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Cobalt, Linac, or Other: What Is the Best Solution for Radiation Therapy in Developing Countries?

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The international growth of cancer and lack of available treatment is en route to become a global crisis. With >60% of cancer patients needing radiation therapy at some point during their treatment course, the lack of available facilities and treatment programs worldwide is extremely problematic. The number of deaths from treatable cancers is projected to increase to 11.5 million deaths in 2030 because the international population is aging and growing. In this review, we present how best to answer the need for radiation therapy facilities from a technical standpoint. Specifically, we examine whether cobalt teletherapy machines or megavoltage linear accelerator machines are best equipped to handle the multitudes in need of radiation therapy treatment in the developing world. © 2014 Elsevier Inc.

Introduction

In a remote village of East Africa, a mother feels a lump develop in her breast. With the closest cancer center thousands of miles away and barely enough resources to survive daily life, months go by, and the mass enlarges and metastasizes until she eventually dies. At an overworked radiation center in West Africa, exhausted doctors and physicists work from 4 AM to 11 PM, doing all they can for the never-ending crowds of patients seeking treatment; yet they cannot afford a source change for their machine, causing treatments to take an extra 30 precious minutes per patient. A woman who was turned away sadly informs us, "I am going home to die." At the other end of the continent, a new facility in South Africa just upgraded to a new linear accelerator (linac), which is now down for the third week because of power shortages and inadequate engineering support for their new machine.

A global crisis is emerging as thousands upon thousands go untreated everyday in developing countries around the world. When resources do become available and outreach efforts prove effective, determining how best to proceed continues to be an issue of debate. Is newer technology, such as a linac, more appropriate for developing countries, or should cobalt teletherapy be implemented? Cancer is a leading cause of death worldwide, and the number of cases and deaths per year is increasing. Currently, the World Health Organization estimates 12.7 million people are diagnosed with cancer annually worldwide (1, 2). An estimated 7.6 million people die from cancer worldwide every year, of which 4 million people die prematurely (aged 30-69 years) (3). This number is increasing significantly, and by 2030 the number of deaths will increase by 45% and reach 11.5 million

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deaths annually (4). More than 70% of all cancer deaths occur in developing nations where lack of access to cancer care is a significant problem. Approximately 64% of cancer patients in the United States receive some form of radiation therapy (5), but lack of equipment in Third World countries make this therapy virtually inaccessible. The worldwide standard for cancer care is that there should be 1 radiation megavoltage machine for every 100,000 to 200,000 people living in a region. However, in some countries, there is no availability at all; in Africa, 29 countries have no machines, Senegal has 1 machine for 12 million people, Ghana and South Africa have 1 machine for 1 million people each, and Ethiopia has 1 machine for 70 million people (6-8).

Countries' economic status is closely linked to the availability of cancer treatment. A report of the status of pan-Asian countries demonstrated a clear link between the country's economic status and the availability of radiation facilities. In some of the countries surveyed, the radiation oncologist also covered duties of diagnostic radiologist, medical oncologist, and medical physicist. A lack of treatment planning systems and simulators was also observed. For example, in countries such as Bangladesh, <1 in 5 departments had a treatment planning system (9). This leads to either no care or increased waiting time in areas that do have a functioning machine. Even tertiary care medical centers that are privileged with a higher level of comprehensive cancer care resources are often burdened with patients from inside and outside of their country who travel in by foot to receive care. For example, in New Delhi, India, an audit performed at a tertiary medical center described increased waiting time with a median time for registration of patient and time to start radiation therapy course of 41 days, with 25% of patients unable to complete their course (10).

Transitioning internationally to high-level, cost-effective, and available radiation therapy

After the discovery of the therapeutic potential of radiation in the late 1890s, cobalt teletherapy was one of the first methods of delivering radiation therapy clinically. The first reported Cobalt-60 (Co-60) teletherapy machine was introduced into clinical use in London, Ontario, Canada, in 1951. Since that time, cobalt teletherapy machines have been constructed around the world and have been in popular use. The incorporation of the cobalt teletherapy machine was part of cancer treatment regimens that cured and palliated millions of individuals around the world successfully for the past 60 years. Nearing the end of the 20th century, cobalt teletherapy fell out of favor because of the superior dosimetry that a linac could provide. As improved techniques and modalities became available, cobalt teletherapy machines have over time been retired and replaced with more up-to-date equipment and are now mostly extinct in the United States. However, many countries only have access to cobalt machines. A review from Hungary (8) reveals cobalt machines continue to be the mainstay of treatment in Eastern Europe.

