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APPLICATIONS AND OPPORTUNITIES
FOR RADIATION SOURCES

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Introduction

An important spin-off benefit from the nuclear energy industry has been the ability that has been acquired to produce a wide variety of ionizing radiation sources for industrial, medical and scientific applications.

These sources include radionuclides, produced by irradiation of target material in nuclear reactors and cyclotrons or recovered from spent reactor fuels. Techniques developed in nuclear research laboratories have also given us machines for accelerating electrons and other charged particles to high energies, and to produce high energy x-rays at high power levels.

Once these sources became available, practical applications were quickly discovered which have become the basis for many profitable and beneficial businesses.

Canada can take some pride in its contributions to these developments. For example, as early as 1949, the Commercial Products Division (now known as the Radiochemical Company) of Eldorado Mining and Refining Ltd. contracted with the National Research Council for the production of radioisotopes in the NRM reactor at Chalk River.

In the same period, the pioneering work of Dr. Harold Johns on the medical applications of cobalt-60 here at the University of Saskatchewan, led to the development, in collaboration with RCC, of the world's first production cobalt-60 teletherapy machine for the treatment of cancer. This machine was installed in the Victoria Hospital, London, Ontario in 1951. It was the first of over 2,000 machines built in Canada and sold in over 30 countries, establishing Canada as the originator of modern supervoltage radiation treatment of cancer.

In the following years, RCC became a division of Atomic Energy of Canada Limited and continued to develop both medical and industrial application of ionizing radiation. Annual revenue generated by this division of AECL now exceeds \$80M and production of radioisotopes in several Canadian nuclear power reactors make a significant contribution to their operating costs. Many other countries with nuclear industries have now developed their own radioisotope and radiation based business ventures, and it is estimated that as many as 15,000 jobs have been created world-wide as a direct result.

The Situation Today

As with any technology, the radiation source and radioisotope business has seen evolutionary changes. In the early days, the major application was in cancer treatment using both externally applied radiation from cobalt-60 and x-ray machines and internally administered small sources based on various isotopes for therapeutic or imaging purposes.

Industrial applications which were soon established included use of radioisotopes as tracers, for radiography, and in instruments for measuring thickness, density, smoke detection, etc. These remain important uses, especially in the case of radiography. For example, AECL supplies about 75% of the more than 800 iridium-192 radiography sources used in Canada each year.

The availability of increasing amounts of cobalt-60 in Canada stimulated research into potential new uses for the unique properties of gamma radiation energy. The Radiochemical Company Division of AECL supported this work by making available commercially many different types of self-contained laboratory irradiators based on cobalt-60. These are now in use in over 450 institutions throughout the world for research into radiation effects and possible applications of gamma irradiation.

AECL also conducted its own research into practical uses for cobalt-60 gamma radiation energy, covering applications as diverse as biological sterilization, chemical processing and electric power sources for underwater use.

A major breakthrough which resulted was the widespread adoption in the early 1960s of cobalt-60 gamma radiation as a method for sterilizing pre-packaged disposable medical supplies. This has become the fastest growing application for gamma irradiation in the world. As in the case of cobalt-60 teletherapy, Canada played a leading role in developing this application through its commitment to production of large quantities of cobalt-60, and the development of safe, economical and reliable irradiation systems. AECL worked with users to solve radiation related material problems and to satisfy regulatory authorities as to the safety and reliability of the process.

At this time there are over 130 gamma sterilizers installed world-wide in over 40 countries, and it is estimated that 40% of all medical disposables are now sterilized in this way.

Figs. 1 and 2 illustrate the dramatic increase in shipments of AECL industrial cobalt-60 which has resulted from this application, and the growth in the number of plants in service. Gamma sterilization has succeeded because of its clear economic and technical advantages over alternative processes, and it is

expected to take an ever-increasing percentage of the medical product sterilization market.

Radiation has also been found useful in many processing industries for curing and cross linking of plastics, rubber, inks, adhesives and paints. Both cobalt-60 gamma radiation and electrons are used for such purposes, although relatively low energy electron beam generating accelerators have been most commonly employed.

A number of major manufacturers now routinely use electron beam processing for such purposes as curing wire and cable insulation, manufacture of heat shrinkable plastics, rubber vulcanization and paint curing. It is estimated that some 400 machines are currently in use for these purposes.

Evolution of medical applications has been no less dramatic than in the industrial area.

The success of cobalt-60 teletherapy in cancer treatment stimulated the search for improvements, particularly higher photon energies which have advantages in the treatment of deep-seated tumors. Although treatment systems based on high energy devices such as the Betatron had been in limited use even before the development of cobalt-60 teletherapy equipment, they had not gained wide popularity because of their complication, low dose rates, cost and general inconvenience of use. However, the needs of nuclear research has led to the development of the high energy linear electron accelerators driven by klystrons or magnetrons. These devices offered the possibility of building compact high energy teletherapy equipment which was competitive with cobalt-60 systems.

