IMPROVING ACCESS TO RADIATION THERAPY BY REIMAGINING TECHNOLOGY

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Abstract — **The paper outlines some of the technology-associated challenges associated with delivering high-quality care in the LMIC environment. It describes an unique redesign of radiotherapy delivery technology aiming to address the specific needs of the LMIC setting.**

Keywords— **Radiotherapy, Healthcare in Low and Middle Income Countries (LMIC).**

I. GROWING GLOBAL NEED FOR CANCER CARE AND RT

Oncology is a growth area for healthcare on the global scale. The World Health Organization (WHO) estimates that there were 9.6 million cancer deaths worldwide in 2018 and continuing to grow [1]. This burden falls disproportionately on low- and middle-income countries (LMIC) as shown in Table 1. There are many factors driving this change such as population growth, aging and a shift in the burden of disease toward non-communicable diseases. Now a majority of cancer cases appear in LMICs, and also the mortality rate in these countries is much higher as shown in Figure 1. The cancer-specific mortality rate is nearly twice as large in a low-income country as in a high-income country (Figure 1).

Year	% of newly reported cancers in LMI-countries
1970	15 %
2008	56 %
2030 (expected)	70 %

Table 1: The proportion of newly reported cancers case in low- and middle-income countries by year (adapted from [2-4])

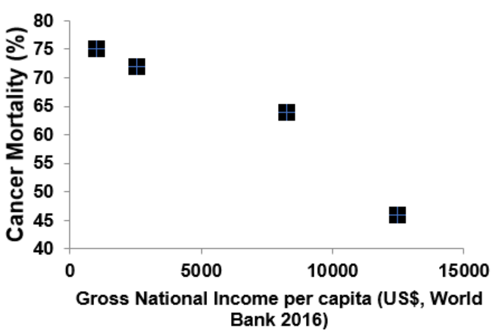

Figure 1: Cancer mortality vs. gross national income per capita as defined by the World Bank. Rates are estimated as the ratio of mortality to incidence per year (adapted from [2])

Globally more people die each year from cancer than from tuberculosis, malaria and AIDS combined [2].

This bleak picture is driven by many factors, arguably the most important of which is access to care. Of the global resources invested in cancer care, it is estimated that less than 5% are spent in LMICs [3]. This is especially true for radiation therapy which is one of the key pillars of oncology care. Studies indicate that overall more than 50% of cancer patients should receive radiotherapy based on evidence and guidelines [5]. However, this rate is determined by the way diseases present in Australia and other high-income countries and is likely a large underestimate of the need in LMICs [6]. For example, the recommended utilization rate in head and neck cancer is 78% and 76% for lung cancers [5], both of which are prevalent in LMICs.

Not only is radiotherapy clinically important in the management of disease, it is also cost-effective. It is non-invasive, allows for organ preservation and has a lower risk profile for morbidities such as infection or lymphopenia which can be challenging to manage. A 2015 report from the Global Task Force on Radiotherapy for Cancer Control studied the potential impact of providing radiotherapy in LMICs from the economic impact point of view [6]. The report concluded that a benefit of US$11 billion to $280 billion per country could be realized if radiotherapy access were scaled up to full need over the 2015-2035 period.

For the above discussion it is clear that there is a strong and growing need for cancer care especially in LMICs, that radiotherapy plays a key role and that it is a particularly cost-effective modality to employ. In spite of all this, however, access to radiotherapy is extremely limited in many LMICs. A 2013 report from the IAEA, for example, noted that of the 52 countries in African only 23 were known to have radiotherapy services available [7]. In India, a country of 1.3 billion people, there are 438 centers providing radiotherapy and 650 treatment units [8]. To fulfill the World Health Organization recommendation of 1 treatment unit per million people, India would need to approximately double the capacity to 1,300 treatment units.

Against this picture of unmet need, however, is a ray of hope. Access continues to grow. In 1991 there were 63 radiotherapy treatment units in Africa. By 2010 there were 277 and continuing to grow [7]. This article outlines some of the technology-associated challenges associated with delivering high-quality care in the LMIC environment and asks the question "can we do better by reimagining the technology"?

II. Current RT technology in the LMIC environment

Since the Clinac-4 was introduced in 1968, the technology for external beam radiation therapy has evolved in a stepwise fashion., although there are also specialized technologies that pre-date the C-arm linacs (e.g. Leksell Gamma Knife unit for stereotactic radiosurgery) the machines that one would see in a modern radiotherapy clinic look largely like the 1968 commercial C-arm unit from Varian Inc. At various points over the intervening decades the technology has been re-imagined in various ways. In 1994 the Cyber Knife radiotherapy system was introduced and commercialized by Accuray Inc., incorporating a robotically-mounted X-band linear accelerator along with co-planar imaging [9]. In 2003 a helical tomotherapy unit was introduced by Tomotherapy Inc. (later Accuray Inc.), using a modified CT ring gantry with a binary MLC and megavoltage CT imaging [10]. More recently radiotherapy units with MR-guidance have become available such as the system from ViewRay Inc [11].

