A RETROSPECTIVE OF COBALT-60 RADIATION THERAPY: *"THE ATOM BOMB THAT SAVES LIVES"*

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Abstract — **The first cancer patients irradiated with cobalt-60 gamma rays using external beam radiotherapy occurred in 1951. The development of cobalt-60 machines represented a momentous breakthrough providing improved tumour control and reduced complications, along with much lower skin reactions, at a relatively low cost. This article provides a review of the historic context in which the advances in radiation therapy with megavoltage gamma rays occurred and describes some of the physics and engineering details of the associated developments as well as some of the key locations and people involved in these events. It is estimated that over 50 million patients have benefited from cobalt-60 teletherapy. While the early growth in the use of cobalt-60 was remarkable, linear accelerators (linacs) provided strong competition such that in the mid-1980s, the number of linacs superseded the number of cobalt machines. In the meantime, other technological advances on linear accelerators provided increased capabilities such as intensity modulation and image guidance, developments which were *not* implemented on cobalt-60 machines until decades later. The simplicity and relatively low cost of cobalt teletherapy provided an incentive for its use in lower-income situations where financial resources are constrained and cancers are often more advanced, generally requiring simpler treatment techniques. Cobalt-60 sources continue to be used in a variety of other treatment contexts including high-dose-rate brachytherapy and stereotactic radiosurgery. However, radiation safety and security concerns with the possibility of malicious applications has developed a mentality of removing these sources from usage as much as possible. Furthermore, with the increased demand for cobalt-59 in other contexts, the future supply of cobalt metal will be strained. The combined concerns of greater complexity and potentially reduced reliability for cobalt-60 machines with add-on devices, and the security concerns for cobalt-60 radioactive sources have significantly reduced the early advantages of cobalt-60 over linacs and, thus, has resulted in a significant decline in their use.**

Keywords — **cobalt-60, radiotherapy, history, teletherapy, brachytherapy.**

CONTENTS

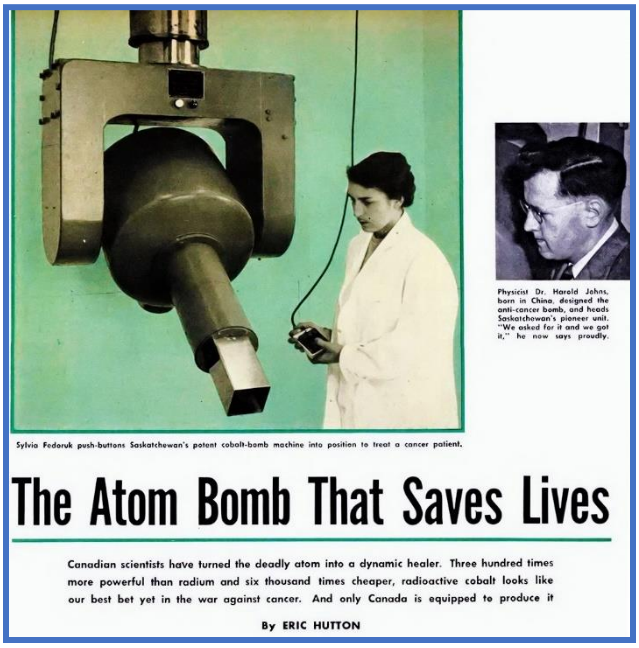

Figure 1. Opening page of an article written by Eric Hutton for MacLean's magazine, Canada's premier current affairs magazine. The picture on the left is the cobalt-60 machine designed by Harold Johns who is shown on the right. The medical physicist operating the machine is Sylvia Fedoruk who eventually became the lieutenant governor (the Queen's representative) for the Province of Saskatchewan, Canada (1988-1994) [66].

I. INTRODUCTION

The headline and the opening sentences of an article in MacLean's magazine, Canada's premier current affairs publication, written by Eric Hutton and published on 15 February 1952 read: **"The Atom Bomb That Saves Lives"** "Canadian scientists have turned the deadly atom into a dynamic healer. Three hundred times more powerful than radium and six thousand times cheaper, radioactive cobalt looks like our best bet yet in the war against cancer. And only Canada is equipped to produce it." (Figure 1) [66]. It was clear that cobalt-60 radiation therapy was considered the new breakthrough and game-changer for treatment of cancer patients and it was considered international news. In this review, we will provide the historical development of cobalt-60 radiation therapy, placing it into a context with other relevant developments and provide a sense of the global impact on improvements in cancer treatment. Major references for this historical development include: a detailed paper by Robison [109] who provided an excellent overview of the quest for the development of megavoltage beams, both x-ray and gamma ray; four articles published in 1999 in the newsletter of the Canadian Organization of Medical Physicists, *InterActions* [33-35;96]; a book and editorial by Peter Almond outlining the history of development of the first cobalt-60 unit in the United States [3;4]; a handbook from London, Ontario on early experience and guidance for cobalt-60 teletherapy [118]; an encyclopedia contribution by J.R. Cunningham [36], a couple of history articles [63;115], in addition to the many other references cited in this paper.

II. BRIEF HISTORY OF RADIATION THERAPY

X-rays were discovered in 1895 by Wilhelm Conrad Röntgen and this was followed shortly thereafter with the discovery of radioactivity by Antoine Henri Becquerel in 1896. Already in 1896, consideration was given to the use of radiation for medical purposes [109]. In 1898, Becquerel along with Pierre Curie and Maria Sklodowska-Curie were able to separate two radioactive isotopes from uranium: polonium and radium. It was very shortly after these discoveries that both x-rays and radioactive isotopes were used to treat a variety of cancers, initially primarily for dermatological conditions. With Coolidge's introduction of "deep therapy" tubes of 200 kV in 1922, the subsequent period until the 1940s used mostly low energy x-rays (perhaps up to 400 kV but generally in the range of 50-250 kV) and radium and radon for the treatment of cancer patients. Radon sources were used for interstitial treatments and radium was used for both external beam radiotherapy as well as brachytherapy. High voltage generators were also developed by Van de Graaff and Trump and attained megavoltage levels (1-2 MV). The first megavoltage x-ray cancer treatment took place in Boston on 1 March 1937 [115]. A 1.2 MV generator was later installed at Massachusetts General Hospital in 1939 and operated until 1955. These were colossal electrical devices with limited dose rates and were intimidating for cancer patients. It is historically interesting that John D. Trump, uncle of present-day United States President Donald Trump, collaborated with R.J. Van de Graaff at the Massachusetts Institute of Technology (MIT) on megavoltage electrostatic x-ray generators; 43 generators were in use clinically until 1969 [115]. Their research also addressed synchronous field shaping [123;139], which is discussed more later in the context of cobalt-60 teletherapy.

III. LIMITATIONS OF RADIATION THERAPY UNTIL THE 1950s

The limitations of x-rays included high skin doses and a lack of deep penetration as would be needed for tumours deep inside the body. Furthermore, the dose rates were such that the x-rays needed to be applied with fairly short treatment distances, which resulted in shallower depth of dose penetration. The outputs of x-ray tubes and generators were quite variable resulting in complications in their dose calibration [109].

The problem with the alternative radiation source, radium, was that it was difficult to produce in high enough activities for external beam therapy; as part of its nuclear decay process, it emitted a radioactive gas resulting in radiation safety concerns; and it was prohibitively expensive (about $885 per mgm in 2020 US dollars!) [109]. A typical therapy radium unit required a radium pack in the range of 5 to 10 grams affordable only in well-endowed hospital or research institutions with the equivalent of million-dollar budgets (2020 currency). Treatment machines needed to operate at short treatment distances to maintain high enough dose rates and to keep patient treatment times reasonable. A typical dose rate was still only ~3 cGy per minute at a depth of 10 cm in tissue. Finally, these units had poor source shielding resulting in radiation exposures to the staff. Although low-activity cobalt-60 sources in the range of 100 Ci were considered as replacement for radium in tele-radium treatment units, the optimal use of cobalt-60 required much higher activity and completely redesigned equipment as described in Section VII.

IV. RADIOACTIVE SOURCE DEVELOPMENT

The discovery of the stable form of cobalt, i.e., cobalt-59, occurred circa 1735 and is attributed to the Swedish chemist Georg Brandt (1694–1768). Cobalt metal is found in the earth's crust generally in a chemically combined form and is often produced as a by-product of copper and nickel mining. The word *cobalt* is derived from the German *kobalt*, from *kobold* meaning "goblin", a superstitious term used for the ore of cobalt by miners. Cobalt-based blue pigments (cobalt blue) have been used since ancient times for jewelry and paints, and to impart a distinctive blue tint to glass [135]. Currently, the Democratic Republic of the Congo produces about 63% of the world's cobalt with an expectation that this will rise to 73% by 2025. The next top three producers of cobalt are Russia, Australia and Canada. Raw cobalt metal is relatively inexpensive. Prices peaked in 2018 at almost US$100.00 per kg but currently trade at $30.00 per kg. The demand for cobalt is expected to rise with the increased production of electric cars as cobalt continues to be used in their lithium-ion batteries.

It was prior to and during the Second World War in the 1930s and 40s that nuclear reactor developments were at an embryonic phase with the resulting discovery that when uranium was bombarded with neutrons, it broke into separate fragments, with a process known as nuclear "fission". This paved the way for producing "artificial" radioactive isotopes with potential biomedical applications.

An early report, perhaps the first, concerning cobalt-induced radioactivity was published by Rotblat in *Nature* in 1935 [111], although the estimated decay scheme and half-life was far from as we know them today. Sampson et al in 1936 from Princeton University were the first to observe a long-lived isotope of cobalt-60 by *irradiating cobalt-59 with neutrons* and reported a half-life to be more than one year [113]. Inconsistent results on the gamma energy spectrum and half-life persisted in experimental results reported by Risser [3;108] and Livingood et al. from University of California, Berkeley [88;89;135]. The half-life riddle was finally resolved by Nelson et al in 1937 [3;108].

In England in 1937, Arthur Eve (formally of McGill University, Canada) and Leonard George Grimmett reported on therapeutic medical applications of artificial radioactive sources *versus* x-rays [46]. Grimmett was a visionary medical physicist with prior clinical experience in the United Kingdom with radium devices. A detailed biography and record of his achievements can be found in the book "Cobalt Blues" by Peter Almond [4]. Starting in 1929, Grimmett worked at the Westminster Hospital in London, England. During World War II, Grimmett became convinced that cobalt-60 would be an exquisite replacement for radium in a practical radiotherapy machine [3;25], a proposal that was punctuated by J.S. Mitchell [95]. Starting in 1948, Grimmett played a key role in the design of an early cobalt therapy unit to be installed at the M.D. Anderson Hospital in Houston, Texas, as will be described later. He collaborated with Marshall Brucer, research chairman of the Oak Ridge Institute for Nuclear Studies (ORINS) and Dale Trout of the General Electric X-ray Corporation (Milwaukee, Wisconsin). He published the first article describing a cobalt therapy machine design in 1950 in a local journal [3;57], preceding a key paper by Harold Elford Johns et al of Canada [71] (Figure 2).

The activation of cobalt-60 is represented by the following nuclear reaction:

$$^{59}_{27}\mathrm{Co} + \, ^{1}_{0}n \rightarrow \, ^{60}_{27}\mathrm{Co} \qquad (1)$$

The nuclear cross-section reflective of the probability of capturing a slow neutron in cobalt-59 is large (i.e., 37 barns) so that sources of high specific activity could be produced in a nuclear reactor in reasonable time. The neutron flux in the Canadian NRC NRX reactor described later was considered intense for that era, ~10^{13} neutrons per cm^2 per second. The first cobalt-60 sources reached a net activity of ~1,000 Ci with an exposure time of approximately 1.5 years [71].

The decay of cobalt-60 which then yields the megavoltage gamma rays is denoted by:

$$^{60}_{27}\mathrm{Co} \rightarrow \, ^{60}_{28}\mathrm{Ni} + \, ^{0}_{-1}e + \bar{\upsilon}_e + 2\gamma(1.17 \,\&\, 1.33 \text{ MeV}) \qquad (2)$$

where $^{0}_{-1}e$ represents a beta particle with a maximum energy of 0.32 MeV and $\bar{\upsilon}_e$ is an antineutrino. The half-life of this decay process is 5.27 years and, as indicated, two megavoltage photons are emitted with energies of 1.17 and 1.33 MeV. Hence, cobalt-60 yields an ample supply of quasi-monoenergetic megavoltage photon radiation [71].

