The Legacy of Radium

M S S Murthy

M S S Murthy retired as Head, Radiological Physics Division, BARC, Mumbai a year ago. His professional interests are radiation biology, radiological safety and molecular biology. He occasionally writes popular science articles in both English and Kannada. He was also the Editor of *Journal of Medical Physics.*

The discovery of radium, its use in radiation therapy for cancer and its modern replacements are described.

Introduction

Show any person any thing that fluoresces in the dark and ask what it is. Snap comes the reply 'Radium'. In most cases it is not radium. Most people have not seen radium and even fewer have ever handled it. But this testifies the extent to which radium has remained a household word even a century after its discovery. Its discovery on December 26, 1898 heralded a new era in the treatment of cancer, which until then was managed only by surgery. Today, a hundred years after its discovery, radium is no longer in use, but *brachytherapy*, the science of treating of cancer, for which radium laid the foundations, remains one of the best hopes for patients suffering from cancer of the cervix, ovary, bladder, breast, head and neck and oesophagus, etc. The history of the discovery of radium, its initial application in the treatment of cancer, and its final replacement by more suitable radiation sources all make a fascinating story.

The last decade of the nineteenth century was sizzling with new and far-reaching discoveries in physics. The first was the discovery of X-rays in 1895 by W C Roentgen, a German physicist. In fact, he produced the first ever radiograph of his wife's palm in which the bones clearly showed up. It made a tremendous impact on the practice of medicine. Within months after the discovery of X-rays, Henri Becquerel, a French physicist, demonstrated that many salts of the element uranium emit rays similar to X-rays. However, the intensity of the radiation was so low that it could not find any immediate applications. It remained quiescent, waiting to be explored further. Then came the next explorer, an outwardly frail, young woman by the name of Marya Sklodowska.

The Discovery

Marya Sklodowska was born on November 7, 1867, in Warsaw, Poland. After completing her initial studies brilliantly, she went to Paris in 1891 to pursue higher studies in physics at the Sorbonne University since in those days women in Poland were not admitted to the universities for higher studies. Her progress was excellent. By the end of 1897 she had become Marie Curie marrying Pierre Curie who was a noted physicist in the University, had become the mother of a baby girl, and more importantly had earned two university degrees – one in physics and the other in mathematics. The next step in her career was a doctoral degree. For this she had to choose a topic yet unexplored, but fertile enough to produce original work. It was at this stage that she came across Becquerel's papers on 'uranium rays'. Marie Curie immediately realized its potentiality for further investigations. With the consent of Becquerel she set out to investigate the properties of uranium rays.

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Earlier Roentgen and Becquerel had used only photographic plates and fluorescent screens to study the properties of X-rays and uranium rays. Marie, for the first time, adapted an ionization chamber coupled to a piezoelectric quartz electrometer, designed by her husband, to measure the ionization power of uranium rays. This enabled her to make quantitative measurements and arrive at some important conclusions. She discovered that not only uranium but also thorium emitted similar rays. More importantly she observed that these radiations were unaffected by the temperature of the salt, ambient light, or even the chemical nature of the salt formed by uranium or thorium. She realized its fundamental importance and named the phenomenon 'radioactivity'

After investigating all the compounds available to her for their property of radioactivity and finding them to be non-radioactive, she turned her attention to the ores, which contained uranium

Marie Curie isolated from the ore pitchblende two new radioactive elements – polonium and radium.

or thorium. In hindsight this appears to be a very momentous decision, because it led her on to the road to radium. To her surprise she found that pitchblende, an ore of uranium, was about four times more radioactive than expected on the basis of the amount of uranium contained in it. Since she had already concluded that no other known element (expect thorium) was radioactive, she argued that the excess radioactivity might be due to a new element, yet undiscovered. She also realized that the new element might be present in extremely minute quantities in pitchblende. At this stage her husband joined in the investigations. After separating all known elements in pitchblende, they found radioactivity taking refuge in two fractions. This suggested to them that pitchblende contained not one but two new radioactive elements. They called one of these 'polonium' in honor of Marie's native land Poland and the other 'radium' which in Latin meant 'rays'.