While these technologies have been made to function well in North America, Europe and other countries, there are many challenges that arise when employing them in the LMIC environment. They are dependent on the local infrastructure in many ways. McCarroll et al [12], for example, have studied the effect of power outages on the efficiency of treatment. An average daily power outage of 2 hours can cause patient throughput to drop to approximately 60%. The effect is dependent on technique and technology, with the biggest impact being with the more complex techniques such as intensity modulated radiation therapy (IMRT) delivered with a linear accelerator. Interestingly, simpler technologies such as conformal therapy with 60-Cobalt teletherapy device are much less subject to such effects according to this study and can maintain throughputs of over 90% even with average power outages of 8 hours per day. There are also infrastructure-related safety concerns with some technologies. The well-known 2001 radiation therapy accident in Poland [13], for example, was precipitated by a failure in the power grid.

There are also requirements in terms of staffing and expertise that are needed to deliver high-quality care. One key component of this is quality assurance, typically performed by a medical physicist. An enormous effort is required, however, to adhere to adhere to IPEM 81 and other best-practices. A 2012 survey of radiotherapy centers in the UK, for example, found that the average time required from a medical physicist for quality assurance is 19.5 hours per month per machine and 1.5 hours per patient [14].This difficult to achieve in any environment and is all but impossible in the LMIC setting.

One might ask the question of whether all this quality assurance from highly trained specialists is really necessary. To put it simply, can't we do "good enough" by simply "pushing the button"? The answer, unfortunately, is no. We know from cooperative group trials that treatments with inferior dosimetry and treatment planning have much worse patient outcomes [15] and this is not just an effect in one trial is borne out when one looks across trials [16, 17]. We also know that the commissioning and validation of treatment planning system is crucial and even with highly-trained staff many systems are flawed. In validation tests from the Imaging and Radiation Oncology Core-Houston (IROC-H) over 20% of institutions have failed relatively simple measures [18].

III. The case for intensity-modulated radiation therapy (IMRT)

The above considerations provide strong motivation for re-imagining radiation therapy technology in a way that is less dependent on the expertise and availability of highly trained staff including engineers, the ready availability of maintenance equipment, and the reliability of the local infrastructure. In considering technology requirements, the first task is to determine what is needed. In particular, is the ability to provide intensity modulated radiation therapy (IMRT) a requirement? We argue that it is.

IMRT allows for complex dose distributions that allow for organ preservation. The use of IMRT emerged in the late 1990's and the evidence for its use has been well-established [19, 20]. In head-and-neck cancer therapy, for example, IMRT allows for sparing of the salivary glands. If these glands are not spared xerostomia results after a dose of approximately 23 Gy [21, 22] and this results in morbidities for patients such as fissures, infections and osteonecrosis which can be very debilitating and costly to manage [23-25]. In North America IMRT is offered in essentially every radiotherapy center [26, 27] and is used in approximately 50% of treatments [28].

If IMRT is necessary the question is how best to deliver it? The technique that has evolved from the 1990's onward employs moving multileaf collimators (MLCs) to modulate the radiation fluence. There are, however, many disadvantages to using MLCs for IMRT deliver. These include mechanical failures (leading to downtime and reduced throughput), stringent requirements for quality assurance and highly trained staff, challenges with commissioning including the measurement of small treatment fields, and inefficient use of dose leading to long treatment times. One of the possible approaches explored in the next section is the elimination of the MLC.

IV. IMRT TECHNOLOGY RE-IMAGINED

There are many possible alternative ways to modulate fluence for the purposes of IMRT. The approach that we are exploring is the use of physical compensators, i.e. metallic objects inserted in the beam to modulate the dose. Compensators-based IMRT is not new. It was employed to deliver IMRT in the 1990's[29-32]. There were, however, some limitations to the way that compensator-based IMRT was implemented in the 1990's and it was largely abandoned in favor of MLC solutions. Our thesis is that these limitations are not fundamental, that compensator-based IMRT designs were never explored to their full potential, and compensator-based IMRT is an especially attractive option for IMRT delivery in resource-limited settings. Because compensators have fewer moving parts, they should lend themselves to a simplified quality assurance approach that is based on some form of mechanical measurement. This could be automated in some way and may not require the presence of a medical physicist or other highly trained staff.

