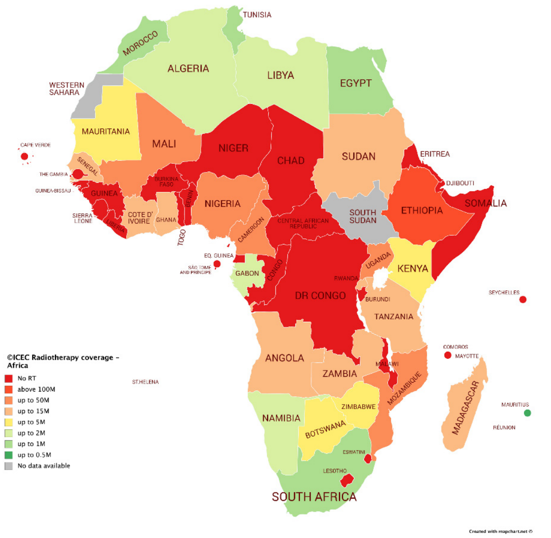

Figure 1: Shows the variation in RT capacity across Africa in number of people per linac with a severe shortage especially in the Sub-Saharan region.

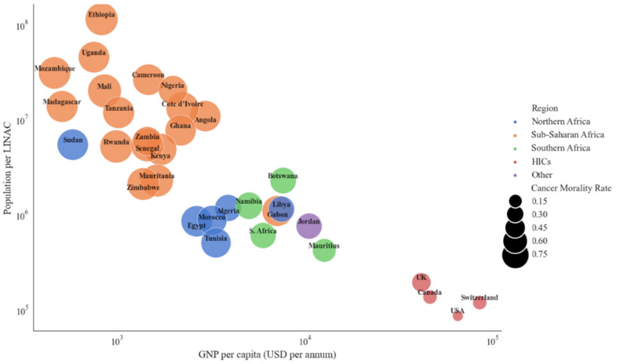

Figure 2: LMIC and HIC countries in the study plotted graphically by GNP per capita and the ratio of inhabitants to RT machines [4].

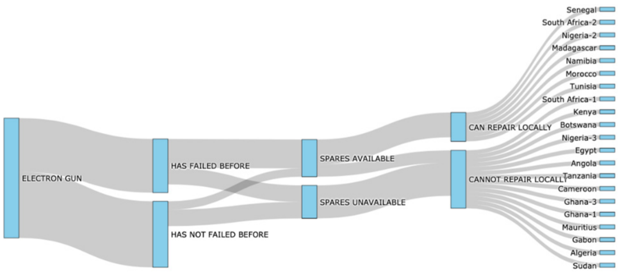

Figure 3: Sankey Plot for the electron gun tracing the problems/issues regarding performance and failure to perform. (Figure provided by Alexander Jenkins from data gathered in [4].)

The Southeast European Study [5]

The Southeast European (SEE) region of 10 countries consisting of about 43 million people differs from Western Europe in that most SEE countries lack active cancer registries and have fewer diagnostic imaging devices and radiotherapy (RT) units. The Balkan study obtained detailed on-the-ground information for three SEE groups: a) ONCO - oncologists regarding cancer treatment modalities and the availability of diagnostic imaging and radiotherapy equipment; and b) REG - national radiation protection and safety regulatory bodies regarding diagnostic imaging and radiotherapy equipment in SEE facilities and c) Research community (Figs. 4 and 5).

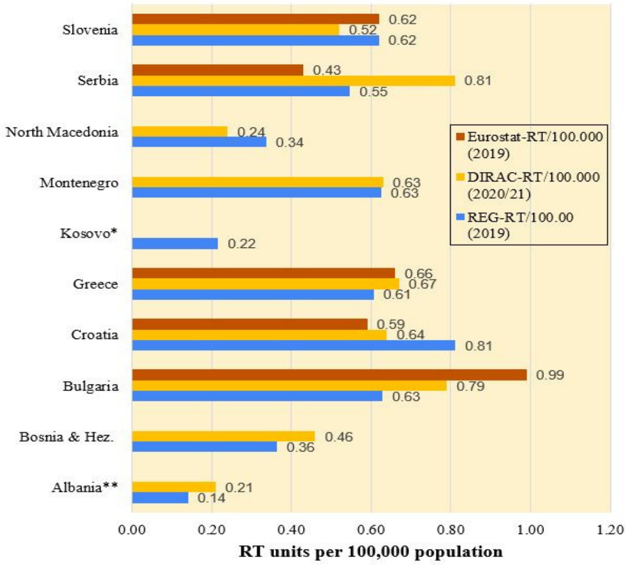

Figure 4: RT units per 100,000 population results from 3 different sources; Eurostat-RT, DIRAC (IAEA)-RT and REG-RT (from this survey). Not all 3 were available for each country. In addition to showing the variation across the region, this points out how the source of data can vary among the various data bases.