Introduction of these machines in the late 1960s reduced the demand for cobalt-60 teletherapy equipment, and while cobalt teletherapy remains an important tool for the radiotherapist, accelerators now represent more than 90% of new sales in North America. Nevertheless, the simplicity and reliability of the cobalt machine ensures that it will maintain a basic role in markets where these qualities are paramount requirements.

Canada has played a significant role in developing linear accelerator technology for research purposes, and currently AECL sells a technically advanced high energy therapy accelerator based on a unique double pass concept developed at the Chalk River Nuclear Laboratories. It has not, however, captured the dominant position in the present cancer therapy market that was once held with cobalt-60.

Developments in other applications of radioisotopes in medicine have provided many rewarding opportunities. The wide use of diagnostic imaging processes based on the use of specific radiopharmaceutical compounds has led to a rapid growth in the

radiopharmaceutical industry and the supporting supply of bulk radioisotopes.

Canada's NRX reactor was first used to supply I-131 to U.S. medical researchers in 1947. Thirty-seven years later, NRX is still producing isotopes and Canada has become one of the world's largest producers of bulk radioisotopes to the radiopharmaceutical industry.

By far the most widely used medical diagnostic isotope at the present time is Technetium-99. It emits a single gamma photon with an ideal energy for organ imaging. It has high specific activity and a short six-hour half life which minimizes radiation exposure of patients, and its compounds can readily be used for visualizing a variety of specific body organs. Technetium-99 is used for approximately 90% of the total 350,000 nuclear medicine procedures performed annually in Canada.

Technetium-99 is usually drawn as required from chromatographic generators loaded with fission product Molybdenum-99. Canada has become the world's largest producer of fission-product Molybdenum-99 and in 1983, AECL shipped some 250,000 curies to manufacturers of Technetium Generators.

The recent completion of the new AECL isotope production facilities at Kanata, Ontario, provides the resources needed for expansion of this business and for diversification into the manufacture of products such as Technetium-99 generators.

In addition to Molybdenum-99, AECL markets several important reactor-produced isotopes used extensively for medical diagnosis, including Iodine-131, Iodine-125 and Xenon-133.

The cyclotron, originally developed as a tool for high energy nuclear particle research, now provides a means for making a number of medically useful isotopes which are not obtainable from nuclear reactors. Among these are Thallium-201, used in an effective diagnostic technique for cardiac malfunctions, and isotopes such as Gallium-67 and Iodine-123.

Canada is entering this business with isotopes produced in an AECL-operated facility based at the TRIUMF cyclotron laboratories in Vancouver.

Radioisotopes also play an important role in medical immunoassay procedures, and in recent years this has been a significant growth market.

Antigen antibody complexes are formed by mixing radioisotopically labelled antibodies with unlabelled natural antigens in

blood or other samples. The amount of radioactivity found at equilibrium is a measure of the naturally occurring antigen in the sample. These in-vitro tests are rapid, simple and inexpensive to perform and can be used in small de-centralized clinical laboratories. Carbon-14 Iodine-131 and Iodine-125 are all used for these assays, although Iodine-125 is the current isotope of choice. AECL supplies about 50% of the world demand for each of these three isotopes.

There are, however, indications that new, non-radioisotope based assay procedures may soon begin to replace the present techniques.

Future Trends and Opportunities

During the next decade, radiation derived from radioisotopes and accelerator sources, may still be expected to play significant roles in medical and industrial applications, but significant changes of emphasis will occur as new technology develops and economic factors exert their influence.

Medical Applications

Radiation is likely to remain an important treatment method for cancer for many years ahead unless some unexpected breakthrough occurs in chemotherapy or immunology.

For external application of radiation, the linear electron accelerator is likely to continue to displace isotope sources because of its greater versatility in terms of radiation type and energy delivered.

The technology is relatively mature and the industrial world is already well supplied with equipment, so that we do not see this as a major growth market for radiation sources in this area.

Many third world countries will, however, be building up cancer therapy capability and this may provide growth opportunities for supplying competitively priced isotope and accelerator based teletherapy machines or the technology to build them.

Similarly, the radiopharmaceutical market is maturing in the industrial world and total productive capacity exceeds demand, so that strong downward pressures exist on profits and prices as producers compete for market share.

The producer of bulk isotopes is vulnerable in these circumstances and has a strong incentive to seek for new radioisotope applications and new products.

Developments in bio-technology may provide several significant opportunities for radioisotopes in the medical area.

