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The history of the Norwegian Radium Hospital

Norwegian Radium Hospital's history team (RADHIST) 2024





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Preface

This book provides a brief historical overview at an important time in the history of the Norwegian Radium Hospital (later The Radium Hospital) when a new clinic building and a proton center are under construction. The new buildings are scheduled to be commissioned in 2024. Some main features of the hospital's exciting history are described, as well as the professional development and the hospital's main role in cancer care, cancer treatment and cancer research in Norway.

The Radium Hospital history team (RADHIST) has produced this book on a voluntarily basis. RADHIST was established in 2021 with the purpose of preserving all types of historical material from the Radium Hospital. This material will be presented to employees, patients, relatives and the general public both digitally and physically. This book, together with our website (**radhist.no**), is an attempt to convey some of the hospital's history.

The practical work on the book has been carried out by an editorial committee consisting of Jan F. Evensen, Tor Green, Ole Nome, Gunnar Tanum and Kristin Øwre (in alphabetical order). All of them have long experience as employees at the Radium Hospital. In addition, several others have contributed with input and content to the book.

Many thanks are extended to the Norwegian Radium Hospital's Foundation that have contributed funds that have made it possible to publish this book. Without their goodwill, the book could not have been published.

The Norwegian Radium Hospital, April 2024

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Introduction

This book describes the history of the Radium Hospital from the idea of building a cancer hospital, or "Country Hospital" which it was also called, to the completion of today's cancer center. It is a turbulent history of protests and resistance already from the first plan to establish radiotherapy for cancer diseases in Norway.



Figure 1. The Norwegian Radium Hospital at its opening in 1932.

The many subsequent development projects have not aroused unanimous enthusiasm from all quarters. However, the pioneers behind the establishment of the hospital persevered and were also helped by some key people and some fortunate circumstances. The first building was completed in 1932 and was named

"The Radium Hospital"after the radioactive element radium. Today, it has been developed into a cancer center of high international quality with access to modern diagnostics, several surgical specialties, modern drug treatment, various forms of radiation therapy and research.

Radiation therapy is widely discussed here because it was the direct reason why the Radium Hospital was built. Irradiation from radioactive radium was then a main treatment for cancer. Since then, the technical development of radiation machines has been the premise for the largest development projects, including the billion kroner investment in the 2020s that includes a proton center. Surgery and drug therapy have greatly contributed to better treatment outcomes. Not least, combination therapy with surgery, drugs and radiation has yielded good results, with better survival and fewer side effects.

In parallel with the treatment-oriented development, diagnostics and research activities have also acquired their contemporary buildings. Modern research has opened for new and improved diagnostics and new treatment options. The first pioneers' visions of a close interaction between research and clinic have proved to be very fruitful. It is most often research that is behind improved outcomes for patients. International contact and open exchange of research results have been essential for this progress.

The hospital has had and still has both regional and national tasks. In recent years, the Radium Hospital has become part of the large hospital conglomerate Oslo University Hospital (OUS).



Figure 2. The Radium Hospital - 2015

What has improved for patients?

When two new buildings at the Radium Hospital worth almost NOK 5 billion open in 2024, it is natural to ask: What makes life easier and better for patients today compared to when the Radium Hospital was built in the 1930s? We can try to form a picture of how a cancer patient felt in the early 1900s and how medical developments have affected the patient role in the years leading up to today.

In the book "Det Norske Radiumhospital" (The Norwegian Radium Hospital) (1932), Dr.med. S Poulsson begins as follows: "Among the many diseases that plague man, cancer occupies a special position. Its causes still rest in darkness; Preventive or protective precautions are therefore unknown. Left to itself, it always ends in death, after a couple of years of often great suffering, which is exacerbated by the fact that it has hitherto been said that with the word 'cancer' the death sentence has been handed down." His grim and elaborate description probably coincides with people's perception of the disease. To put this in perspective with the other dreaded disease at the time, tuberculosis, 4563 died of tuberculosis and 3300 of cancer in 1926. The statement is devoid of hope. But a hope was kindled by the discovery of X-ray radiation and radioactive radium. Medical developments have been driven on many fronts. The improvement in cancer treatment is formidable. The driving force behind this development can largely be attributed to the technological development throughout the 1900s and up to the present day. Treatment outcomes for all cancers have improved significantly. The prerequisite has been the introduction of scientific methods for mapping efficacy, side effects and sequelae. An overall national organization is an important prerequisite. Today, national standards have been established with the distribution of tasks between hospitals and national cooperation for continuous updating of knowledge. Fortunately, the knowledge base is freely available international property.