In Africa, radiation therapy has changed over the past decade. Information regarding the availability of equipment is maintained through the Directory of Radiotherapy Centers, a database provided by the International Atomic Energy Agency (IAEA) Regional and African and Interregional project reports. There are a total of 277 megavoltage machines in Africa, 32% (88 machines) are cobalt teletherapy machines, and 68% (189 machines) are linacs. This is in stark comparison to the past when, in 1998, approximately 60% of the machines in Africa were cobalt machines. Furthermore, installation of radiation machines have increased significantly over the past decade; in 1998, there were only 155 recorded radiation machines in all of Africa, and by 2010, this number had risen to 277 machines. Of the 189 linacs registered in the Directory of Radiotherapy Centers, almost half of those machines were <5 years old in 2010, whereas about half of the cobalt machines were >20 years old and needed to be replaced (5, 11). Most of these countries do not have the resources to replace their cobalt machines with new ones. A few countries have been able to acquire "new" machines from countries that send their old cobalt machine to be reused. Cobalt machine manufacturers have decreased in number, but a few thriving companies exist, including Best Medical International, a Canadian company, and Medway Technology, a Chinese company. Both of these companies have continued to manufacture and supply cobalt machines with options for new technological advances. Companies and engineers with knowledge of cobalt machine maintenance are now fewer in number, but the IAEA has replaced sources in several situations. For coordinating transport and installation, the World Health Organization has purchased sources from other countries in collaboration with IAEA to install the new sources. After source replacement, the output of the machine should be verified by the manufacturer, measurement by local physicists using a calibrated chamber and electrometer, and IAEA thermoluminescent dosimeters (TLDs). The IAEA has coordinated international quality assurance measures and published results of several quality assurance audits (12, 13). In cases in which audit results are outside of tolerance, assistance should be requested from IAEA or other volunteer physics experts. In addition, fly-in engineers from countries such as South Africa, Germany, France, and other European countries have been contacted by nonprofit organizations, and many have volunteered to fly in to help maintain machines if these become available. Expert fly-in engineers are essential for work in and around the source drawer due to the potential of high exposures. To keep costs down, minor machine maintenance and repair away from the source drawer may be performed by local engineers with some training.

Linac versus cobalt machines in developing countries

Deciding how best to address the growing and critical need for cancer care in developing countries is an ongoing debate. One of the areas of focus is the installation of megavoltage

Table 1 Practical factors in consideration of a cobalt versus linac machine[†]

	Cobalt	Linac
No. of units worldwide	2386	8460*
Maintenance	Replace source every 5 years	Frequent QA
Safety issues	Radioactive source—transport, disposal, ensuring functioning off switch	Labor-intensive QA processes
Staffing issue	Easier to perform QA and operate	More staff are educated and can support infrastructure in developed countries
Cost	CO-60 IMRT and linac-IMRT are cost-equivalent	Ongoing maintenance for linac is more expensive
Clinical acceptability	Yes	Yes

Abbreviations: IMRT = intensity modulated radiation therapy; linac = linear accelerator; QA = quality assurance.

* From the International Atomic Energy Agency.

[†] Based on World Health Organization criteria. Adapted from Ravichandran et al (16).

linac versus cobalt teletherapy machines in these countries. Some representatives from international organizations feel that linac-based facilities should be the wave of the future for developing countries because cobalt radiation therapy is thought to provide substandard treatment. Others feel the dire need for access to cancer care outweighs the benefit a linac machine could provide over a cobalt machine.

Linacs and cobalt machines both offer the ability to deliver external beam radiation therapy treatments. The question of which to use and why has been preliminarily studied by several groups (14, 15). The primary discussions in these studies revolve around dosimetric comparisons, including beam penetration, penumbra, dose rate, and dose uniformity and infrastructure comparisons, including requirements for adequate and stable power, machine downtime and repair costs, and security and radiation safety concerns. These differences have been summarized in Tables 1 and 2, which have been modified from Ravichandran et al (16). These studies are of significant value and should be referenced when faced with a decision between a linac and a cobalt machine. The vast majority of external beam machine purchases made in North America are linacs, thus it seems relatively safe to assume that the consensus opinion of the North American radiation oncology community is that linacs are superior to cobalt in terms of treatment quality, despite a significantly increased operational cost (17). This idea is supported by the estimation of Van Dyk et al that only 25% of patients treated in North America would receive adequate treatments if those treatments were delivered on cobalt machines (18).

However, this question continues to be actively debated. Should funds be invested for "outdated" but reliable cobalt radiation therapy machines, or should funds be invested in up-to-date, more dosimetrically acceptable linac megavoltage facilities to answer the call of the hundreds of millions of people with no access to radiation therapy services?