A Daunting Task

The quantities of the new elements were so minute that they could be identified only by their strong radioactivity and not their chemical properties. In the two fractions, polonium co-precipitated with bismuth while radium co-precipitated with barium. To accept the discovery of the new elements, scientists demanded that they be made available in pure form. It was an onerous task. Tons of pitchblende had to be processed. The ore pitchblende was very expensive because of its uranium content. They did not have sufficient funds to buy the ore. Furthermore, it required a large laboratory and equipment to carry out chemical processes for the separation. No known chemical methods were available to separate small quantities of the new elements from other elements with similar properties, but present in much larger quantities in pitchblende. Undaunted the couple took up the challenge. They managed to get free of cost one ton of pitchblende residue left after extracting uranium from the Austrian government which owned a mine. For the laboratory space, all that the University could offer was an old, leaky shed that was once used for dissection of cadavers by the faculty of medicine. The chemical-processing job was backbreaking. In Marie Curie's own words "I came to treat as many as twenty kilograms of matter at a time, which had the effect of filling the shed with great jars full of precipitates and liquids. It was a killing work to carry the receivers, to pour off the liquids and to stir for hours at a stretch, the boiling matter in a smelting basin." They applied a series of chemical separation techniques such as dissolution, precipitation, filtration, crystallization, etc., employing thousands of litres of alkali and acid solutions. At the end of forty-five months, they were able to isolate about a decigram of pure radium chloride – a white powder that could easily be mistaken for common salt!

Radium mixed with zinc sulfide emits bright light.

The Curie Therapy

Following the separation and purification of radium, it was made available in small quantities for experiments. In the hands of renowned scientists like Ernest Rutherford and Frederick Soddy, radium laid the foundations of nuclear physics and radiochemistry. Marie had observed that radium chloride could glow in dark, emitting blue light. Later, it was found that radium mixed with zinc sulfide could emit brighter light. Thus started the application of radium in dial painting industry. Dials of wrist watches, alarm clocks, aircraft instrument dials, and anything that needs to be read in the dark were painted with radium paint. Thus, radium reached the common man and that is why he attributes anything that fluoresces to radium. However, the focus of our attention here is its medical applications. Two German biologists found that radium had physiological effects. Subsequently, Pierre Curie exposed his arm for 10 hours to the action of radium and 'to his joy a lesion appeared' in the form of a burn. Marie Curie and Henri Becquerel also reported similar effects. Pierre Curie soon collaborated with medical men and discovered that radium rays destroyed living cells and certain forms of cancers. The first treatment using radium was reported by M Danols, a dermatologist at St. Louis Hospital in Paris . He treated some lumps. Soon many others in Europe and USA reported treatment of similar cases using radium. Goldberg in

The rays from radium kill tumour cells, but can also cause cancer.

London first treated skin cancer in 1903. Alexander Graham Bell, the inventor of the telephone, suggested in 1903 that a small amount of encapsulated radium may be embedded in tissues to treat cancers inaccessible to X-rays. Following this, the first gynaecological treatments were undertaken for fibrosarcoma and uterine cervical cancer in 1905. Curie therapy was born. Thereafter, gynaecological cancer and cancers of the head and neck became the main targets for treatment by Curie therapy. To facilitate the placement of radium in close contact with the tumour, sealed tubes and needles of platinum containing a radium salt were developed at the Curie Foundation in Paris. Soon they became standard materials for treatment of cancers and the procedure came to be popularly known as brachy therapy. By 1930s brachytherapy could successfully challenge surgery as a modality for managing various types of cancers. Marie Curie was personally involved in setting up Radium Institutes in Paris and in her native Poland. Similar centres came up all over the world. In all, about 2 kg of radium was put to service. India too contributed to this, with nearly 60 radium departments using about 20 grams of radium. It has been estimated that some 360,000 cases of cervical cancer had been treated the world over by the year 1955. However, all were not cured with radium.