There are, however, many challenges to employing compensators. One is the need to perform block exchanges for each field. If this requires entering the room after each beam the treatment delivery time will be negatively impacted (see McCarroll et al. [12]). This is not a fundamental limitation, however. Several groups have explored mechanisms that would provide an automatic exchange of devices between fields [33, 34]. These were envisioned as add-ons to a C-arm gantry design. We are exploring a more extensive redesign which involves a ring model and associated exchange mechanism.

A second potential challenge is in the production of the patient-specific compensators themselves. The approach that found favor in the 1990's was a mail-order system whereby one would provide the compensator design specifications for each plan and a company would mill the required compensators out of metal (typically brass) and mail them to the clinic. This had many disadvantages, all of which would likely be amplified in the LMIC setting. A possible alternative of milling the compensators on-site at the clinic is also not attractive as this is outside the typical expertise in a clinical setting and would require a large shift in practice.

We are exploring a system whereby negative molds for the compensator are made out of plastic and these molds are then filled with metal beads. The technologies for forming plastic are more widely available and could be implemented on site. Other groups have explored such an approach[32, 35] but it has not become widespread likely because the associated technology was not widely available until quite recently. Figure 2 shows a Monte Carlo simulation of the device (60-Cobalt based in this case) and the associated transmission through a thin, flat compensator. Clearly the solid metal offers less transmission, but a bead formulation is acceptable at the expense of extra thickness. The disadvantages of thicker compensator can be partially obviated by the fact that they can be made divergent with the beam.

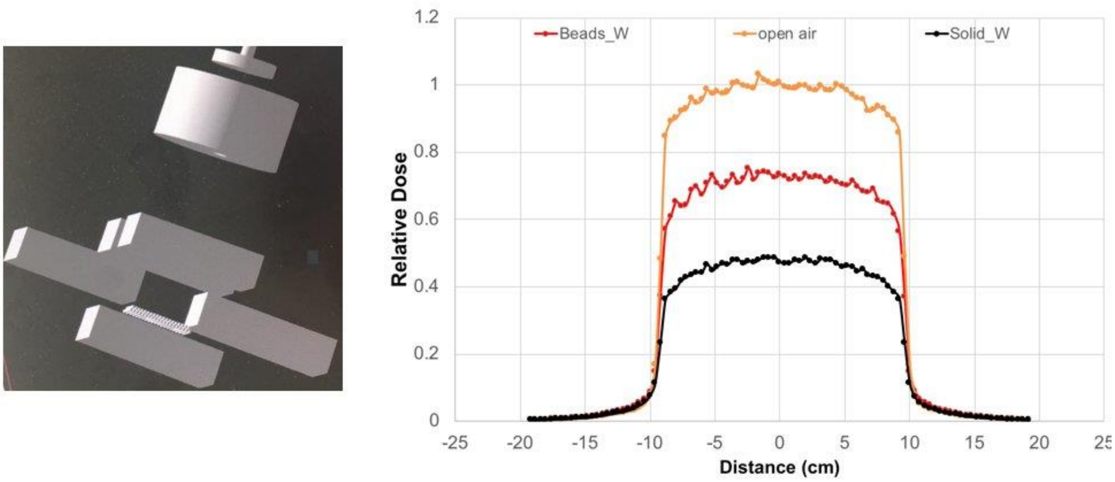

Figure 2:Monte Carlo simulation of the proposed device showing the geometry (left) and the transmission results (right) through 1 cm-thick tungsten either in sold for solid material (black) or beads (red).

Our initial simulations of treatment plans with this system [36] show that even with a 60-Cobalt source acceptable tumor coverage and organ-at-risk sparing can be achieved, that treatment times are reduced by approximately a factor of two compared to even linac MLC-based IMRT, and that the increase in skin dose is not clinically significant. The main reason for these gains is that compensators do not have the mechanical limitations of MLCs (they can be made with high resolution and fully divergent) and they also use radiation dose extremely efficiently, as opposed MLCs which are closed over many parts of the beam for long periods of time.

V. Technology and beyond

The redesign of radiotherapy delivery technology described here aims to address the specific needs of the LMIC setting. To our knowledge this has never been done before in a deliberate way and the potential impact is enormous. As important as technology is, however, it is also important to consider the whole care path when imaging a large-scale conversion to IMRT delivery. There will be educational needs and potentially a different mix of staffing. Key infrastructure components in the healthcare system will also be required. For example, a CT scanner and a treatment planning system. The conversion is well-justified, however, given the clear need for cancer therapy and radiotherapy in particular, the enormous benefit of IMRT in many disease sites and the potential health and economic benefits. Our hope is a thoughtful redesign of treatment technology will allow for high-quality cancer care in areas of the world where it is desperately needed.

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