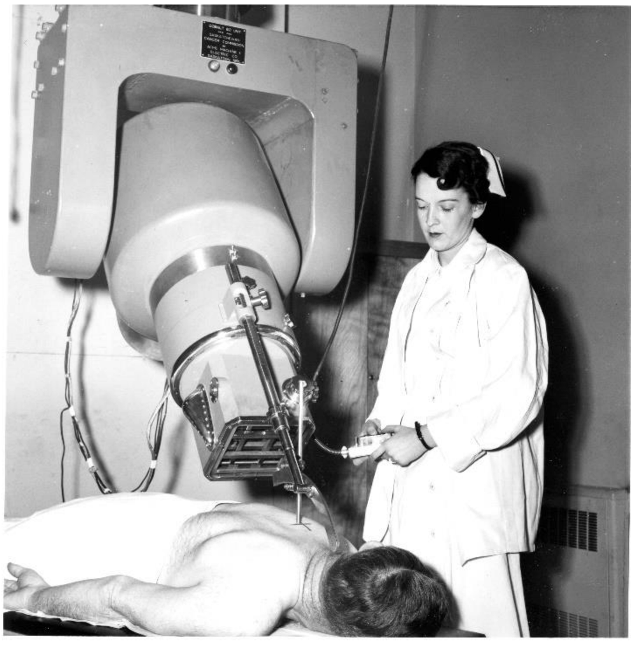

Figure 2. The Saskatoon Unit designed by Harold Johns and students, and John MacKay of Acme Machine and Electric of Saskatoon. From University of Saskatchewan, University Archives and Special Collections, University Photograph Collection, A-2244.

Assuming a typical source size of 6 cm^3 weighing ~55 grams, the yield from the NRX reactor was ~20 Ci of cobalt-60 per gram of original *cobalt-59* metal assumed to be of high purity. As Professor Harold Johns [74] might have stated "It is left to the student to show that the fraction of NRX-activated cobalt-60 was only ~2% of initial cobalt-59". If this exposure had been prolonged (impractically) to several *decades*, this fraction would have equilibrated at ~8%, yielding of ~100 Ci per gm of *cobalt-59.* If it were possible to increase the reactor neutron flux significantly by a factor of 10 (i.e., 10^{14} neutrons per cm^2 per s) to outpace the source decay, the theoretical limit is the specific activity (1,100 Ci per gram of cobalt-60*).* It cannot be reached practically because of limited exposure time, and self-attenuation and scatter within the source capsule. However, sources of ~500 Ci per gm of cobalt-59 are routinely produced today for current manufacturers of cobalt medical devices [36].

Important events in the development of nuclear reactors that preceded the clinical implementation of cobalt therapy machines are now described. Enrico Fermi helped build the first nuclear reactor in Chicago in 1942 as part of the Manhattan project. He noted that neutrons travelling at slower speeds were more effective at splitting nuclei compared to faster ones. Hence, they developed "moderators" to slow the neutrons. While the United States used graphite as a moderator, the team in Montreal, Canada, working under Canada's National Research Council (NRC), used heavy water, D_2O [87]. The uranium used for these reactors was mined and processed by Eldorado Mining and Refining Ltd. The Canadians built a research reactor in an outpost known as Chalk River, approximately 190 km (120 miles) northwest of Ottawa, the nation's capital. The first small heavy water reactor was the Zero Energy Experimental Pile (ZEEP) and on 5 September 1945 the first successful, peaceful atomic reaction occurred outside of the United States, just one month after the atomic bomb explosions in Hiroshima and Nagasaki. The subsequent "big brother" to the ZEEP reactor also located in Chalk River was to be known as the National Research Experimental (NRX) and first went critical in 1947. The reactor emerged from the World War II alliance of Canada, Britain, and the United States [4]. It also used natural uranium and heavy water to provide a significant neutron flux capable of producing a variety of radioactive isotopes including cobalt-60. The heat generated by the reactions was cooled by water drawn from the adjacent Ottawa River [87]. *The neutron flux at that time was ten times greater than any other known reactor in existence,* thus allowing for faster production of isotopes along with higher specific activities and placing Canada at the forefront of nuclear reactor and efficient isotope production for medical research and applications. This was *the* enabling technology for the development of clinical cobalt-60 teletherapy machines for the world.

During this same time period, Harold Elford Johns, a physicist, who was then with the Saskatchewan Cancer Commission, recommended the procurement of a betatron (22 MeV) and also the *de novo* development of a cobalt-60 teletherapy unit. His original cost estimate for constructing a new cobalt unit was between $2,500 and $7,000 in 1950 dollars or $25,000-$70,000 in today's dollars [63]. He found enthusiastic financial support for *both* devices from the Premier of the government of Saskatchewan, T. C. ("Tommy") Douglas. Douglas is recognized for establishing Canada's socialized national medical care program, in addition to being the grandfather of actor Kiefer Sutherland.

In the autumn of 1949, Chalk River scientists A.J. Cipriani and W.B. Lewis began the activation of enough cobalt material to prepare three radioactive teletherapy sources in the NRX reactor, each with a goal of one kilocurie. Johns assembled his physics research team in Saskatoon, Saskatchewan and with clinical colleague, Dr. A.T. ("Sandy") Watson, submitted a request to the NRX staff for a cobalt-60 teletherapy source on 13 August 1949. The second source request came from Donald Green and Roy Errington of Eldorado Mining and Refining Limited for integration into a commercial unit destined to Dr. Ivan Smith. The installation was planned for the Ontario Institute of Radiotherapy, then located in the War Memorial Children's Hospital across the street (South Street) from the former Victoria Hospital in London, Canada. The first two cobalt sources were made from thin wafers, 0.052 cm thick and 2.55 cm in diameter (i.e., the size of a Canadian 25-cent coin). Once removed, they were to be stacked to an overall thickness of 1.3 cm and sealed in a metal cylindrical capsule to produce the final teletherapy source. The requisition for the third source was ambiguous. It was originally requested by physicist W.V. Mayneord and reserved for the Royal (now Marsden) Hospital in England [87]. However, export restrictions forced a cancellation of that order. The third source production was then re-assigned to satisfy a custom order received from Gilbert Fletcher and Leonard Grimmett of the M.D. Anderson Hospital in Houston, Texas, working in collaboration with the Oak Ridge Institute of Nuclear Studies (ORINS) and General Electric X-ray Corporation (Milwaukee, WI). This source was designed differently by Grimmett as a stack of four plaques, each 2 x 2 x 0.25 cm^3. These plaques were initially exposed in the Oak Ridge reactor, but it would have taken over five years to achieve the desired total activity of 1,250 Ci. The plaques were therefore eventually transferred to the "hotter" NRX reactor, but net activity after a 10-month exposure was still disappointing (650 Ci) due to excessive self-attenuation. A secondary "top-up" irradiation in the reactor was applied for six months, and the sources were not ready until summer of 1952, with a final activity of 876 Ci. There was additional misfortune for the M.D. Anderson group with Grimmett's untimely death due to cardiac arrest in May of 1951 [3]. He did not live to see his dream of a cobalt machine materialize in the United States and beyond. Cross-border regulatory issues, dosimetry studies at the Oakridge Institute for Nuclear Studies (OINS), and bunker construction delays resulted in final clinical installation of the General Electric unit at the M.D. Anderson Hospital in September 1953. Meanwhile another machine was installed in Los Angeles, leading to the first case treated in the United States (23 April 1952). That unit remained in service until 1962.

V. THE RACE TO FIRST CANCER TREATMENTS

In 1947, Mayneord and A. Cipriani, a Canadian biophysicist, measured the absorption characteristics of cobalt-60 gamma rays and determined that the incident radiation consisted of two spectral lines at 1.1 and 1.3 MeV [92]. Mayneord had also delivered a series of lectures in a two-week course on the physics of radiotherapy at Toronto General Hospital in 1946 at which time he also spoke enthusiastically about the possibility of cobalt-60 as a source of radiation for a teletherapy unit. In the audience was Harold E. Johns who was visiting from the University of Saskatchewan. As a point of historical financial interest, Dr. Johns' salary at that time was reported to be $3,600 per annum, or $54,000 in today's dollars, evenly split between the two collaborating institutions [63]. The profession of medical physicist was at its infancy and its societal value was not yet fully recognized. Cobalt-60 developments played a large role in changing this perception. The Mayneord lectures piqued Harold Johns' interest in cobalt-60 teletherapy. The combination of a stronger, spectrally simpler, smaller and cheaper radioactive source in comparison to radium provided multiple reasons to make it a tremendous substitute for radium and megavoltage x-ray generators.

As a positive side effect of the Mayneord lectures and associated notes, Harold Johns went on to write the first edition of *The Physics of Radiation Therapy* which eventually evolved to four editions with subsequent editions being entitled *The Physics of Radiology* and published with co-author John Robert (Jack) Cunningham [73;74;130]. This became the classic textbook for medical physicists in training around the world for many decades.

As noted previously, Grimmett was a creative visionary physicist who was known for having designed and built an innovative 5-10 gram teleradium unit in which the source was pneumatically moved into the unit. When Grimmett moved to Houston in early 1949, he and Gilbert Fletcher planned to purchase one of the units, without the radium, and load it with a 50 Ci cobalt-60 source. When on a visit to Oak Ridge in August 1949, Grimmett was told that a 1000 Ci source was possible, he knew that an extended treatment distance, compared to the teleradium unit was possible and he immediately started to design a brand new unit to take full advantage of such a large amount of activity. From a radiation safety viewpoint, he also realized that such source in a radium unit would present a radiation hazard.

In February 1950, the isotope division of the Atomic Energy Commission (A.E.C.) and Oak Ridge called a meeting in Washington D.C. to discuss and solicit designs for a cobalt-60 irradiator. Thirty-three people attended from around the U.S. and Canada made up of radiologists, physicists, governmental agency representatives and industry. It was at this meeting that the U.S. became fully aware of the extent of the Canadian program and that contrary to earlier promises, the Oak Ridge reactor would not be able to deliver on a 1000 Ci source. Grimmett immediately started to make arrangements to get the cobalt-60 sources for his unit transferred to the Canadian reactor to be activated [49].

It was at this meeting that Grimmett and Johns met for the first and only time and there is no record that they corresponded afterwards. Both were extremely busy with research and development duties and Grimmett unfortunately passed away 15 months later [4] – this being an era well before the availability of e-mail! However, the two groups continued to be in contact. In July 1951, Brucer and Kerman, the radiologist, from the Oak Ridge project visited Canada to follow up on the status of the cobalt sources and took the opportunity to visit with Johns and the radiation oncologist, Sandy Watson, in Saskatoon. In addition, Watson and Fletcher, who were good friends, were constantly in contact.

Roy Errington had been hired by Eldorado Mining and Refining Limited in 1944 to setup a sales department to sell uranium. He also became aware of Mayneord's theoretical proposal and its strong commercial potential, with a favourable half-life, ideal for recurrent sales as a supply item. When Eldorado Mining won the right to sell cobalt-60, Errington decided to develop equipment to help sell his new product [87]. On his way to a meeting in Chicago in 1949, Errington met with Dr. Ivan Smith in London, Ontario, Canada and was assured that cancer therapists (now called radiation oncologists) would actually use a teletherapy cobalt-60 machine. It is not clear if this meeting was pre-planned or simply serendipitous, but it most certainly was appropriate. London had become the second largest cancer centre in the province of Ontario. Smith was a surgeon-pathologist and Chair of the Department of Therapeutic Radiology at the University of Western Ontario. Radiation oncology was not an established specialty in Canada at that time. His positive reaction to a clinical cobalt unit led Errington to seek internal corporate funding that accelerated commercial development for such a machine.

A prototype commercial unit was designed by Donald T. Green of Eldorado Mining and Refining Limited and built under contract by the Canadian Vickers company of Montreal, Canada. With improvements in manufacturing, production of the first commercial units (Eldorado A, a product name resonating with an eye-catching Cadillac vehicle) transferred back to Eldorado Mining. The ***Eldorado A* became the first cobalt-60 teletherapy unit in the world to be used clinically on a cancer patient on 27 October 1951 in London, Ontario, Canada** (Figure 3). This first unit was purchased with a special grant from the Ontario Cancer Treatment and Research Foundation (OCTRF) for the Ontario Institute of Radiotherapy of Victoria Hospital in London, Ontario, Canada, with a special price tag of $25,000 dollars in 1951, equivalent to $250,000 today. The first *rotational* unit, called the Theratron Model B, was designed in 1952 and sold at a price that was double the Eldorado A. This was the beginning of the Theratron series of cobalt units sold by Commercial Products Division (CPD) of Atomic Energy of Canada Limited (AECL) [5], which eventually became MDS-Nordion, and, now, is Best Theratronics.