Most conditions have become much better for cancer patients. But the diagnosis of cancer still creates fear, even though today we cure many and can often keep the disease under control for many years. Treatment will by many feel like a great burden and cause both temporary and lasting side effects. Today's cancer treatment can be long-lasting and extend over several months, perhaps years. Some may feel very tired, and powerful side effects are still common. It is still difficult to become ill even though we have more effective remedies for unpleasant sequelae of both the cancer and the treatment programs. At the same time, we would like to emphasize that the possibilities for better symptom relief, especially pain relief, where new drugs and forms of administration give us a larger register to play on. Openness, communication and attitudes between patients and healthcare staff have also changed dramatically for the better and will certainly evolve further. The hope of a good and successful outcome is far more realistic today.



Figure 3. Technology development after WW2 made new treatment methods possible. The picture shows treatment with an X-ray machine and beam machine (betatron) in the 1950s.

Since World War 2, there has been an incredible medical progress. This is due to better biological knowledge and understanding. But it is important again to point out that the medical improvement is largely due to technology development with radiation machines, computer equipment, X-ray machines, blood tests, tissue samples, etc. Medical research is closely linked to technological developments. History has many examples where basic research has lit a "spark" that has led to groundbreaking medical discoveries. The discovery of X-rays is one such example that we shall see later.

We owe a debt of gratitude to the many who have given us new medical and technical insights. This is an international collaboration in many fields, which together provide great progress in cancer treatment. The pharmaceutical industry is the most important developer of new drugs, but their research builds on other research that is happening around the world. It is the welfare state that makes it possible for all people, regardless of background, to receive the same good cancer treatment that in our country is paid for by society.

All patients who have participated in clinical trials and trials of new treatments have also made major contributions to this development. They have made themselves available for new, experimental treatments and made all their personal data available. This makes it possible to draw up results on efficacy, course, side effects and risk of complications. This source of new knowledge is the prerequisite for medical progress. Our tribute therefore goes especially to the many thousands of patients who have been included in the medical scientific investigations.

New knowledge gave the idea for a new cancer hospital

Why would anyone build a new hospital with radiation machines and radium "far out in the countryside" in the early 1900s? This became a long story and controversial history that caused bitter controversy in the medical community.

The scientific discovery that set it all in motion was Wilhelm Conrad Röntgen's discovery in 1895 of what he called "X-radiation", an unknown type of radiation. Around the same time, married couple Marie and Pierre Curie managed to isolate radium from pitchblende (1898). Radium emitted radioactive radiation similar to the X-rays. This was the beginning of a remarkable development in medical diagnostics and treatment. In most countries.



Marie Curie

Pierre Curie

It was quickly discovered that X-ray and radiation from radium had an effect on cancerous tumors. Xray treatment of cancer was adopted in several countries. Some strongly argued that this form of treatment should also be established here in Norway, while others were more skeptical. There are many examples that new knowledge can be met with resistance, delaying its implementation. On the other hand, there was very limited knowledge about radiation, radiation doses and how the radiation treatment should be given to the patients. Side effects and damage could therefore be very serious. In the initial phase, radiation therapy was also tried for several benign disorders, but it was soon discovered that this could go completely wrong. "Burns" to the skin were the most common. Enthusiasts and sceptics were in a way both right and wrong but seen in the light of the long lines of history, we must be able to determine that it was right to establish radiotherapy as a form of treatment in Norway. Radiotherapy still has a very central place in many types of cancer.

Wilhelm Conrad Röntaen

Figure 4. Key researchers in the history of radiotherapy



Figure 5. The discovery of X-ray radiation and radium brought new possibilities for cancer treatment. The picture shows an X-ray machine and radium cannon from the 1930s.

The pioneers step into action

Severin Andreas Heyerdahl (1870-1940) and Hans Ludvig Carl Huitfeldt (1876-1969) were both employed at Rikshospitalet. As young doctors, they followed all the reports from Central Europe about new methods of diagnosis and treatment. They believed that Rikshospitalet had to acquire both an X-ray machine and radium. X-rays could be used for both diagnostics and treatment. Not everyone was equally eager and influential groups at Rikshospitalet opposed the young doctors' ideas. The Diakonisseanstaltens Hospital in Oslo received an X-ray machine in 1907, the year before Rikshospitalet received its apparatus.

When radium was used a little later in cancer treatment in several European countries, the two pioneers wanted to make this also available to Rikshospitalet's patients. They succeeded in getting the procurement into the hospital's budget proposal. However, they again encountered resistance from important professional groups at Rikshospitalet, but received good support from the medical director. The Ministry overruled the budget proposal from Rikshospitalet and removed the allocation from the budget, but there was clearly a great commitment among the population. Aftenposten wrote about the issue just before the budget was to be finally adopted by the Storting (1912). Amandus Schibsted, who was editor and owner of Aftenposten, was also the father-in-law of one of the most important driving forces, H.L.C. Huitfeldt. The parliament (Stortinget) allocated the money despite the Ministry's negative attitude. There were probably quite a few who had "talked" before the vote in the parliament!