For example, it is now possible to produce monoclonal antibodies from the hybrid cells created by fusing lymphocytes with tumour cells. These antibodies are very specific in their action and react only with one antigenic determinant. They offer greatly enhanced sensitivity and specificity for immunoassays when tagged with isotopes.

When tagged with suitable radioisotopes they can also be used for accurate tumour location and may also offer the possibility of actually carrying therapeutic quantities of radioisotopes for tumours.

Successful developments in these areas could reduce the demand for current diagnostic isotopes such as Technetium-99 and may increase the demand for new isotopes, especially those produced in cyclotrons, such as Iodine-123. Success in treatment of tumours via monoclonal antibodies - the so-called "magic bullet" approach could even have a major impact on the demand for both teletherapy and implantable radioisotope sources in future.

Industrial Applications

In the industrial application areas, it appears likely that cobalt-60 gamma sterilization of medical disposables will continue to increase its share of the available market. The reasons for this are that photon radiation has a unique advantage in its ability to penetrate large volumes of pre-packaged materials, and when delivered from a cobalt-60 source, offers a high degree of reliability in terms of delivered dose and hence in guaranteed sterility.

Furthermore, the most competitive alternative for bulk sterilization of medical disposables, is coming under increasing scrutiny because of possible toxic side effects of residual amounts of the ethylene oxide sterilant which it uses. Stricter controls on residual levels and permissible exposures to processing plant operators will increase the costs relative to gamma processing.

Nevertheless, it must be recognized that the medical sterilisables' market is a finite one and that growth will taper off as processing demand is saturated. Thereafter cobalt-60 replenishment for existing sterilizing irradiator sources will be the most important feature of this market.

Growth prospects for radiation processing in the plastics and coating industry, do not appear to be large at the present time. Unless some significant breakthrough applications, such as

production of a unique material unavailable by other means, is discovered, the electron beam curing or vulcanization processes will continue to develop relatively slowly and only when it can show good economic competitiveness with alternatives.

A significant potential does however exist for irradiation in the area of food processing. This has long been recognized in Canada, and much pioneering work has been done in the past 30 years.

In 1960 the Canadian government was the first in the western world to approve irradiation of potatoes to inhibit sprouting.

Since that time, research and development has continued in laboratories world-wide with support both from governments and international agencies such as the Food and Agricultural Organization (FAO), the International Atomic Energy Agency (IAEA) and the Organization for Economic Co-operation and Development (OECD).

As a result of these programmes it has been shown that radiation can be usefully employed for four main applications:

- sprout inhibition in stored root crops;
- shelf life extension of fresh fruits, vegetables and fish;
- disinfection of insects in foods such as grain;
- elimination or reduction of microbial pathogens, such as salmonella in poultry.

In spite of the demonstrated positive benefits, commercial exploitation of food irradiation has been very slow to develop. Initially, government regulatory agencies required extensive testing to ensure that irradiated food was safe for human consumption. Even when that had been proven beyond reasonable doubt, food processors remained reluctant to adopt the technique because of uncertainty about public acceptance of the product.

As a result, development of commercial food irradiation has largely been through the medium of operators of service irradiation facilities, such as Gammamaster in the Netherlands, who for several years have been successfully irradiating various foods and spices for microbial decontamination. Limited programmes have also been operated in Israel, Italy, Japan and the U.S.A. By 1983, 33 foods were approved for irradiation in 19 countries (see Table I). About 10 industrial food irradiators are known to be in operation at present, utilizing about two million curies of cobalt-60 in total. However, we believe that this market is on the verge of a major

expansion and that within 10 years the total installed cobalt-60 capacity may well exceed that currently in place for medical product sterilization.

To illustrate the potential in just one area, it is worth noting that in some countries food loss in storage due to infestations can amount to over 30% of crop yield. The National Academy of Sciences has estimated that such losses, by 1985, could amount to 107 million tons of food worth \$11.5 billion. Even a modest reduction in this loss by using radiation would have significant economic and social benefits in these countries. Furthermore, radiation disinfection avoids the risks associated with other commonly used disinfection techniques using toxic chemicals, such as ethylene dibromide.

Another major industrial potential for irradiation lies in the sterilization of waste materials containing pathogenic organisms or toxins. The effectiveness of radiation for such purposes has been demonstrated in a number of laboratory and pilot scale experiments, but much development is needed before widespread commercial use occurs.

Because of the very large doses of radiation required, especially to destroy viruses, coupled with the large amounts of material to be treated in many cases, cobalt-60 may not be an economic source of radiation for these purposes, and indeed demand for cobalt-60 could quickly outstrip the finite supply available from installed nuclear power reactors, if radiation treatment of waste was widely adopted.

For this reason, we believe that a large scale waste irradiation project is most likely to be carried out by using high power linear electron accelerators based on the same principles as the smaller units developed for medical use, even if initial piloting and demonstration is done with cobalt-60 or fission product sources such as cesium-137.