In parallel with these developments, Harold Johns led an independent research group in Western Canada at Saskatoon. His machine design (Figures 2 and 4) was later adopted by the Picker X-ray Company and featured a Johns-McKay collimator to produce variable field sizes without the use of individual lead cones (see Figure 13). The collimators (known as Johns-McKay collimators) were built under contract by the Acme Machine and Electric Company in Saskatoon [77]. The first treatment in Western Canada occurred on 8 November 1951 – just a few weeks after the world's first treatment in London, Ontario. The Saskatoon patient was a 43-year-old woman with a cervical tumour, treated at Saskatoon's University Hospital (now Royal University Hospital). She lived to be over 90 years of age! This led the Saskatoon group to claim bragging rights for the first *successful* cobalt patient treatment. To be fair, it is not known how many curative cases were treated in London between 27 October and 8 November 1951. Saskatoon's cobalt machine treated 6,728 patients until it was replaced in 1972. Meanwhile, Dr. Johns left Saskatoon in 1962 to become the Head of Physics at the Princess Margaret Hospital (PMH) and Ontario Cancer Institute (OCI) in Toronto. Anecdotally, it was reported in the recent Hollywood movie, *First Man*, that Neil Armstrong attempted to consult with Dr. Johns regarding the possible cobalt-60 treatment for his very young daughter who had developed a brain tumour. Dr. Johns continued his creative work with innovations in radiation chemistry, ultraviolet damage to DNA, and medical imaging (CT). As an aside, two authors of this article (JVD, JJB) worked in the same institution with Dr. Johns for many years in Toronto and have benefited immensely from his exceptional attention to computational and experimental details in medical radiation physics research.

The close timing of the initial treatments led to the designation that London and Saskatoon were engaged in a "race" to achieve the world's first cobalt-60 irradiation of a cancer patient; it clearly became a photo finish considering all the interim delivery logistics and source calibration issues for a novel source. London's source had undergone extensive radiation measurements, including the first depth-dose curves, at Canada's National Research Council in Ottawa [43;44]. In effect, the Eldorado A arrived in London *pre-calibrated* in 'plug-and-play' configuration on 23 October 1951. This neutralizes unfair

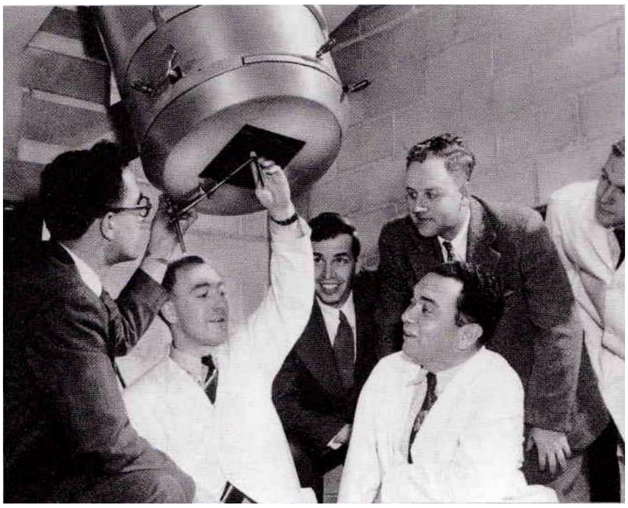

Figure 3. The Eldorado A at Victoria Hospital in London Ontario in 1951. The first patient treatment was given on 27 October 1951. Don Green (far left) was an engineering physicist involved in its design. Roy Errington (second from right) became the founder of MDS Nordion and heavily involved in the initial development and sales of cobalt teletherapy. Dr. Ivan Smith (right foreground) was a surgeon-pathologist and Head of the London cancer clinic. Dr. Frank Bately (with arm up below the Eldorado unit) was the radiation oncologist. From [87].

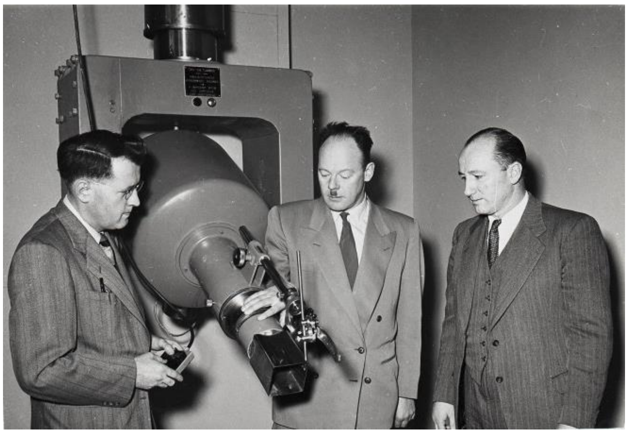

Figure 4. Saskatchewan cobalt unit with initial lead plug collimator system. From left to right: Dr. Harold Johns, John MacKay and Dr. T.A. Watson admiring their handiwork. Reproduced with permission from [63].

criticism that clinical commissioning of the London therapy unit had been “skimpy”. The dosimetry was rechecked locally by Dr. J.C.F MacDonald who was urgently recruited to replace Jack Brown who had contracted tuberculosis while traveling in the United Kingdom to investigate British medical physics practice. At that time, the United Kingdom was considered the epicenter for training of medical doctors and physicists in the field of radiation oncology. The world’s first treatment of a cancer patient indeed proceeded quickly on 27 October 1951 under Dr. Ivan Smith’s leadership. This first patient was treated for palliation with a very poor prognosis and only lived a limited time. An interesting video summarizing some of this history can be found on the Saskatchewan’s Western Development Museum website [134].

The unit destined for the M.D. Anderson Hospital was built by the General Electric X-ray Corporation of Milwaukee and ready to be displayed at a meeting of the American Roentgen Ray Society in 1951. For a variety of technical and military reasons due to the Korean war, and the premature death of Grimmett, the first treatment at the M.D. Anderson Hospital, Houston, Texas, was delayed until 22 February 1954 (Figure 5). After the Washington meeting in February 1959, the M. D. Anderson Group realized they were never in the running to deliver the world’s first cobalt teletherapy treatment. In fact, the first patient treatment with a cobalt-60 unit in the United States occurred on 23 April 1952 at the Los Angeles Tumor Institute. The US unit was designed by Russell Hunter Neil with a source consisting of six stacks containing 18 pieces constituting 108 individual micro-sources. The six stacks were arranged in a single cylinder, 4.33 cm high, 3.5 cm diameter for a total weight of cobalt of 181.74 gm and a total activity of 1080 Ci (February 1952). The machine output was 32 r/min at 70 cm from the source [4]. This late entry to the race does not belittle the leading contributions of all three pioneering groups (Saskatoon, London, Houston) who started this fast-paced competition to improve radiotherapy for the world.

A surge of similar technical developments also occurred in other countries including the Soviet Union, Japan, Denmark, Holland, and Sweden. By 1956, 218 machines were in operation in non-Russian countries and an estimated 160 were assumed in use in countries behind the “iron curtain” [23].

Table 1 summarizes key dates and times of the three locations in the race for cobalt-60 treatments and Table 2 compares timelines and the characteristics of the world’s first two clinical cobalt-60 machines.

Evita Peron Story: On 21 May 1952, the Montreal Gazette newspaper published a story under the headline *Ontario Hospital Denies Evita Peron Treated There.* (Figure 6).

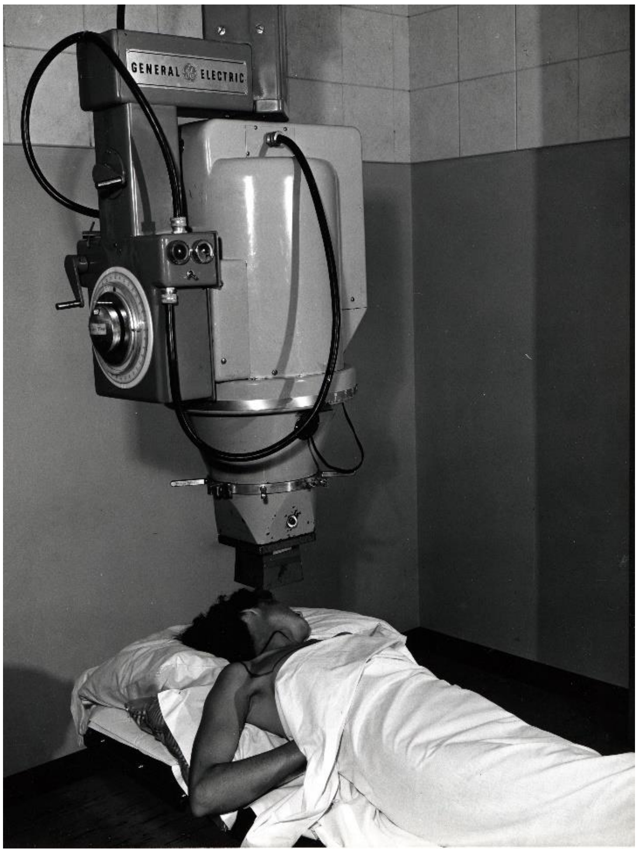

Figure 5. The Grimmett designed cobalt-60 unit marketed by General Electric and located at the MD Anderson Hospital in Houston, Texas. Image courtesy of the University of Texas MD Anderson Cancer Center Historical Resources Center.

Ontario Hospital Denies Evita Peron Treated There

London, Ont May 20. —(CP)—The Toronto Telegram said today that Mrs. Juan Peron, wife of the Argentine dictator, underwent treatment with the cobalt bomb at Victoria Hospital here about three weeks ago. Officials at the hospital said they had no knowledge she had been there.

The report gave no hint of the ailment of the vivacious blonde first lady of Argentina. Radiation from the Canadian-developed cobalt bomb is generally a treatment for cancer.

The Telegram said Mrs. Peron was flown here under "the tightest of security cloaks."

Dr. Augustin Nores Martinez, the Argentine's ambassador to Canada, said in Ottawa that Mrs. Peron was in Buenos Aires all during the last month.

Dr Carman J. Kirk, Victoria Hospital superintendent, said he had no knowledge of Mrs Peron ever being admitted to the hospital, "even incognito" He said Dr. Ivan Smith, director of the cancer clinic, and Dr. Frank Batley, who directs treatment with the cobalt bomb, scoffed at the report. Dr. Batley denied that Mrs. Peron had received treatment at the clinic.

The politically-prominent Mrs. Peron, variously reported as 30 or 33, underwent a major operation in Buenos Aires last November. The one-time movie actress, known as Evita (little Eva) to millions of citizens of Argentina, had been ill several weeks with what doctors called acute anaemia. Indication that she had been suffering from cancer came when it was learned she had been treated by Dr. George T. Pack, a leading cancer specialist from New York.

A cobalt bomb similar to the one here is in operation at the University of Saskatchewan in Saskatoon. Doctors in Saskatoon said today Mrs Peron was not treated there.

Publication of the Toronto report brought to light the information that Argentina tried to buy the cobalt bomb before it was delivered to the clinic here. It is said to have offered up to $1,000,000 for the radioactive instrument produced in Canada for $50,000.

The bomb, powered by a core of cobalt made radioactive by being placed in Canada's atomic pile at Chalk River, Ont., produces radiation equal to that of $50,000,000 worth of radium.

Figure 6. A section from page 10 of The Gazette newspaper in Montreal.

To quote the opening sentences “The Toronto Telegram said today that Mrs Juan Peron, wife of the Argentine dictator, underwent treatment with the cobalt bomb at Victoria Hospital here (i.e., London, Ontario) about three weeks ago. Officials at the hospital said they had no knowledge she had been there.” During that time Dr. John C.F. MacDonald was a physicist at the London cancer centre and, as described earlier, had been involved in the original commissioning and dosimetry of the Eldorado A. (As a side note, in the early 1970s, Dr. MacDonald was also the graduate student supervisor of two of the authors (JVD, JJB) of this historical review.) As a follow-up to the Evita story, one of the authors (JVD), prior to a conference in Argentina, contacted Dr. MacDonald to obtain more background information. To quote from Dr. MacDonald’s e-mail of 9 May 2011, “Evita had ca uterus, and when the Argentines heard about the cobalt unit, they sent the Argentine ambassador to see Roy Errington (leader @ AECL) and to order one to be shipped to Buenos Aires immediately to save 'the poor shirtless ones of Argentina'. But Roy had to tell him that a source wouldn't be available for about a year. So, when AECL Commercial Products threw a big bash in London, the ambassador was invited, and the press took note. The next day, a Saturday, Frank Bately, the oncologist, and I were in the Clinic, and between us took innumerable calls from all over the world about Evita. - but that didn't stop the reports. She died soon after.” A further corroboration of this story can be found in a historic article in the Canadian Medical Association Journal [78]. Furthermore, one of the authors (JJB) was given access to archived files from Dr. Ivan Smith’s office in 1994 and was unable to find any clinical or communication documents whatsoever referring to Evita’s treatment. Case closed!

VI. COBALT TRUTHS AND CONSEQUENCES

The progression from kilovoltage to megavoltage energy was considered a giant leap forward in the practice of radiotherapy [126]. We previously noted some key physical advantages of cobalt-60 sources over radium and kilovoltage x-ray systems, such as cost-effectiveness, higher dose rates at a longer source-to-surface distance (SSD), and skin-sparing in the dose buildup region. The era of differentially targeting the tumour while limiting the radiation dose to surrounding tissue and organs at risk had arrived and there would be no turning back [105;107;123;139]. The following is an interesting quote from the British Medical Journal of 26 September 1959 (page 566), in the Section of Radiology on Supervoltage Radiotherapy, “Dr. IVAN H. SMITH (London, Ontario) reviewed the use of cobalt-60 in the treatment of oral cancer in the first 50 patients treated on a radical basis by means of the original 1-kilocurie Eldorado A unit. Five main conclusions could be drawn: (1) Tumour invasion of the mandible could be controlled. (2) Complete regression of disease recurring after previous treatment was possible.