Ellen Gleditsch



Severin Andreas Heyerdahl



Hans Ludvig Carl Huitfeldt

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Heyerdahl and Huitfeldt encountered several obstacles along the way. Radium was in high demand and very difficult to obtain. One also feared rogue marketing. The quality of the radioactive substance had to be ensured. Here we come to two interesting people. Pharmacist and chemist Ellen Gleditsch (1879-1968) was described as a brilliant mind. She was educated in Kristiania (later Oslo) and, after strong international competition, had the opportunity to work at Marie Curie's laboratory in Paris. She was there from 1907-to 12. The two ensured satisfactory quality control and calibration of the radioactive substance. Once again, it was a fortunate coincidence, and Rikshospitalet obtained its radium with the help of Gleditsch. The first patient to complete radium treatment at Rikshospitalet was discharged in October 1912.

The influx of patients was significant. Heyerdahl and Huitfeldt wanted to expand their activities so that more people could receive treatment. They again met resistance. The atmosphere hardly improved when the two young doctors established Kristiania Radium Institute in 1913. This was a private clinic outside the walls of the National Hospital. In an anniversary publication from 2015 by former department head Tor Brustad, a note is depicted with the following text: "A Norwegian private radium fund. At the meeting of the Medical Society in Kristiania on 12 March. a notification from the Kristiania Radium Institute is made that a radium fund of NOK 15000 has been established by gift from editor Schibsted. for the purchase of radium." The background was obvious namely that H.L.C.Huitfeldt was the son-in-law of Aftenposten's editor Amandus Schibsted. It further states: "The purpose of the fund is to have access to free radium treatment for less fortunate patients, especially those, who suffer from malignant tumors." There was hardly any doubt as to what Aftenposten's editor thought about the radium issue. We must be able to say that it was a «good party» for the radiation issue both in the first phase before the construction of the Radium Hospital, but also on later occasions in the hospital's history. Perhaps we should date this event in 1913 as the start of the Radium Hospital, even though the building itself was long in coming. There were many who saw the need for "nation-building" in health care after the dissolution of the union in 1905. The Norwegian Committee for Cancer Research, founded in 1907, established a board in 1916 with the intention of building a new

Hospital for Radiation Therapy of Cancer Patients. They were behind a petition to the Norwegian people and placed an advertisement in Aftenposten on 5 June 1917 under the headline: "National hospital for the treatment of cancer with radium and X-ray rays". Heyerdahl and Huitfeldt were constantly involved. Many of the other supporters have since made a name for themselves in Norwegian medical history. The medical director had also signed the petition, and the initiators once again drew important support from him. There must also have been a great deal of popular involvement since they managed to raise enough money for the purchase of both land at Montebello outside Kristiania and for a new building. Heyerdahl and Huitfeldt, with good support from many colleagues and a large part of the population, had achieved their goal of a national cancer hospital. However, the dispute with some leading figures at Rikshospitalet was just as deadlocked and lived on for many years.



Figure 7. Picture of the site where the Radium Hospital was built in 1929. Ullern church in the background.

The project was mainly dependent on the funds raised. In due course, the Storting and the Government granted funding of NOK 120,000 annually for 8 years. It was a lot of money and a strong signal. The enthusiasm for giving among the population continued, and by the end of 1928 more than 2.8 million had at their disposal. The difficult 30s were at the door. Fortunately, no funds were lost: "Losses on distressed banks are completely avoided."



Figure 8. Fundraiser image

On 15 June 1929, His Majesty King Haakon VII was finally able to lay the foundation stone of the Radium Hospital. The construction process encountered difficulties due to labor conflicts, but in 1932 it was ready for opening. The hospital had 71 beds and its own gynaecological department. In total, there were 49 employees and for the standards of that time an advanced laboratory with pathology. However, there was no surgical department, cancer operations had to take place at another hospital. At that time, there were no effective chemotherapy sessions, so the hospital was centered on radiotherapy. The name of the hospital – the Radium Hospital – testifies to the purpose of establishing the hospital. Although radium is no longer used as a treatment today, the name has been retained.