Advantages to a linac megavoltage machine include the following:

1. Better quality dosimetry—The Cobalt 60-gamma radiation energy of 1.25 MV and approximate percentage depth of 55% at 10 cm has a less defined penumbra, and its decaying dose rate limits its use in clinical situations compared with more modern megavoltage linear accelerators. Significant differences in grade 3 to 5 toxicities have been reported (17).
2. Security concerns for an active source—Proper security is necessary for compliance with international obligations for nuclear security as outlined by the IAEA (19). In countries where vandalism and theft may be rampant, bolstered security may be an added requirement. Security measures must be in place for source transfers, disposal, and the vault that houses the cobalt unit.
3. Radiation safety—Unlike a linac, a cobalt source always produces radiation, and the source has a high potential of harm. Therefore, an adequate radiation safety framework must be in place to be compliant with the safety standards set by the IAEA.

Table 2 Physical factors

	Cobalt	Linac
Buildup	Equivalent to 4 MV, buildup 5 mm	6 MV: 15 mm; 15-18 MV: 28-35 mm
Skin dose	40%-50%	6 MV: 25%; 18 MV: 15%-25%
Penetration	54% (10 cm)	6 MV: 67% (10 cm); 18 MV: 77% (10 cm)
Penumbra	90%-10% is 1.5-cm field definition, 50%	Sharp beam field definition, 80%
Shape of isodose curves	Rounded (correctable)	Flattened by filter
Integral dose/tumor ratio	More for nonoptimal plans, but acceptable for good plans	Less with simple fields
Irregular fields	Achievable with blocks and MLCs being adapted	MLC
Dose rate	2.5 Gy/min; factor of 4 longer than linac	10 Gy/min
Energy	Lower: greater effect on tissue density and air gap	Higher: less superficial dose and dose bath

Abbreviations: linac = linear accelerator; MLC = multileaf collimator. Adapted from Ravichandran et al (16).

These include requirements for the application of radiation protection principles, government and legal frameworks, regulatory bodies, and management for facilities and activities (18, 20). In addition, local radiation safety measures should be in place to protect the health of workers, the public, and patients. These may include, for example, independent radiation monitors in cobalt vaults, staff dose monitoring, and sufficient shielding.

Advantages of Co-60 units include the following:

1. Dependability—In places with inadequate or unreliable power supply, a cobalt machine is more dependable. Linacs require adequate and stable power supplies to generate consistent reliable radiation beams, whereas cobalt machines do not. Furthermore, unstable power can cause significant damage to the electronic systems of a linac. A power outage can render even the most sophisticated machines useless.
2. Simplicity of repair—In situations with lack of close or affordable machine repair mechanisms, linac repair is expensive, time-consuming, and requires high-level expertise. This requirement is significantly reduced for cobalt machines. In addition, cobalt machines are typically more robust.
3. Less sophisticated to manage safely—Because of the sophistication of the linac relative to the Co-60 machine, improper training could lead to dangerous situations when using a linac. Machine calibration for a linac is much more rigorous than for Co-60 machines; the need to make changes occurs more often and is less predictable than that for a Co-60 machine. Many factors for Co-60 machines are based on geometry, mechanical stability, and natural decay of the source, whereas linac functionality and calibration are based on a multitude of more complicated factors. From quality assurance to dosimetry planning, and everything in between, linacs are more complicated than Co-60 machines and are thus more prone to errors for staff in developing countries where there is often a lack of training, staffing, support, and resources.
4. Cost—Developing new facilities with access to the economic infrastructure and expertise needed to support a radiation treatment facility, particularly one with a linear accelerator can be cost-prohibitive. The increased cost to maintain linac machines is a severe drawback to cancer care in countries with limited resources. A multinational review reported an average cost to maintain a linac was $41,000 versus $6000 to maintain a Co-60 machine (21). These numbers do not include the cost of power, part replacement, or the startup cost or maintenance of a facility that meets qualifications, as well as the ongoing cost of the expert staff needed to operate it.
5. Easier to learn—Because of the increased technical challenges of running a linac facility, it may be most practical to start with a cobalt machine and advance from there. Previous studies have demonstrated the adaptation of drastically new technology may increase error rates, and more educational programs are being developed. Even established linac programs still need ongoing audits and education. A recent audit by the IAEA conducted in 60 centers in 8 European countries (Estonia, Hungary, Latvia, Lithuania, Serbia, Slovakia, Poland, and Portugal) revealed a 10% rate of dosimetry problems requiring intervention for safe delivery, which included awareness of suboptimal beam modeling, algorithm, and beam quality (12). A similar dosimetric verification in Serbia (13) had the same conclusion. Audits like these, performed by the IAEA, are helping to improve the understanding of new treatment planning systems in an attempt to maximize quality of care in developing programs that do have megavoltage linear accelerators. It also suggests that developing facilities may need to have a reasonable starting point.
6. Potential—Recent innovations in methods to adjust cobalt machines to produce flattened isodose curves using multileaf collimators and development of tomotherapy techniques with cobalt machines have been implemented in several centers throughout the world (16). In answer to the dose rate problem, in India, a teletherapy source has been designed to have high output, as much as 170 cGy/min at 1 meter (19). Innovations such as these could provide the ability to deliver modern radiation therapy utilizing a lower-cost machine. These new higher dose rate sources have to follow the same transport guidelines as IAEA guidelines for brachytherapy sources. A safety officer and transport team for these sources need to be arranged when transporting and installing such sources. Usually the manufacturer of the machine helps arrange the source exchanges, which can be coordinated with IAEA and local safety officers. Another example of modernizing available or adaptable cobalt machines is the use of intensity modulated radiation therapy (IMRT). Utilization of multileaf collimators and intensity-modulated planning can reduce the energy limitations on a cobalt beam, and this can compensate greatly for its physical limitations. In Campobasso, Italy, forward-planned IMRT was analyzed as a feasible method of utilizing teletherapy with field-in-field techniques. This dosimetry study showed the improvement of maximum dose, high-dose volume, and better heart and lung sparing with field-in-field forward planning compared to standard plan with cobalt teletherapy (22). This may allow adoption of newer techniques, such as accelerated hypofractionated techniques for breast-conserving therapy. Ongoing studies have shown equivalent quality-of-life scores in breast cancer patients treated with linac and Co-60 (23), showing that it is possible to treat breast-conserving therapy patients effectively in developing countries with limited resources.