Table 1. The teams in the race for cobalt-60 teletherapy.

	Saskatoon, Saskatchewan, Canada	London, Ontario, Canada	Houston, Texas, USA
Source delivered	30 July 1951	16 Oct 1951	July 1952
Unit Installed	17 Aug 1951	23 Oct 1951	Sept 1953
Calibration & commissioning	11 weeks	Pre-calibrated	
First patient treated	8 Nov 1951	27 Oct 1951	22 Feb 1954

Table 2. Canadian twins (adapted from [109])

	London, Ontario Unit	Saskatoon, Saskatchewan Unit
Manufacturing Company	Eldorado Mining and Refining Ltd	Acme Machine and Electric Co.
Hospital where unit is installed	Victoria Hospital	University Hospital
Lead Physician	Dr. Ivan H. Smith	T.A. “Sandy” Watson
Technical Design by	Donald Green Roy Errington	Harold E. Johns
Physics support	Radiology Lab and Physics Division of the National Research Council of Canada, Ottawa	Physics Department, University of Saskatchewan L.M. Bates, E.R. Epp, D.V. Cormack, S. Fedoruk
Machine support mechanism	Floor mounted	Ceiling mounted
Source shutter (On/Off mechanism)	Liquid mercury shutter	Motorized rotating wheel
Marketed by	Atomic Energy of Canada Ltd.	Picker X-ray Co.
Dedication date	11/12 Nov. 1951	23 Oct. 1951
Date of first patient treatment	27 Oct. 1951	8 Nov. 1951

(3) Nodes which were the site of metastases and which could be included within the treatment beam for the primary tumour could be controlled. (4) A very low incidence of bone necrosis was found. (5) There was no skin reaction, and mucosal reaction too was less. Occasionally high tumour-resistance was found. but of the 50 patients treated by the machine 19 had been free of tumour for periods ranging from 39 to 83 months. Further experience had been gained with the rotating hectocurie Theratron Junior using both rotation and wedge fields, either alone or in conjunction with fixed fields. In general, although the fixed field gave a somewhat better depth-dose with less integral dose and less penumbra, rotation offered an easier technique with no need for plaster fixation.”

The advantage of superimposing multiple overlapping fields emerged quickly, as illustrated in Figure 7. Gains in clinical outcomes also soon appeared with the shift from kilovoltage to megavoltage energy [126]. Convincing evidence emerged from Princess Margaret Hospital in Toronto (now Princess Margaret Cancer Centre), rebutting some sceptics who felt that a novel treatment machine was just “an expensive toy for the physicists”. Figure 8 shows the improved survival of cancer patients with cervical cancer in pre-war and post-war periods [26]. The main reason given for the clinical improvement was the availability of a higher energy beam (cobalt-60 versus 200-400 kV x-rays). Further improvements in survival with an even higher megavoltage energy from a 22 MeV betatron were reported; however, the gain was not only due to beam energy but also differences in patient setup, field size, absolute dose, and fractionation. The exact rationale for the improved survival was never ascertained [2] and later treatment techniques were modified away from the four-field oblique delivery. Megavoltage radiation became the new standard of clinical practice for a variety of tumour sites including cervix, Hodgkin’s disease, head and neck, and prostate. The next significant leap forward came with the introduction of 3-D medical imaging introduced at a much later time (1970s). “Pixel-based” dose modelling based on x-ray computed tomography (CT) became the new norm, significantly improving the accuracy of dose distributions used in treatment planning decisions.

Table 3 provides a more detailed summary of the physical characteristics of cobalt and the corresponding impact on the design of a clinical therapy machine. The first kilocurie activity was made possible by the combination of an intense neutron flux in the NRX nuclear reactor and a generous nuclear capture cross-section of cobalt-59. Hotter, smaller, and cheaper sources, compared with radium sources, set the stage for *practical* megavoltage therapy of deep-seated tumours at reasonable dose rates. Extended SSD made cobalt therapy more comfortable for patients with greater clearance for patient setup, without an intimidating canon-like structure pointed closely at the skin. The early Saskatoon cobalt unit used a Lazy Susan rotating platform built into the floor to turn the patient while being exposed to a horizontal radiation beam. A similar treatment was achieved on the Eldorado A machine using a rotating chair (see Figure 9). Various forms of rotation therapy that have been considered are shown in Figure 10. The C-arm gantry of second-generation cobalt units allowed treatment with a horizontal patient setup – foreshadowing modern rotational techniques such as volumetric-modulated arc therapy (VMAT) and tomotherapy [27;41;91].

The beam penetration characteristics are the result of energetic gamma rays, enhanced by longer distance applications and laterally-scattered photons depending on field size. Percentage depth-dose values approached 60%

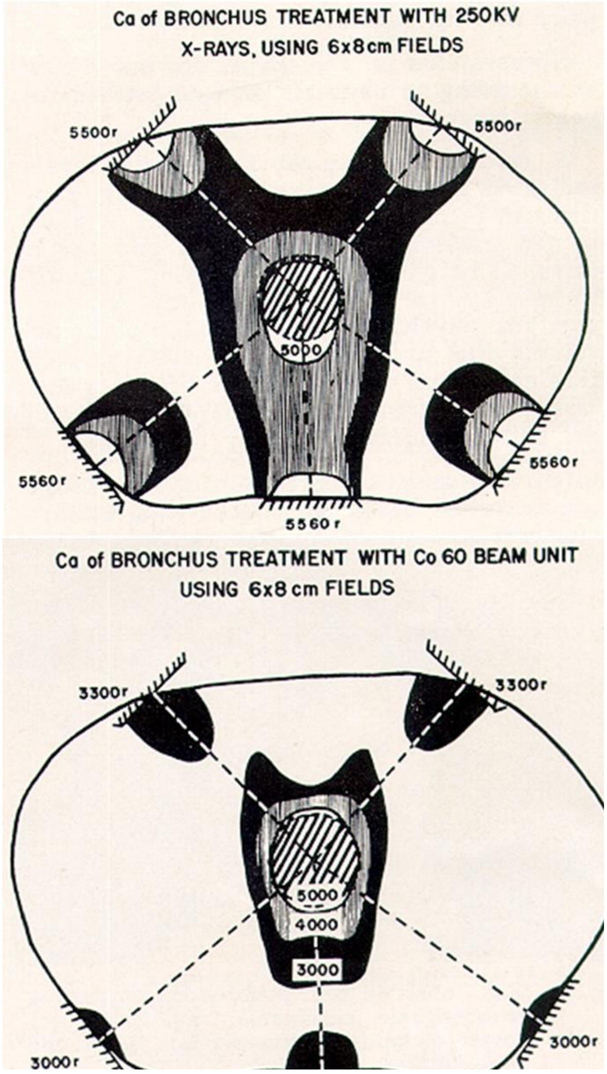

Figure 7 Comparison of dose distributions from 250 kV x-rays (top) and cobalt-60 (bottom).

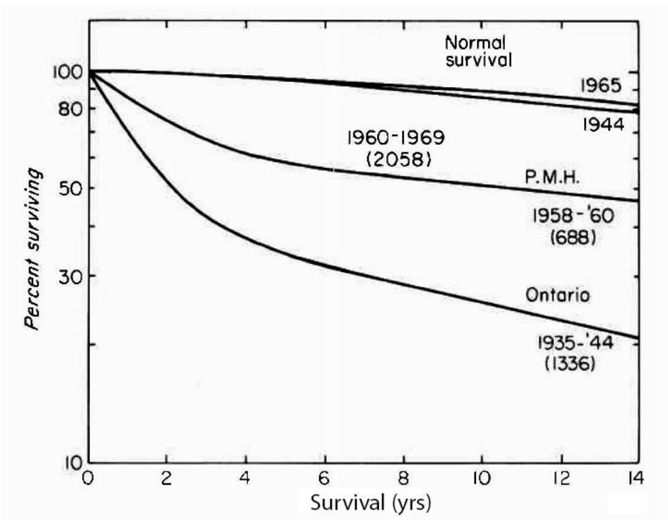

Figure 8. Survival curves for the kilovoltage and megavoltage for cancer of the cervix. With permission from [26].

Table 3. Major attributes of cobalt-60

Attribute	Numerical Values	Practical Consequence
Vivid blue colour	-	Used in glass, pottery, jewellery, ancient Egyptian murals
Cost of raw material Co-59	\$250.00 per kg (1979) \$30.00 per kg (2020)	Affordable and available (at present) Cost expected to rise for electric car battery technology
Nuclear Cross Section (neutron capture)	37 barns (x 10^{-24} cm^2) for cobalt-59	Induce radioactivity efficiently
Activity Yield from NRX neutron flux (10^{13} per cm^2 per s) Activity Yield from modern reactor flux (10^{14} per cm^2 per s) Specific Activity (maximum)	~20 Ci per g of Co-59 (1.5 year exposure) ~300 Ci per g of Co-59 (3 year exposure) 1,100 Ci per g of Co-60	Original source size (56 g) Higher dose rate, smaller sources Smaller geometric penumbra Theoretical limit for ultra-intense neutron flux
Exposure rate constant (Γ_x) Air KERMA rate constant (Γ)	1.29 R h^{-1} m^2 Ci^{-1} 307 µGy h^{-1} m^2 GBq^{-1}	Exposure (R) or Air KERMA (µGy) rate at 1 metre distance per unit activity (Ci or Bq)) Radiation protection vs distance
Source Activity (A) to achieve 256 cGy per minute at SAD = 100 cm (SAD = source-axis distance) RMM source specification (R per minute at 1 meter)	~13,000 Ci ~500 TBq RMM ≈ A (Ci) x Γ_x /60 (theoretical value)	Treatment duration for patient Patient throughput Higher activity enables longer SAD = 100 cm Improved depth-dose Open gantry – ease of patient setup and less stressful Rotational therapy High activity warrants extra security measures
Gamma Rays	1.17 and 1.33 MeV	Skin sparing (< 5mm) and bone-sparing Ease of calibration and dose distribution computation based on tissue electron density (per cm^3)
Half-Value Layer	11 mm Pb	Shielding Blocks/MLC beam shaping Radiation Protection – Room/Barriers
Half Life	5.26 years	Frequent dose rate updates (1% per month) Source replacement costs

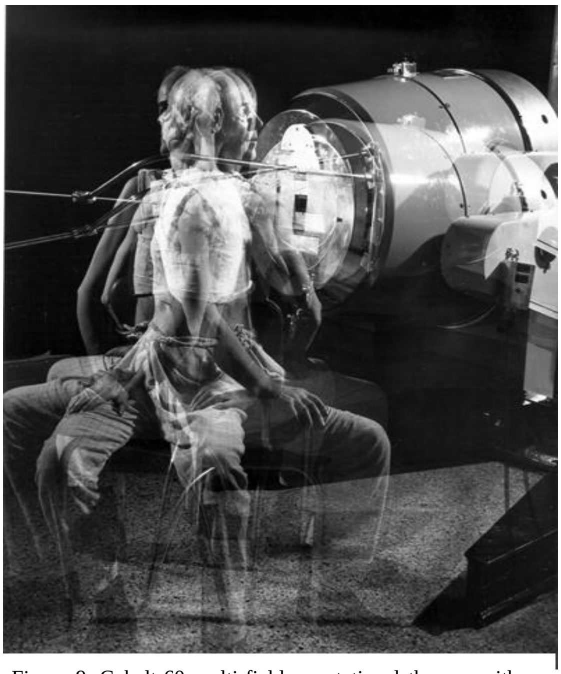

Figure 9. Cobalt-60 multi-field or rotational therapy with a rotating chair and the Eldorado-A. From the archives of the London Regional Cancer Program, London Ontario, held at the library of the University of Western Ontario.

at a depth of 10 cm, doubling the previous value for 'deep' x-ray beams (Figure 11).