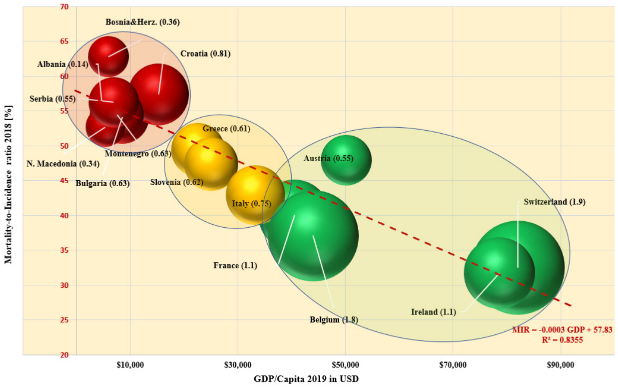

Figure 5: Mortality-to-Incidence ratio (MIR) versus the GDP per capita and the density of conventional RT equipment. The radius of the spheres is proportional to the density of RT equipment per 100,000 population in the respective countries. The number in the parentheses represents the LINAC density in the country. MIR data are from 2018. The GDP per capita are from 2019.

PROPOSED SOLUTION

Figure 6 shows a schematic of a standard medical linac and its components. With the need determined for a RT linac that requires less maintenance, has fewer failures and offers fast repair concluded in ITAR CDR, emphasis on

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STELLA linac design is on developing a modular system with easily replaceable parts, and to select components with longer lifetime to minimise downtime and reduce repair and maintenance costs. Some of the examples of Project STELLA include:

- The design of the RF cavity has been optimised to increase beam-capture and transport the electron beam onto the target [11]. Increasing beam-capture has a dual advantage: first, it reduces the peak current required from the gun to deliver the required dose; and second, it reduces "back bombardment" on the cathode. This design concept allows for simpler replacement of the electron gun's cathode by trained personnel, whereas current designs require replacement of the full electron gun or even the full linac. The ITAR linac cavity geometry is shown in Fig. 7.
- The electrical power supply in LMIC can often be variable and protection equipment to isolate harmonics between pieces of equipment are not always installed, hence its critical to consider this when designing the electrical system for RT machines.
- The multi-leaf collimators (MLCs) that alter the intensity of the radiation so that it conforms to the tumour volume have several thin leaves which are individually actuated. Their failure is a major linac downtime issue. Designing MLCs that are less prone to failure will play a key role in improving up-time in the future.
- Making it simpler to diagnose and repair faults on linacs is another key area that needs improvement. The level of technical staff training often is limited in some LMICs compared to HICs. Hence when a machine fails it can be challenging for local staff to repair it. In addition, that components are degrading can be missed by staff leading to loss of valuable time to order spares.

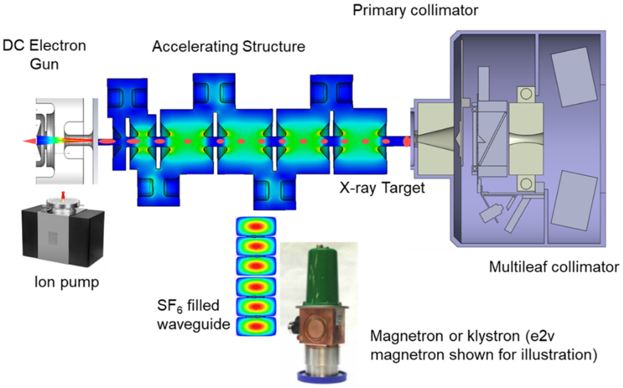

Figure 6: Shows a schematic of a standard Medical Linac showing the electron gun, accelerating structure, target and collimation. Also shown as the RF source to power the linac, the waveguide to transport the power between the linac and RF source, and the vacuum pump to keep everything under vacuum.