A Double Edged Sword

It was soon realized that the rays, which kill cancer, could also cause cancer. Many radiologists in the early part of the 20th century, who had exposed their hands to excessive amounts of X-rays, developed skin cancer. Even Marie Curie died, in 1936, of pernicious anaemia, a form of blood cancer, caused by excessive exposure to radium. By the year 1956, more than 360 persons had succumbed to the ill effects of radiation. Hence, it was necessary to protect the personnel handling radium. Because of the high penetrating power of the radiation, protection became very expensive. Furthermore, the rigid needles and tubes, after constant use, could rupture releasing radium powder and causing extensive radioactive contamination. This was a serious health hazard since radium could remain active for thousands of years. Loss of radium sources into toilets and sewage during the treatment produced horror stories. Even from the clinical point of view, the needles and tubes were too large and inflexible to take the contours of large tumours. Hence, by the year 1950 interest in brachytherapy declined. If new life was to be breathed into it, alternatives to radium were to be found. The search was on for more suitable sources with properties such as high specific activity, malleability, moderate penetrating power, and a more convenient active period (half-life). The discovery of artificial radioactivity had the answer.

The discovery of new radio-isotopes has led to several substitutes for radium in cancer therapy.

New Sources

Irene Curie, the eldest daughter of Marie and Pierre, was interested in science like her parents. From a young age she worked as an assistant to her mother in the laboratory. Later, she and her husband Frederic Joliot, working in Marie's laboratory, discovered in 1934 that many stable elements could be made radioactive by bombarding them with charged particles. This enabled new radioactive substances, not occurring in nature, to be produced artificially. However, with the outbreak of World War II, further research in this area suffered a setback. After the war, with the advent of nuclear reactors, a variety of new radioactive substances could be produced in large quantities and at much lower cost. Many of them were potential radium substitutes. Chief among them were cobalt-60, caesium-137, iridium-192, gold-98, iodine-125, palladium-103, yttrium-169, samarium-145, and americium-241. In recent years automation and computers have stepped in to revolutionize the art of brachytherapy. These highly radioactive, tiny sources can be precisely placed at the exact locations in the tumour by remote operation, thus making brachytherapy safer, quicker, and more accurate. A treatment that took 2 to 3 days with radium can now be completed in just a few minutes. Computer aided treatment planning systems precisely map the radiation dose inside the tumour.

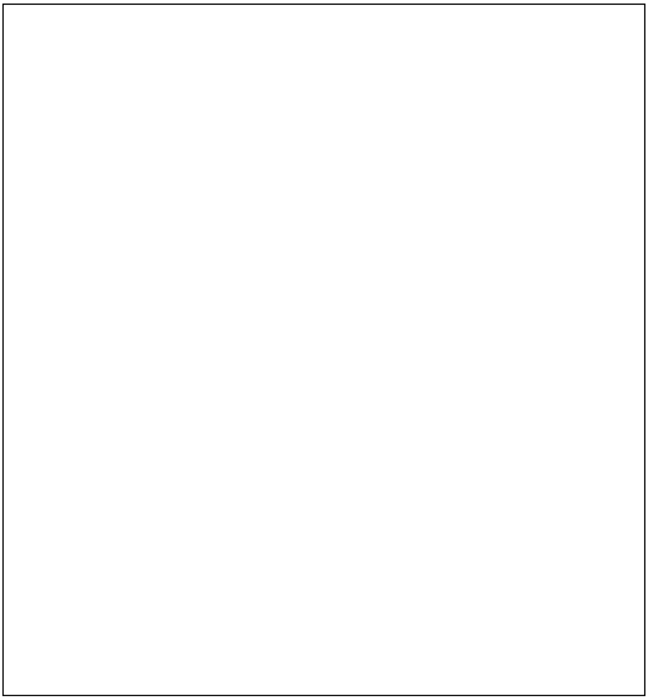

Figure 1. Marie Curie in her laboratory.

Today radium is no longer in service. Out of the 2kg radium that was extracted since its discovery, most has been withdrawn from use and stored safely in underground vaults. But the legacy of radium continues. Brachytherapy of cancer, whose foundation was laid by radium a hundred years ago, remains a beacon of hope for millions of patients all over the world. In addition to the treatment of cancer, it is also finding applications in the management of nonmalignant conditions such as blocked coronary and other arteries.

Address for Correspondence
M S S Murthy, B104
Terrace garden apartments
2nd Main road, BSK lllrd Stage
Bangalore 560 085, India

Truly, as light manifests itself and darkness, thus truth is the standard of itself and of error.

— *Spinoza*