Megavoltage photons liberate electrons in tissue with a finite range giving rise to the dose build-up (i.e., d_{max} = 5 mm) thereby achieving "skin-sparing". In addition, atomic interactions with all types of tissue, including bone, occur quasi-exclusively by the Compton scattering

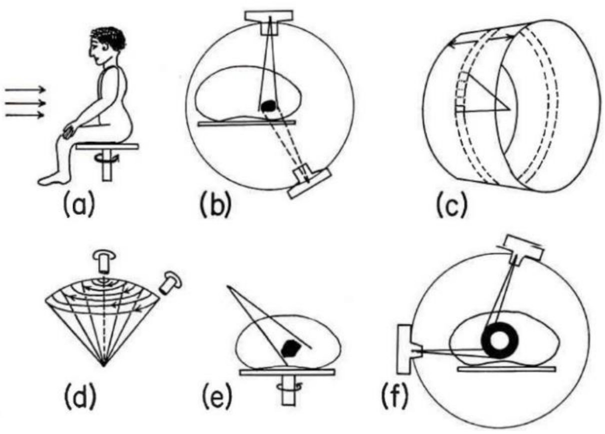

Figure 10. Schematic diagram illustrating the various forms of moving field therapy. From reference [73]. Courtesy of Charles C Thomas Publisher, Ltd., Springfield, Illinois

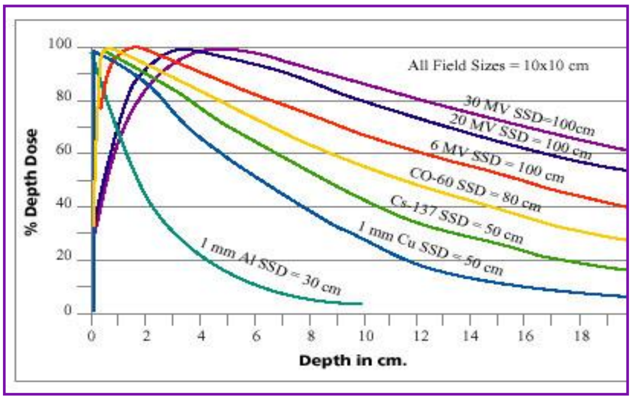

Figure 11. Percentage depth dose curves for kilovoltage and megavoltage beams for a field size of 10 cm x 10 cm.

effect *without* a photoelectric boost. This had a major clinical consequence, enabling dose escalation that had been previously limited by serious skin or bone reactions with kilovoltage x-rays. The close pairing of the two cobalt-60 gamma ray energies simplifies accurate dose calibration and computation of dose distributions, assuming a single effective energy of 1.25 MeV. Compton and Coulomb scattering both dominate the radiation interactions in heterogeneous tissue, and the key parameter for predicting primary beam penetration, scattering, and dose deposition is the tissue electron density (electrons per cm^3). Concern for beam hardening and electronic disequilibrium effects which are prevalent at higher beam energies [42] is greatly diminished, sidestepping considerations of atomic number variations in the body [9]. Electron density information is easily extracted from CT numbers obtained in kilovoltage or megavoltage CT scans [10;110]. Interestingly, the megavoltage Compton scanner that was originally used to generate *in vivo* electron densities [10] used a cobalt-60 source. The Compton image quality [32] was soon surpassed when kilovoltage CT scanners became available.

VII. COBALT TELETHERAPY MACHINE DESIGNS

A typical early cobalt-60 teletherapy machine consisted of the following components [118]:

1. An encapsulated radioactive cobalt-60 source.
2. A source shield or housing.
3. Some device to turn the useful beam on and off (could be a rotating drum, a mercury reservoir, or sliding source drawer).
4. A diaphragm system (collimator) to limit the size of the useful beam.
5. A support mechanism by which the useful beam can be oriented with respect to the volume to be treated.
6. Ancillary devices attached to the source shield or the support mechanism to facilitate beam alignment.

Cobalt-60 teletherapy source: Figure 12 shows typical cobalt-60 source components. The original activity of the first sources was approximately 1,000 Ci although the source capsules could eventually contain up to 15,000 Ci. Prior to 1955, cobalt-60 source capsules came in all sorts of sizes and shapes. This made replacing the old sources a complex and time-consuming process. In October 1953, representatives of 14 x-ray equipment manufacturers met with representatives of the U.S. Atomic Energy Commission, Atomic Energy of Canada Limited, Oak Ridge National Laboratories and the Oak Ridge Institute of Nuclear Studies (ORINS) at the ORINS Medical Division to discuss the issue. As a result of this meeting, the source capsule shown in Figure 12 was developed and adopted as the standard configuration. This example came from Oak Ridge Associated Universities formerly known as the Oak Ridge Institute for Nuclear Studies. As such, it might date from the period when the design was being standardized [21;22;100]. In recent years, most teletherapy sources have diameters ranging between 10 to 20 mm.

Source shielding or housing: Since the radioactive source is emitting radiation all the time, the source shielding has to be designed in such a way that the radiation levels transmitted through the shielding must be low enough to be acceptable in terms of exposure to the staff working with these machines. For a source in the kilocurie range of activity, this requires an attenuation factor of about 10^6, or about 20 half-value thicknesses [118]. The usual shielding material was steel-encased lead, although some units incorporated shields of tungsten alloy or uranium. The Grimmett unit was constructed entirely out of a tungsten alloy called Hevimet, which resulted in a considerably smaller unit than lead shielded ones, allowing better maneuverability of the machine around the patient. Kerman, the radiation oncologist, noted this when he saw the John's machine but thought that the Johns' collimators were superior (see figures 2, 4, and 13). Some of the machine heads with lead shielding contained heavier

Figure 12. Cobalt-60 source capsule. The assembled source is shown on the left. The source components are shown on the right. The cobalt source itself is shown on the lower right-hand corner of the right figure and is about 2.5 cm in diameter whereas the total capsule is about 5 cm in diameter. The top of the source housing (on the left) contained an opening through which the stainless-steel source container can be seen. From [100].

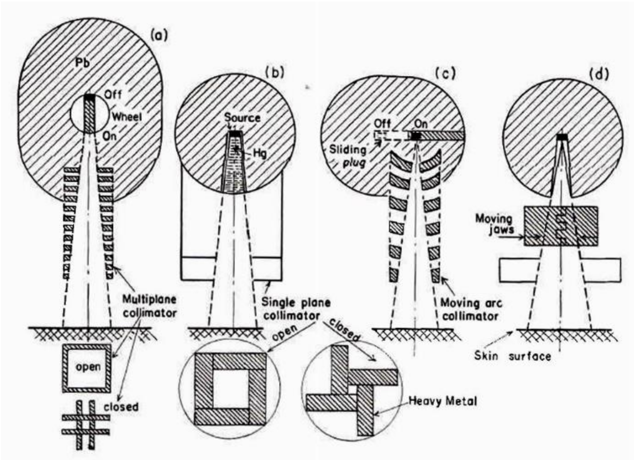

Figure 13. Four types of source shutter arrangements: (a) rotating cylinder with multiplane collimator based on the Johns and Mackay design (b) liquid mercury drawn from a reservoir (not shown), as in Eldorado A design with single plane collimator, (c) sliding drawer design (shown in more detail on the postage stamp of Figure 14) with moving arc collimator, and (d) moving jaw mechanism and single plane collimator. From reference [73]. Courtesy of Charles C Thomas Publisher, Ltd., Springfield, Illinois

metals immediately near the source, where they are more efficient in attenuating the radiation [118].

Source shutter (beam on-off mechanism): The means of turning the beam on and off has become known as the source "shutter". Various designs were used. Four examples are shown schematically in Figure 13. Figure 13(a) shows the source mounted on the circumference of a wheel near the centre of the head, so that by rotating the wheel it can be brought opposite an opening in one end of the head through which the radiation beam can emerge. Figure 13(b) shows a radiation beam emerging through a conical opening in the head. When the beam is "off", this opening is filled with liquid mercury. When the beam is turned "on", an air compressor built into the horizontal arm is started, and air pressure forces the mercury up into a reservoir. If the beam is turned "off", or if there is a power failure, the reservoir valve opens and the mercury returns, under gravity, to block the beam [71]. Figure 13(c) shows the source mounted on a sliding drawer. In the "off" position, the drawer is slid away from the collimator opening such that the radiation is shielded by the head of the machine. In the "on" position, the drawer is moved such that the source is above the collimator opening. Figure 13(d) shows a moving jaw mechanism. The first unit in Saskatchewan used the rotating cylinder and the first unit in London, Ontario, the Eldorado A, used the mercury reservoir. The sliding drawer mechanism was developed later and was probably the most frequently used mechanism in cobalt machines sold around the world. The cobalt-60 developments were recognized by the Canadian government with a postage stamp in 1988 in honor of Harold Johns. Figure 14 pictures the postage stamp with the machine using a sliding drawer mechanism.

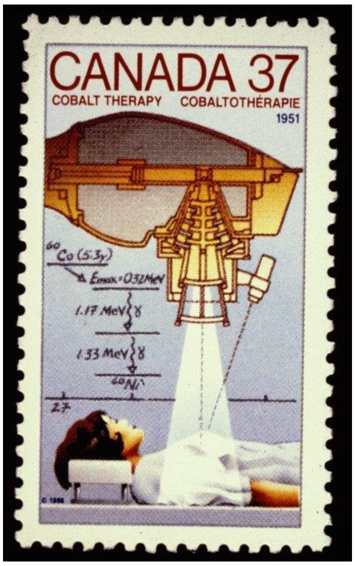

Figure 14. Canadian postage stamp recognizing the development of cobalt-60 radiation therapy in Canada and the involvement of Harold Johns in that development. The stamp includes a schematic of a typical head of a cobalt-60 machine. The source shutter mechanism is a sliding drawer. The source is shown in the "on" position. To turn the beam "off", the source drawer is slid to the left. Also shown is the decay scheme of cobalt-60 with a beta decay with a maximum energy of 0.32 MeV followed by 2 gamma rays of 1.17 and 1.33 MeV. This style of machine was the most produced and used globally. Canada Post © 1988. Reproduced with permission.

Anecdotally, there were several reports describing some technical issues with the mercury shutter mechanism [1;53]. At the time of the development of these cobalt-60 machines, the toxic nature of mercury was not well recognized. Even in 1971, when one of the authors (JVD) began employment at the Princess Margaret Hospital in Toronto, there was still an Eldorado A in operation, along with 9 other cobalt-60 machines. However, the unit was soon taken out of service after one of the patients indicated that he could feel the radiation. In reality, he felt very small droplets of mercury from the reservoir which had developed a very minor leak, hence, causing the end of this machine's life!

Diaphragm system (collimator): A diaphragm system was needed to provide the appropriate field size necessary to cover the target volume requiring irradiation. Examples of such field definition are shown in Figures 13 and 15. Figure 15(a) shows vertical rectangular blocks. This also represents shielding provided by lead blocks placed on a tray under the head of the machine. Figure 15(b) shows

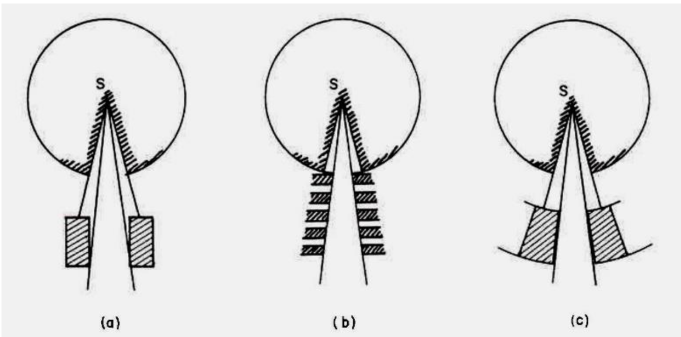

Figure 15. Idealized representation of three common types of diaphragm systems: (a) rectangular blocks, (b) multiple interlocking vanes, and (c) concentric blocks. From [118].

interleaved bars [also shown in Figure 13(a)]. The advantage of this system is that the perpendicular collimator has similar interleaved bars with the distance of the perpendicular bar pairs being only one bar thickness different, thereby minimizing the difference in geometric penumbra in the two orthogonal directions. Figure 15(c) shows the use of concentric blocks. The concern in this situation is that the perpendicular collimator has to be below or above the one shown in the figure such that the source to the bottom of the collimator distance is different by the thickness of the blocks and thus yielding a significantly different geometric penumbra in perpendicular directions. Figures 13(a) and (b) show the collimation systems as were used on the early Picker and AECL cobalt-60 machines, respectively.

Machine support mechanism: The head of the machine contains the source, the heavy shielding and beam collimation system. The machine support mechanism controls the direction and orientation of the machine head. Of the two original cobalt-60 machines, the Eldorado A had its head attached to a floor mounted column. The Saskatoon machine was ceiling mounted as shown in Figures 2 and 4. Eventually (1953) machines were developed such that the head was mounted on a rotational gantry allowing the centres of the beams to rotate about an isocentre. This permitted stationary beams to be aimed at the same point in the patient from different directions as well as dynamic rotational therapy with the beam "on" while the gantry is moving. The Grimmett-designed cobalt machine is shown in Figure 5. It also had a source mounted on a rotating cylinder and was mounted on the ceiling as in the Saskatoon unit.

Ancillary devices: A variety of ancillary devices have been developed over the years, primarily divided between those that help shape the beam and those that help direct the beam. The beam-shaping devices initially consisted primarily of lead shielding blocks placed on a shielding tray which was either mounted on a stand on the floor for machines pointing down vertically (like the Eldorado A or later the Eldorado 8) or attached in some way to the collimation system. Another major ancillary device used for many years was the wedge filter which helped shape the dose distribution inside the patient especially when multiple fields were used from various directions. Later missing tissue compensators were implemented [39;85]. Various forms of conformal shielding using Styrofoam cutouts were also developed [132].