Some of the more promising waste irradiation applications currently being developed or in the early stages of commercial exploitation are:

- decontamination of food waste and garbage dumped at international airports. These wastes must be incinerated or otherwise decontaminated to avoid importation of dangerous infections, such as African swine fever or hoof and mouth disease;
- destruction of persistent toxic chemicals such as P.C.B.s;
- sterilization of liquid sewage waste so that it can be used for irrigation in arid countries where water is valuable;

- sterilization of waste material from laboratories handling viruses and other dangerous pathogens;
- Elimination of sulphur and nitrogen oxides from stack gases.

Commercial success in any of these applications depends a great deal on the successful parallel development of suitable and economic radiation sources, and our Company hopes to be in the forefront of such developments by building on its knowledge of both the industrial irradiation business and accelerator technology.

In summary, the uses of radiation in both medicine and industry can be expected to continue and to evolve. Traditional uses such as cancer therapy will mature and in some cases be displaced by new technology. Major new applications, including food processing and waste treatment, are however expected to maintain the demand for isotopes such as cobalt-60 and to stimulate the development of economical and reliable accelerator systems to deliver large amounts of radiation power, especially if cobalt-60 production capacity growth limits are reached.

TABLE 1

FOODS CLEARED FOR GAMMA IRRADIATION - 1983

<u>PRODUCT</u>	<u>BENEFIT</u>
1. Potatoes	sprout inhibition
2. Onions	sprout inhibition
3. Wheat, flour, whole wheat flour	disinfestation
4. Garlic	sprout inhibition
5. Mushrooms	growth inhibition
6. Grain	disinfestation
7. Dried fruits	disinfestation
8. Dry food concentrates	disinfestation
9. Hospital meals	sterility
10. Powdered battermix	microbiological reduction
11. Poultry	elimination of salmonella, shelf life extension
12. Cod, haddock, whiting, plaice, coal-fish	shelf life extension
13. Strawberries	shelf life extension
14. Spices	microbiological reduction
15. Cacao beans	disinfestation
16. Asparagus	shelf life extension
17. Shrimp	shelf life extension
18. Fresh fruits	shelf life extension
19. Fresh, tinned and liquid foodstuffs	sterility
20. Fresh vegetables	shelf life extension
21. Vegetable filling	microbiological reduction
22. Raw beef, pork and rabbit	shelf life extension
23. Cooked meat	shelf life extension
24. Shallot	sprout inhibition
25. Mixed dry ingredients for hashed meat	decontamination
26. Peeled potatoes	shelf life extension
27. Endive	shelf life extension
28. Frozen frogs legs	microbiological reduction
29. Rice and ground rice products	disinfestation
30. Papaya	shelf life extension
31. Mango	shelf life extension
32. Dried bananas	disinfestation
33. Avacados	delayed ripening

COUNTRIES

1. Bulgaria	11. Netherlands
2. Canada	12. Philippines
3. Chile	13. South Africa
4. Czechoslovakia	14. Spain
5. France	15. Thailand
6. West Germany	16. United Kingdom
7. Hungary	17. Uruguay
8. Israel	18. United States
9. Italy	19. USSR
10. Japan	

FIGURE 1

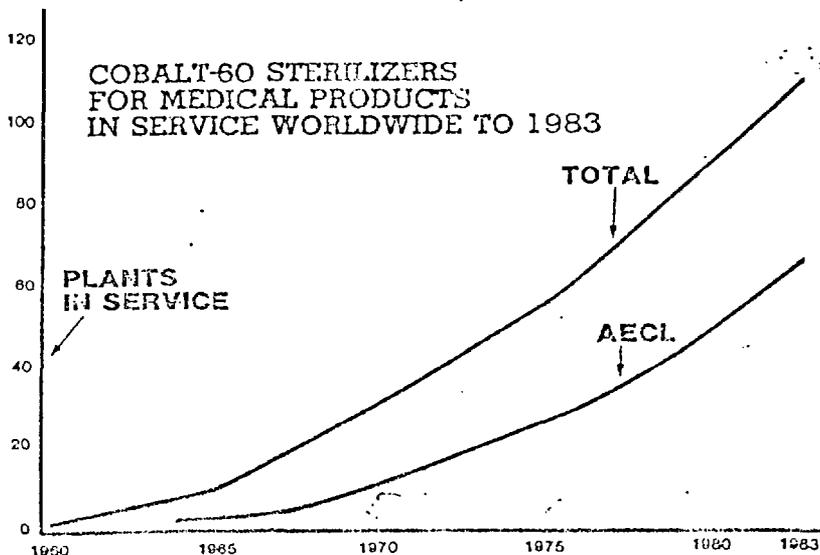


FIGURE 2