Moving toward quality improvement

Given that cobalt machines will be the most viable option for many countries as a starting point for developing a radiation therapy program, it is worthwhile to discuss other areas of the treatment process that may improve treatment quality at low cost and effort. Whether a cobalt or linac machine is constructed at an existing radiation therapy site, improvement in several areas of radiation therapy should continue to be a focus.

Some examples are as follows:

1. Improvement on current techniques in all areas of the workplace: patient throughput, patient setup, simulation, prescription, contouring, treatment planning, quality assurance, and general equipment functionality.
2. Implementation of procedures and protocols by ensuring the appropriate establishment of second check systems for all areas of work to prevent “catastrophic” events.
3. Transition from 2-dimensional to 3-dimensional or 3-dimensional to IMRT.
4. Provide additional, more affordable equipment that can supplement a Co-60 machine. For example, a brachytherapy machine can treat a number of sites better than a Co-60

machine, which otherwise would not be possible (or would be less desirable) without electrons or high energy photons—for example, prostate, breast boosts, and skin lesions. In some curative intent scenarios, such as cervical cancer, which is the most common curable cancer among women worldwide, a high-dose-rate or low-dose-rate brachytherapy boost should be included if brachytherapy is available. Skin lesions (eg, Kaposi sarcoma) can be treated in a simple manner by using high-dose-rate brachytherapy (24).

5. Improve patient simulation—better image quality.
6. Adequate data management—ability to transfer simulation images to the treatment planning system.
7. Improve the adequacy and accuracy of treatment planning system—use of inhomogeneities in dose calculations and treatment volume definition.
8. Patient immobilization through simulation and treatment processes.
9. Consideration of add-ons to the cobalt machine (eg, multileaf collimators and setup verification imaging).
10. Ensure adequate source activity for reasonable treatment times.

Conclusion

Since the advent of therapeutic radiation in 1895 and the first clinical use of the cobalt machine in 1951, our field has made significant technologic progress. Comparisons of cobalt versus linac treatments have previously been described. In general, whereas linacs are generally more favorable for dosimetric reasons, the merits of cobalt treatment units with respect to power supply, maintenance issues, and training mean that cobalt units are often the better option in many developing countries. In countries with insufficient security and safety controls, linacs (or no treatment units) are preferable to cobalt units due to the potential risk of harm that could be caused by the source. Despite the dosimetric disadvantages of cobalt treatments, there is a growing body of literature supporting the use of modified cobalt units that can provide equivalent cancer care outcomes. It is possible that cobalt radiation therapy may be the answer to the growing and drastic need for treatment. Because cobalt units around the world have treated millions of people since the inception of the first clinical unit in 1951, it may be unethical to withhold such care a sufficient radiation therapy unit could provide. In addition, the burgeoning development of adaptable technologies as additions to cobalt units may make the differences in linac versus cobalt treatment smaller. Development and implementation of more radiation therapy treatment sites may be best served by starting small, with an easier-to-maintain cobalt machine that can later be upgraded to a more sophisticated linear accelerator.

Ultimately, deciding how best to proceed requires coordination with each country and representatives overseeing radiation therapy, as well as meeting each country where they are at to develop the next step of quality improvement. Cancer care has improved immensely over the past 100 years, yet there are millions of people internationally who remain without the lifesaving and palliating power of radiation therapy.

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