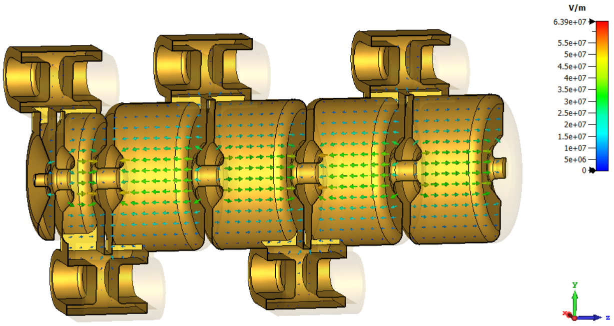

Figure 7: The ITAR Linac cavity geometry, with the short 1st and 2nd cells and strong coupling to the 1st cell to increase capture, showing the electric field contour map [11].

STELLA collaboration is in the process of securing funding for building the prototype of such a modular linac at STFC's Daresbury Laboratory over the next 3 years so that the prototype linac can be tested to see if it meets the design criteria.

People Not Machines Treat Patients

It is not just the radiotherapy machines that are needed to meet the radiotherapy shortage in LMICs, it's also about the availability of trained staff. Indeed, that remains the primary goal of ICEC- to build capacity, capability and credibility in resource-limited settings through mentorship and sustained partnership among an expanding group of centres and nations. It involves working with the major global health agencies including the IAEA and WHO.

PROJECT STELLA

Figure 8 illustrates the interrelated pillars of Project STELLA [12]. Pillar III – program expansion through training, education and mentoring is applicable to any LMIC region interested in capacity building. The current experience with the HIC linacs described above indicates that these highly capable units have shortcomings that have led to the concept design and preparation for prototype construction in Pillar I. Linking machine and treatment is Pillar II that will also be the basis for the global ICEC network and for integration of imaging, biology and data into ever-improving cost-effective and personnel enhancing treatment. In essence it is the person-to-person trusted mentoring network supported by enabling technology designed for the purpose of working in challenging environments. The treatments will be equal to those in HICs as such world-standard treatments are appropriate for all.

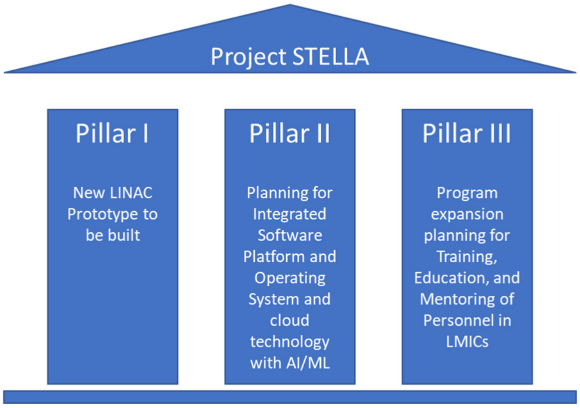

Figure 8: Project STELLA and the three pillars [12].

CONCLUSION

The shortage in global cancer care has persisted for decades with data from the WHO and IAEA continually documenting rate of progress. Cancer is a complex disease in need of fundamental research regarding etiology and treatment. For the majority of patients there are now acceptable treatment algorithms that are known to be successful in HICs. Thus, the gap in LMICs is that of supply of what we know to work.

The ICEC is many years in development as an NGO that can help fill a number of gaps and potentially serve as both an example and a common ground for collaborative global projects. The LMIC solution requires effective full-spectrum cancer treatment that, in turn, absolutely requires effective radiation therapy. For reasons of equity and security a linac that functions well in the challenging environment in LMICs and in geographically remote regions in HICs is essential. Project STELLA has at its goal a robust mentoring network to help build and sustain capacity that is anchored on effective, enabling technology and the robust system for patient management, linac diagnostics, accessing medical literature and treatment guidelines and linking together trusted partners on a global, exponentially expanding network.

The global "we" know the solution to the cancer care gap. The need is obvious and the solution logical. The commitment to finally end this severe deficiency to almost total lack of cancer care in LMICs requires dedication, creativity and persistence to end this human tragedy.

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