Patient support assembly (treatment couch): Along with the development of isocentric cobalt-60 machines also capable of rotation therapy, manufacturers provided an integrated patient support assembly allowing patients to be positioned with the tumour volume generally located near the isocentre of the machine. Such assemblies can have various degrees of freedom including couch vertical motion, lateral and longitudinal motion and rotational motion about a vertical axis. The couch tops had a tennis racket-style window for minimizing intervening materials and allowing skin sparing for posterior beams, with the more modern couches being made of carbon-fiber materials which are relatively radiation transparent.

Different machine designs: Many types of cobalt-60 units have been designed over the years [17;37;44;48;54;55;65;71;72;76;77;84;112]. A partial list of manufacturers is shown in Table 4. In addition to the early units described above, other units were designed with various specialized features. For example, three different types of machines were developed and custom-built at the Princess Margaret Hospital/Ontario Cancer Institute in Toronto in collaboration with Harold Johns and Jack Cunningham. The first of these was a rotational machine, which had a built-in x-ray tube in its head for therapy verification, just above the sliding source drawer [72]. With conventional simulators not having been developed yet, this machine provided treatment simulation capabilities as well as being a forerunner of "image-guided radiation therapy." Furthermore, the counterweight contained an ionization chamber fronted by a 15 cm focussing lead plug with a large number of holes angled towards the source to provide a means of removing scatter and obtaining the radiological thickness of the patient [47]. This system was later modified by one of us (JJB) to provide a rapid means of obtaining an average tissue-air ratio directly, accounting for patient densities [11], thus providing an early method of tissue density correction especially for rotational therapy.

In 1962, Jack Cunningham and Harold Johns designed and built the world's first double-headed cobalt-60 machine capable of delivering simultaneous parallel-opposed fields, an innovative machine that could take

Table 4. Partial list of manufacturers of cobalt-60 teletherapy devices. Adapted and updated from [51]. Some of the vendors no longer market cobalt-60 units or no longer exist.

Country	Company	Device
Argentina	INVAP	Therados 800, Teradi
Canada	Best Theratronics (Formerly MDS Nordion, & AECL)	Equinox & Phoenix of the Theratron line
China	Nuclear Power Institute	GWGP80, GWXJ80
Czech Republic	UJP Praha	Terabalt
Czech Republic	SKODA	Teragam
France	Cisbio International	CIRUS
India	Panacea Medical	Bhabhatron-II & 3i
Russia	Concern "Granit-Electron"	Rokus-R
United States	Advanced Medical Systems (Formerly Picker Corporation)	ATC, C/9, V9
United States	ViewRay	MRIdian System 4.1 (3 cobalt sources)

partially decayed sources from any two of the other eight or so cobalt machines at PMH and use them for another five years, generating a reasonable patient dose rate for this specific treatment modality [37]. Jack Cunningham also developed a scanning beam technique for total body irradiation using the rails on the ceiling mounted Picker unit that was originally designed by Harold Johns [38]. Later, because both total-body and half-body radiotherapy were in such high demand, a special cobalt machine (i.e., the Hemitron) was designed and built to provide very large radiation fields, 50 cm x 160 cm at 90 cm from the source and up to about 90 cm x 300 cm for patients on a stretcher near the floor [84]. The design used large collimators akin to Figure 15(c). The world's largest field tissue-air ratios were determined by one of us (JVD) [131] (up to equivalent squares of 75 cm x 75 cm) and these were incorporated in the British Journal of Radiology Supplements 17 and 25 containing central axis data for use in radiotherapy [19;20]. Clearly, cobalt-60 machine innovations by the Johns and Cunningham team persisted well after the 1950s.

Already in 1965, Takahashi in Japan described the use of multileaf collimators (MLC) and modulated delivery on a cobalt-60 unit as a precursor to today's intensity modulation radiation therapy [122]. Also, in 1965, a group at the Royal Northern Hospital in London, England pioneered conformal radiation therapy by developing cobalt techniques in which the patient was automatically positioned during rotational therapy while moving the treatment couch and machine gantry dynamically. This was known as "The Tracking Cobalt Project" [54]. With a similar intent, Proimos in Patras, Greece [105] and later Rawlinson and Cunningham in Toronto [107], described the use of synchronous shielding in a cobalt-60 beam to make the radiation beam conform to the target while avoiding critical normal tissues.

Later, MDS Nordion developed isocentric machines with options of either an 80 cm or 100 cm source-to-axis distance with high dose rates (Theratron Elite 80/100). Their comparison is described in some detail by Glasgow [51;52].

More recently, several groups have investigated the development of MLCs for cobalt teletherapy, some of which are manual devices, while others are automated with pneumatic or motorized mechanisms [7;82;116]. Prof. John Schreiner and his group in Kingston, Ontario, Canada have considered various high-precision options for cobalt-60 teletherapy including intensity modulation [114], image guidance [110;114], and tomotherapy [27;41;79]. Some of these concepts are starting to be commercialized. For example, Best Theratronics in Canada now provides an MLC as an add-on option. Panacea Medical Technologies in India offers integrated MLCs on their Bhabhatron II and Bhabhatron 3i, with the latter being fully integrated with intensity modulation and image guidance on a ring gantry.

Perhaps the most sophisticated use of cobalt-60 teletherapy is the more recent development of MRI-guided radiation therapy [81]. ViewRay, Inc. (Cleveland, Ohio, USA) has marketed a machine (MRIdian) which integrates a 0.35 T whole-body MR imaging system using a split magnet design along with a radiation therapy system on a rotating gantry, which incorporates three heads, 120° apart, with cobalt-60 sources, each with an identical doubly focussed multileaf collimator (30 leaf pairs) [28;137]. The maximum dose rate is 555 cGy/min at the isocentre. This technology has been clinically implemented with real time anatomy tracking and beam control [56]. It provides sophisticated possibilities for adaptive radiation therapy. The most recent implementation of the ViewRay MRIdian includes a single 6 MV linear accelerator system in lieu of cobalt sources [80]. The rationale given for transitioning from cobalt sources to a linac includes reduced need for inspection, replacement and disposal of cobalt sources and reduced oversight of national agencies for radioactive sources. Furthermore, today, linacs are more common in most radiotherapy centres in high-income countries. The linac system also allows higher dose rates and faster electronic variation of the pencil beam intensities and their placement. The next section provides further discussion on the historic gradual transition from cobalt to linac radiation therapy.

VIII. GROWTH AND DECLINE OF COBALT-60 TELETHERAPY

The tremendous benefits of cobalt-60 teletherapy were recognized immediately with the first use of these machines for the treatment of cancer patients. Megavoltage energy photons along with extended patient source-to-surface distances provided depth dose characteristics previously unachievable with radium isotope machines or "deep" x-ray beams. While >20 MeV betatrons had already been developed and used for radiotherapy by the late 1940s [58;60;69;75;83], these were considered too complex and too expensive for the average radiation therapy department. Under the leadership of H.E. Johns of the Physics Department at the University of Saskatchewan, Canada, an Allis-Chalmers betatron was installed mainly for research in 1948 [63]. The first cancer treatment with a betatron in Canada occurred on 29 March 1949. The betatron remained in service for 17 years until 1965, having treated only 301 patients. One of the main drawbacks was the 'exorbitant' cost per hour of operation. A betatron donut cost $3800 in 1949 ($43,000 in 2020 dollars) and generally needed to be replaced within 150 hours of usage [63].

The world's first patient treated with a medical *linear*

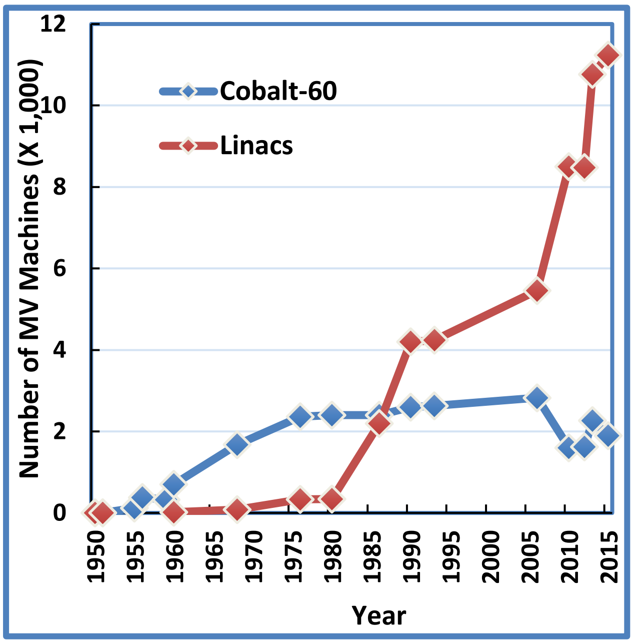

Figure 16. The global number of teletherapy cobalt-60 machines and linear accelerators versus year. The curves are based on publications from various sources of information; hence, the ragged nature of the curves; however, the trends are obvious. See text for references.

accelerator (8 MV) occurred at the Hammersmith Hospital, in London, England in August 1953 [109]. The Van de Graaff generator was also used for megavoltage radiation therapy as noted previously. In the thirty years from 1939 to 1969, no more than 136 megavoltage x-ray units were reported to be sold, whereas in the 10 years between 1951-1961, 1,120 cobalt-60 units were sold, with 422 of them in North America [109]. We have tracked the number of medical teletherapy cobalt machines and the number of medical linear accelerators in use by year based on various publications over the years [4;23;24;29;67;70;109;140]. The results are shown in Figure 16. Using some broad assumptions with significant uncertainties, we can estimate the number of patients who have been treated across the globe. Our data show that *on average*, there were about 1,600 cobalt teletherapy units per year between 1951 to 2020, i.e., over 69 years. If there are 250 treatment days per year and that on average 50 fractions are given per day (more realistically this ranges between 25 to 100 patients per day) and that each patient gets on average 19 fractions per course (This can range between 1 and 35; however, an optimal number has been shown to be 19 [136], although realistically this number has probably been less over the years), then this gives

$$69yrs \times \frac{1600units \times 250 \times 50\frac{fractions}{day}}{19\frac{fractions}{patient}} = 73\ million\ pts$$

Recognizing the uncertainties in these calculations, there have probably been somewhere between 50 to 100 million patients treated globally with cobalt-60 teletherapy; clearly, the clinical impact has been very significant!

IX. COBALT VERSUS LINAC: COMPETING MODALITIES

We now review the arguments normally used to justify and perpetuate this ongoing transition of technology, some of which are based on false impressions leading to an accelerated deployment of linacs. We have provided a more detailed analysis in previous publications [12;128;129]. The most common reasons in favour of accelerators include:

(1) The ALATA (As Long as it is Technologically Achievable) Principle
(2) Sharper Field Penumbra
(3) Better Conformal Dose Distributions
(4) Radiation Safety
(5) Cobalt Source Supply Chain

ALATA principle: In this age of rapidly evolving technology, it is easy to adopt exciting new products "as long as they are technologically achievable" (ALATA), without too much technical or cost analysis. The attitude is described as "Keeping up with the Joneses?". The rapid adoption of more expensive linear accelerators is driven in part by marketing hype from the manufacturers. A more rational justification is based on the acquisition of "two machines for the price of one" with x-ray and electron beam capability, variable energy, programmable beam collimation for intensity modulated radiotherapy (IMRT), and on-board image guidance (IGRT). Cobalt machines have evolved much more slowly with conservative upgrades and are therefore often viewed as a mature technology reaching their end of product life cycle.

Glasgow and Corrigan [51;52] compared the annual costs for a cobalt unit to those of a linear accelerator. The capital and operating costs amortized over a 15-year period for replacement of an AECL Theratron-780 including bunker renovations, maintenance, and licensing fees amounted to $62,000 and $100,000 per year for a Theratron-1000 and Varian 6 MV linac. A prior study by Rawlinson [106] in 1986 reported amortized costs in support of operating a cobalt unit, low energy linac, and high energy linac were ~$38,000, $123,000, and $181,000 per year, respectively. Note that all these units were equipped quite similarly before the advent of IMRT, without MLC collimation and CT image guidance. A more recent analysis [97] reported the *capital* costs for cobalt therapy unit, a low-energy linac, and high energy linac at $750,000, $2.25 M, and $4 M dollars. The annual operating costs including maintenance and source replacement were $50,000, $150,000 and $300,00 per annum. The most economical solution for mono-energetic radiotherapy with minimal maintenance requirements is delivered by a cobalt-60 unit; this has had direct implications for low-to-middle income (LMIC) countries [6;127;140].

The many faces of penumbra: This topic is probably the least understood and the most contentious issue when it comes to the debate on cobalt versus linac purchases. X-ray beams from an accelerator undoubtedly have tighter *geometric* penumbras due to the small focal spot sizes (mms), compared with cobalt source diameters (cms). This effect is responsible for the sharpness of field edges measured "in air", including those shaped by primary or secondary collimators. However, the width of this fundamental penumbra becomes expanded "in tissue" by the lateral scattering of knock-on electrons. This physical or radiological penumbra worsens with increasing photon energy and with decreasing tissue density (Figure 17). The penumbra inside the patient is significantly and inevitably enlarged especially in lung. It should also be noted that the dose fall-off at field edges for optimized dose distributions is due mainly to the overlap of fields, and less affected by the baseline geometric penumbra of individual fields.

The obsession of having a narrow penumbra is further tempered when we consider realistic uncertainties of planning and delivering a fractionated course of radiotherapy. The first limitation occurs in treatment planning with the radiation oncologist's ability to define tissue volumes accurately or consistently [90]. Another consideration is blurring caused by the repeated positioning of the patient and possibly organ motion while the treatment beams are active. Even a "perfect" penumbra (i.e., a Dirac-delta function) will be smeared out by practical beam placement uncertainty and organ motion, such as substantial tumour movement due to the respiratory cycle. These effects are now being mitigated by the use of on-line 3-D image guidance and 4-D treatment planning. A final consideration has to do with the radiobiological response of the irradiated tissues. Tumours and normal tissues respond with a sigmoidal-shaped transform with different sensitivity and slope parameters. It is not unreasonable for cells to produce a 10% change in response to a 5% change in dose for dose levels at mid-sigmoid. The net biological effect is a *re-sharpening* of the physical penumbra. In summary, the instinctive preference for sharp geometric penumbras is intuitive but it must be tempered by the reality of radiation delivery and radiobiological considerations.

*Better conformal dose distributions with increasing higher energy***:** The benefit of an increase in energy is often evaluated by considering depth-dose curves for single fields, dose ratios of the maximum dose and isocentric considerations for multi-field arrangements, or integral dose. However, such findings cannot be generalized for application to all tumour sites. For example, superficial diseased nodes occur in head and neck cancer and Hodgkin's disease and must be treated with a beam that has a shallow build-up layer. The choice of optimal energy therefore does not abide by a "one energy fits all" strategy. Suit [121] concluded that appropriately fitted cobalt-60 units could be "fully acceptable in the treatment of a large majority of the patients undergoing radiation treatment for carcinoma of the head-neck region, breast, and sarcomas of soft tissues of the extremities." Another study [59] showed that access to accelerators is a surrogate indicator of the overall "modern-ness" and infrastructure of a radiotherapy facility. Centres that used accelerators were apt to be well staffed and equipped with ancillary equipment like 3-D imagers, advanced treatment planning systems, electronic portal imaging, and patient immobilization systems. Much of the criticism levied at cobalt can be traced to the lack of progress in adding multi-leaf collimators and image guidance rather than beam energy *per se*. The situation is evolving as considerable advances have now been made with cost restraint [64;86;103;114]. Figure 18 provides an example of a head and neck tomotherapy

(a)

(b)

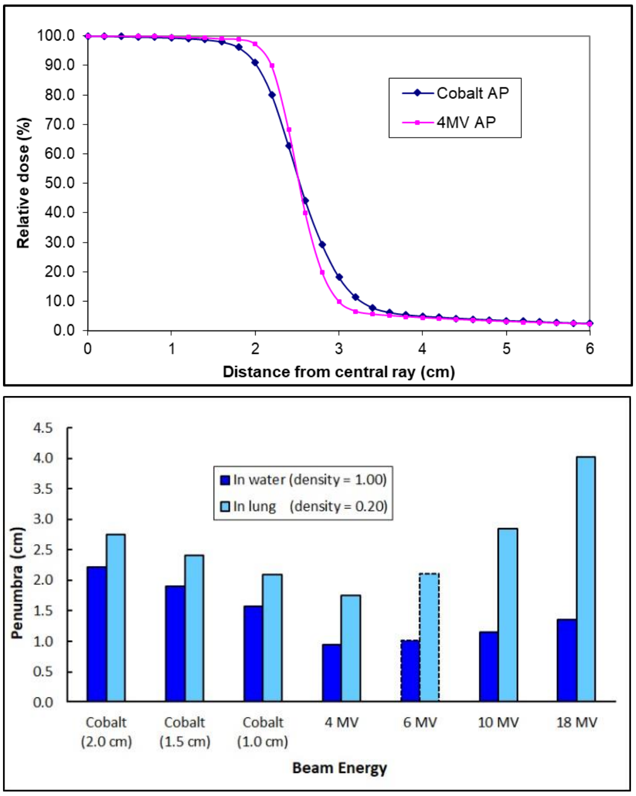

Figure 17. (a) Monte Carlo calculated dose profiles for a cobalt-60 beam and a beam of 4 MV x-rays. (b) Monte Carlo calculated beam penumbra defined as the 90-10 % width at a radiological depth of 10 cm in a homogeneous phantom of water or lung (density = 0.20 g/cc) exposed to a 5 cm × 5 cm field. Cobalt data are shown for 3 different source diameters and an SAD = 80 cm. Figures are adapted from [12]. The 6 MV data were obtained by a linear interpolation between the 4 and 10 MV data.

treatment using cobalt-60 or 6 MV x-rays. As predicted, the differences in target dose coverage and normal tissue sparing appear to be minimal. Furthermore, with multifield and rotation therapy, the differences in dose distributions as a result of different penumbra magnitudes is relatively small as shown in Figure 19. We surmise that if cobalt-60 conformal therapy and IMRT are advanced, beam energy will fade as an important variable in the retrospective analysis of clinical outcome results.

Radiation safety: Modern cobalt machines use sources with over 10 times more activity (e.g., 13,000 Ci or 500 TBq) than the original sources to yield a dose rate of over 200 cGy per minute at an SAD of 100 cm. The advantage of radioactivity is a very predictable and constant dose rate except for monthly source decay corrections. In practice, the cobalt source is retracted into a bulky head assembly when not in use (e.g., Figure 13(c)), but there is a risk of a radiation incident if the source "gets stuck" in the "on" position. Personnel are trained to cope safely with this type of emergency. The shielding attenuates the continuous stream of emitted gamma rays to protect medical personnel in the treatment room and the public beyond. Radioactive sources cannot be switched off and pose human and ecological risks while being transported, placed into medical devices and hospital facilities, and at disposal time. Considering that thousands of cobalt medical sources have been shipped incident-free over past decades by a Canadian company to over 65 countries, source transportation by conscientious manufacturers is a very safe practice. The radioactive source is always radiating, however, whereas a linac beam can be interrupted at a moment's notice, ignoring the low induced radioactivity in collimating and room structures for beams above 10 MV. The production of x-rays is therefore more switchable, although there have been serious accidents with accelerators due to failure of hardware and software controls. The issue of source disposal is of substantial concern if inadequate legislation is in place, as evidenced by incidents that have occurred in Mexico and Brazil [13;99]. These are exceptional occurrences attributed to untrained, incompetent, or unscrupulous individuals.

The theft of a source by unauthorized persons or groups could lead to the fabrication of "dirty" radiological bombs with grave consequences. Following the 11 September 2001 terrorist events in the United States, security measures were enhanced for all facilities housing intense radioactive sources. In 2015, government proposals (yet unapproved) were tabled to phase out *all* radioisotope sources [97]. The intended and unintended consequences of such a directive are immense for the American population and for the rest of the world [31]. In a later section, we describe general applications of cobalt-60 beyond radiotherapy including the irradiation of food, medical devices, blood irradiation for tissue allografts, and consumer products. The total abolishment of cobalt-60 sterilization, without a cost-effective substitute linac technology would lead to a catastrophic global disruption of the food and medical supply chains. Radiotherapy in many low-to-middle-income countries with perhaps 2,000 cobalt teletherapy units, which service a large percentage of the world population, would be in jeopardy. A shift of cobalt-60 activation and manufacturing plants to other countries with less stringent radiation regulations would aggravate security risks on a world scale.

Cobalt-59 supply: The current cost of a cobalt therapy source is driven only partially by the cost of cobalt-59 metal ($30.00 per kilogram), which is expected to rise dramatically within this decade because of heavy demand for electric vehicle lithium-ion batteries. This may impact the cost of cobalt units to a minor extent because the cost of cobalt-59 material is a minor contributor to the overall cost of a therapy machine. Production of a radioactive source requires access to costly nuclear reactor facilities. For example, a cobalt source replacement generally costs between $100,000 to $200,000 [97]. The electric vehicle market is unlikely to impact the cost of a therapy unit, but *it could halt their production line*. It is projected that 10 to 20 million electric cars will be produced *each year*

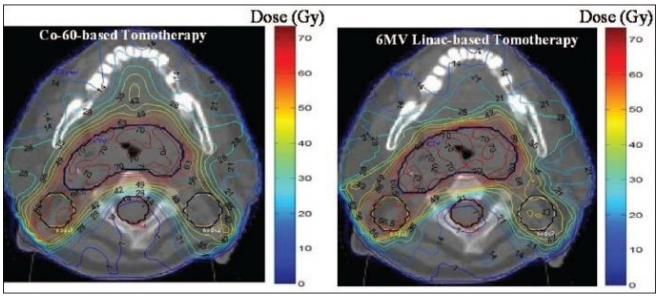

Figure 18. Tomotherapy distributions using cobalt-60 or 6 MV x-rays. With permission from [79].

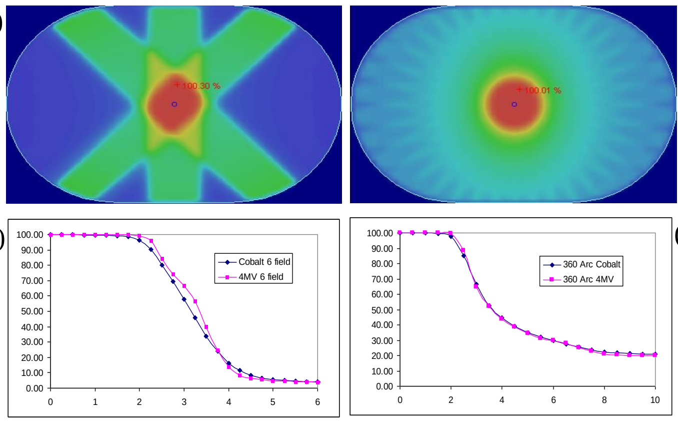

Figure 19. Cobalt-60 dose distributions for: (a) 6-field, and (b) 360° rotational techniques. Below each distribution (c and d) is a plot of the corresponding mid-plane horizontal dose profile (% dose versus distance from the central ray in cm) with a comparison to that achieved with 4 MV x-ray beams, which has the sharpest single-beam penumbra as shown in Figure 17. From [12].

starting in 2025, just 5 years from now. Each car battery requires 10 kg of cobalt and, hence, electric vehicle manufacturing will need 100,000 to 200,000 metric tons of cobalt metal *per year*, comparable to the entire world's current supply (140,000 metric tons per year) [124]. The annual supply will clearly need to escalate in response to the automotive industry or cause a serious deficit for medical needs including sterilization and radiotherapy. This could clearly become a serious issue within this decade; medical and automotive industries need to reach an agreement on the sharing of the world's supply of cobalt-59. In parallel, the development of alternative battery designs that avoid the use of cobalt will likely eventually reduce the demand.

The discussions about the pros and cons of cobalt-60 teletherapy in comparison to radiotherapy with linear accelerators has been on-going for many years [12;62;68;102;128;129]. Table 5 provides an overall, abbreviated, high-level summary of these factors of comparison between cobalt and linacs [68;128]. Note that as a high-level view and as indicated by the earlier discussion, there are a lot of details that provide variations on these broad perspectives.

To summarize these considerations, the general arguments against cobalt are large geometric penumbra, changing dose rate due to source decay, source replacement every five years, radiation safety concerns with a radioactive source that emits radiation continuously, security concerns regarding the radioactive source and possible malicious abuse, lack of modern technology such as built-in multileaf collimator (MLC), shallower depth of penetration, and radiation safety concerns associated with appropriate source disposal. In contrast, cobalt offers lower cost and greater simplicity for less sophisticated techniques.

X. OTHER USES OF COBALT-60

Cobalt-60 sources have been used for several other clinical applications in addition to external beam teletherapy. Some examples are summarized here.

Gamma unit for stereotactic radiosurgery: It was already in the 1950s that Swedish professors Borje Larsson of the Gustaf Werner Institute, University of Uppsala, and Lars Leksell at the Karolinska Institute in Stockholm, Sweden, began to think about combining proton beams with stereotactic devices for small targets in the brain. They gave up on this approach because it was complex and costly. Instead, in 1967, they designed the first Gamma Knife device using cobalt-60 as the source of energy and had it constructed. This new focused radiation therapy technique became known as "stereotactic radiosurgery." The prototype unit was in clinical use for 12 years in Sweden, with specific clinical applications for functional neurological surgery, e.g., for treatment of patients with pain, movement disorders, and certain behavioral disorders.

Prof. Leksell and his collaborators manufactured a

Table 5. Abbreviated comparison of cobalt and linacs

Issue	Cobalt	Linac
Technique types	Simpler	More complex
Penumbra	Larger (1-2 cm)	Smaller (~1 cm)
Dose at 10 cm	Lower (~56%)	Higher (67-80%)
Dose uniformity	Not flat for large fields	Flat for large fields
Depth of max. dose	~0.5 cm	1.0-3.5 cm
Impact of surface contour and density variations	Significant	Lower (4-10 MV). Higher (>10 MV) due to electron transport in lung
Relative dose to bone	0.96-1.14	0.97-1.04
Dose rate	1.2-2.6 Gy/min	2.0-25 Gy/min
Patient collimator distance	30-50 cm	~50 cm
Isocentre height	~115-136 cm	~110-134 cm
Photon source	Gamma rays – decays ~1%/month	X-rays, constant dose rate
Output	Stable – constant radioactive decay	Possibly variable due to electronic instabilities
Beam shaping/MLC	Not standard, add on MLC available for some products	MLC optional
IMRT/VMAT capable	Not standard	Optional
IGRT capable	Not standard	Optional
Local infrastructure	Simple power source	Stable power source
Room requirements	Simple	Possible air conditioning, chilled water
Shielding	Less	More
Service availability	Important	Important
IT infrastructure	Basic	Important
Source transport/ disposal	Every ~5 yrs, Stuck source risks	
Cardiac implantable devices	No risk except radiation dose	Dose risks & possible electromagnetic interference
Security	Source is possible security risk (e.g., dirty bombs)	No radioactive source
Capital cost: Building	Lower than linac	Dependent on energy and options
Capital cost: Equipment	Less expensive	Dependent on energies & options
Personnel	Less for simpler techniques	Dependent on options and techniques
Maintenance	Lower cost	Higher cost

second Gamma Knife in 1975, which was installed at the Karolinska Institute for its neurosurgical service there. Subsequent units, which were built in the early 1980s, were installed in Buenos Aires, Argentina; Sheffield, England; the University of Pittsburgh (through the efforts of Lundsford et al [93]); and the University of Virginia.

With the development of stereotactic angiography, arteriovenous malformations (AVMs) and cranial-based tumours became appropriate targets for stereotactic irradiation. In the 1980s, an increasing number of patients had radiosurgery for AVMs, some benign tumors, and some small-volume malignant tumors. Currently, based on the information on the Elekta website, over one million patients have undergone Gamma Knife radiosurgery and over 75,000 patients per year receive the treatment.

While the original Leksell prototype unit used 179 cobalt-60 sources arranged over a spherical segment of 60° x 160°, the later U, B and B-2 gamma units are manufactured by Elekta (Stockholm, Sweden) and incorporate 201 sources housed in the central body of the unit. These sources produce 201 collimated beams directed at a single focal point at a source-focus distance of ~40 cm (Figure 20). The main components of these gamma units are: the radiation unit with upper hemispherical shield and central body; the operating table and sliding cradle; a set of collimator helmets; and a control unit [104].

In the U, B, and C models of the Gamma Knife, the beam collimation is split between an internal collimation and a removable external helmet-based collimation system. Each external collimator helmet has an array of removable tungsten collimators (one for each source) with circular apertures that are used to create different diameter fields at the focus point. Four, 8, 14, and 18 mm collimator helmets are available. A subset of the collimators may be removed and replaced with solid tungsten "plugs" to block individual beams in cases where additional shielding is required. Modification of the isodose distribution is achieved by using combinations of isocentres using different collimators, different stereotactic locations, and differing dwell times.

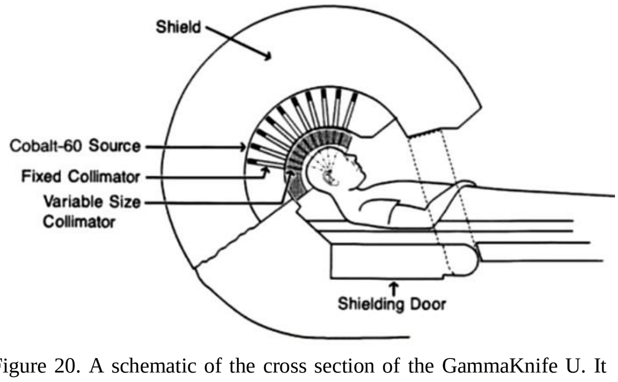

Figure 20. A schematic of the cross section of the GammaKnife U. It shows the structure of the central body in which the 201 cobalt-60 sources are positioned.

In the new Gamma Knife Perfexion, the external helmet collimators have been replaced by a single internal collimation system. In the Perfexion, the cobalt-60 sources move along the collimator body to locations where 4, 8, and 16 mm apertures have been created. (The above descriptions of the gamma units are largely extracted from [104;125].)

The most recent model of the Gamma Knife series is the Icon (Figure 21), which has the same delivery and patient positioning system as the Perfexion, but has the addition of a cone-beam computed tomography imaging arm and an intrafraction motion management system [45].

Brachytherapy: Cobalt-60 needles were used for a short time after the second world war but fell out of favour later on [8;14;50]. In 1962, Walstam introduced the first concept of a remote afterloader equipped with cobalt-60 [133]. Remote controlled afterloading was introduced clinically in the 1970s mostly using caesium-137 sources for low-dose rate treatments. In 2003, Eckert & Ziegler BEBIG successfully designed and introduced the first miniaturized cobalt-60 source. Since then they have sold over 270 high-dose rate (HDR) brachytherapy systems equipped with cobalt-60 sources.

In 1988, Mesina et al described their acceptance testing of the Nucletron Selectron HDR cobalt-60 unit [94]. HDR brachytherapy has most often been used with iridium-192 sources that have to be replaced on regular basis several times per year because of its relatively short half life of 74 days. Hayman et al performed a cost comparison between the use of cobalt-60 and iridium-192 HDR treatments over a 10 year period and concluded that there were significant economic benefits of cobalt-60 over iridium-192 and that there was no significant difference between these two isotopes in dose prescription or

Figure 21. Most recent version of Elekta's Gamma Knife Icon which includes cone-beam CT image guidance capabilities.

treatment planning [61]. A separate dosimetric comparison concluded that there are no clinical advantages or disadvantages of cobalt-60 versus iridium-192 but there are potential logistical advantages of cobalt-60 due to its longer half life, making it an interesting alternative especially in low-to-middle income countries where source replacements can be a significant administrative challenge [120].

While surgical management with enucleation was the primary treatment for uveal melanoma (UM) for over 100 years, brachytherapy has now become a standard of care as an eye-preserving treatment modality [18]. Chronologically, the following isotopes have been used in rings or plaques [18]: radon-222 encapsulated in gold seeds (began 1939) [119], cobalt-60 radioactive scleral plaques (Stallard reported on 99 patients treated up to 1964 [119]), ruthenium-106 β-emitter, iodine-125 plaques, and palladium-103 seeds. Stallard's cobalt-60 radioactive plaque technique revolutionized treatment and was also used for retinoblastoma patients [18]. The UM patients were treated with cobalt-loaded circular, crescentic, or semicircular applicators that were sutured to the sclera over the neoplasm with a 1 mm margin. Most of the patients received a radiation dose of 20,000–40,000 R at the tumor base over 7–14 days; the optimal dose was still under investigation. In 1984, it was reported that the "average" UM patient treated with cobalt-plaque therapy did not completely regress to a flat, depigmented scar, leaving concern that the remaining tumour may be viable and capable of metastasizing [18]. Furthermore, cobalt-60 plaques are high in energy and cannot be shielded effectively on their external surface, as other isotopes could. By 1985, cobalt plaques were no longer regularly used in London, England [18].

Gamma irradiators for research and medical purposes: Self-shielded cobalt-60 gamma irradiators are in use in many hospitals around the world. These units can be placed in any room without adding shielding. They date back to 1959 and can be used by researchers wishing to perform mutation and other biological effects studies; studies in the area of radiation chemistry; radiation dosimeter testing; research in the sterilization of food materials, soils, sediments and other media; gamma radiation damage studies; and for many other applications [101]. They can be used to irradiate blood used for blood transfusions for immuno-deficient and immuno-suppressed patients to minimize the impact of graft-versus host disease, possibly in association with bone marrow transplants. Already in the 1960s, these irradiators were used for extracorporeal blood irradiation where a portion of a patient's blood was shunted through the irradiation field of the gamma irradiator. Applications included study of: (1) radiation response of circulating elements of peripheral blood, (2) radiation injury of circulating plasma proteins, (3) kinetics of blood cell production, particularly the lymphocyte type, (4) therapy of selected leukemias, and (5) cardiac output and flow through selected organs by radioisotope techniques [30;117]. These irradiators can contain cobalt-60 activities up to 24 kCi (e.g., for the MDS Nordion Gammacell 220). Today many of these gamma irradiators use caesium-137 sources although the cobalt-60 option is still available.

Other cobalt-60 uses: There are a variety of other applications using cobalt-60 although these are not medically related, other than sterilization of medical products; hence, they will only be listed here without much explanation:

- *Industrial radiography* as a form of non-destructive testing for assessing metal welds in pipes and other metal containers, especially for the oil exploration industry and in the printing industry to monitor the flow of inks and thickness of paper
- *Food irradiation* for extending the shelf life of various fruits and vegetables. This started at AECL in Canada in 1961. Even a mobile potato crop irradiator with 16 kCi of cobalt-60 was proposed [87]
- *Sterilization* of medical supplies and devices, e.g., surgical gowns, latex gloves, catheters, scalpels, bandages and implants
- *Chemical processes*, e.g., polymerization of plastics
- *Decontamination* of cosmetic raw material and applicators
- *Treatment of fresh produce* to prevent the spread of disease and consumption of crop by invasive species of insects
- *Preservation* of cultural heritage items
- *Treatment of gemstones* to improve their colour.

XII. SUMMARY AND CONCLUSIONS

The development of cobalt-60 radiation therapy for cancer patients beginning in 1951 was a historic breakthrough, moving radiation therapy into a new age with very significant improvements in patient outcomes both from the perspective of tumour control and reduced normal tissue complications, including a great reduction in skin reactions. While we estimate that between 50 to 100 million patients have benefited from cobalt-60 treatments since its implementation into clinical practice, it is not easy to estimate what impact cobalt-60 has had on quality-adjusted life years. In the meantime, linear accelerator developments have competed with cobalt-60 to the extent that in the mid-1980s, the number of linear accelerators surpassed the number of cobalt-60 machines (Figure 16). Furthermore, the technological advances on linear accelerators significantly increased their capabilities with IMRT and IGRT. Similar developments on cobalt-60 machines occurred decades later, leaving cobalt-60 teletherapy far behind for many years in terms of technical capabilities. Furthermore, the concerns about cobalt-60 being a radioactive source and the possibility of terrorist activity, in the context of using these sources as "dirty bombs", has prompted a mentality of removing these sources from usage as much as possible. This awareness became more acute with the terrorist activities that occurred on "9/11" 2001.

One of the very significant advantages of cobalt-60 therapy in earlier days was its simplicity and its relatively low cost compared to the less stable and more complex linear accelerators. However, as the new options of MLCs, IMRT and IGRT are added and as linear accelerator technology has provided more stable beams and improved reliability, this relative simplicity is fading. Thus, the combined concerns of greater complexity for cobalt-60 machines with automated collimation and on-board imaging technologies, enhanced stability of linear accelerators, and the security concerns for cobalt-60 sources have significantly reduced the remaining advantages of cobalt-60 compared to linacs.

In summary, we have reviewed the post-war developments of cobalt-60 radiotherapy equipment. This was truly an international effort, driven largely by the nuclear reactor technology that emerged after the war and the human appetite for using radiation as a peaceful and benevolent agent for curing a major disease threat. Cobalt-60 has given hope for a normal life to over 50 million cancer patients since 27 October 1951. More importantly cobalt therapy provided a stimulus for catapulting megavoltage therapy forward, which is the current standard of practice in high-income countries (HICs). Cobalt-60 radiation therapy continues to evolve and play a role in LMICs dealing with 70% of world cancer deaths [138] but only using 35% of the world's radiation therapy facilities; or stated another way, LMICs have 0.7 machines per million population versus 7.6 machines per million for HICs [40]. Within the African continent, around half of the countries have no radiotherapy services and most of those that have cannot adequately cover the population which needs them [98]. The cost-effectiveness and ease of maintenance of cobalt units has contributed to the cause of treating cancer worldwide. While treatment techniques will improve as a new generation of IMRT-ready cobalt units emerge, security of cobalt installations and proper disposal of radioactive sources remain a genuine concern and top priority for strict government oversight. The future supply of cobalt metal will be drained by the electric automotive revolution, perhaps as early as 2025. It might enhance the shift to accelerators, possibly continuing the stress on LMICs.

Clinical outcomes in terms of disease-free survival and fewer treatment complications continue to improve with image-guided IMRT, VMAT, high precision radiosurgery, along with automation and artificial intelligence. There undoubtedly will be new imaging and accelerator developments in the future. One can dream of high-LET beams such as carbon ions eventually becoming available for national use in every country or that the recent excitement about FLASH radiation therapy [15;16] will provide new, cost-effective treatment modalities that can be readily implemented globally.

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