Another event in 1929 later proved to be a prerequisite for the quality of radiation therapy and the hospital's future operation. Heyerdahl contacted physicist Nelius H. Moxnes (1897-1956) with a desire to hire him as a radiation physicist at the hospital. Moxnes used the construction time to further perfect the knowledge of the time in radiation physics. He obtained his doctorate in Germany. We might call this the cornerstone of radiation physics at the Radium Hospital. Heyerdahl had realized a fundamental lack of knowledge about radiotherapy, and he chose the right person. Moxnes became a pioneer in several areas of radiation physics and radiation biology at the Radium Hospital. Radiation as a treatment would not have been possible without physicists. Moxnes was also engaged in radiation hygiene, i.e. measures that protect both patients and staff from unnecessary radiation. He was also instrumental in the establishment of what is today called *the Norwegian Radiation and Nuclear Safety Authority (DSA)*. Gradually, there have been many different professional groups behind the technological development in radiation therapy.



Figure 9. In the 1930s, radiation therapy with radium cannon and radium needles was one of the most important forms of treatment for cancer. To the right is a picture of the physicist Nelius Moxnes (1897-1956) who was central to the establishment of radiation therapy at the Radium Hospital.

The fundraiser succeeded in raising money for buildings, but they also had to raise funds to purchase more radium. It also became gift from the people. It received wide coverage in Aftenposten on "Radium Day" on Tuesday 9 June 1931. Support for the fundraising was very good. The raw material for radium came from the Belgian Congo. "In 15 to 20 tons of crude mineral there is 1 gram of radium," writes Poulsson. The hospital owned 2.5 grams in 1932. The cleaning processes were very expensive. The price was NOK 50 per mg radium. The radioactive substance was molded into completely dense, hollow platinum needles. They could be cast in a "radium mask" that was made from beeswax and adapted to the area to be treated, such as the chest wall. The mask was applied directly to the skin. Needles could also be inserted into the tumor or inserted into the body cavities, such as in the treatment of cervical cancer.

A "radium cannon" was also provided with Moxnes's help. This was a kind of precursor for the later radiation machines. The patient waiting lists became long, and they planned expansion by furnishing the attic of the Radium Hospital. New fundraising was started in 1938, and the population once again gave money to the hospital. The attic was fully furnished in 1940, and the number of beds increased to 110.



Figure 10. Various types of radium preparations were used for radiation therapy in the 1930s. The picture shows an overview of needles, tubes and plates with specified filtration and mg Ra.

Science is emerging.

The history of science and the Radium Hospital are closely linked. Radiotherapy with radioactive radium and X-ray apparatus was used when the Radium Hospital opened in 1932. The equipment was primitive and unreliable from today's point of view. An important shortcoming was that radiation doses could not be measured, and the accuracy of the treatment was therefore relatively poor.

Knowledge in radiation biology was even worse, i.e. the study of radiation's effect on cells, tissues and organs. Both patients and staff could suffer radiation injuries that reduced their quality of life. The long-term effects on both patients and staff were unknown. This was an international problem, and knowledge building has taken many years.

Today we have a far better and in-depth knowledge of the tolerance limits for radiation in various organs. We have a better overview of the risk of sequelae, and how the treatment can be administered in a gentler manner. In addition, we have technical equipment in the form of radiation machines and systems that control the radiation dose to the right level. Gradually, we have also got specially trained personnel who control the machine park, keep track of all complicated calculations and supervise the radiation machines. Radiation therapy today is given with very high accuracy. The risk of errors and accidents during treatment is therefore dramatically reduced. There is still considerable interest in improving treatment and gathering more knowledge, both at hospitals and at the companies that produce the equipment. Digitalization is also an important keyword for this business. The machines in diagnostics and treatment have become so advanced that previously manual routines are now automated. The staff controls computers, which in turn control the machines. Although computer technology has made the equipment more automated, it is still very important to have well-qualified staff who can control the machines and provide care to patients.

Research projects and patient safety

An important aspect that safeguards patient rights is the obligations to comply with international agreements in research and testing of new treatments. The Declaration of Helsinki establishes the ethical guidelines that everyone must follow. It was first adopted in 1964 and has since been revised and improved several times. These are internationally binding agreements that also include cash flows and sources of funding for the development of new medical methods. The world now has common ethical and professional guidelines to ensure patient safety and provide all relevant information.

If we go back to the start of radiation therapy and the establishment of the Radium Hospital, the principles followed were based more on trial and error. The patients sometimes barely knew what diagnosis they had. Information from the doctors was inadequate, and the patients were to be "spared" from the truth. At that time, scientific thinking and ethical use of scientific methods were not very developed compared to today's situation. The development of accepted international regulations is one of the most important developments to protect patients. This also requires documentation so that as much information and learning as possible is obtained when experimental treatment is given. Independent professional groups assess the research projects both ethically and academically. International research is the foundation of the progress we see today. Testing new treatments is always very time-consuming and resource-intensive, but in the long run the only viable route to reliable new knowledge. This applies to all forms of medical treatment. The requirements for openness and information to patients are key values.

The Declaration of Helsinki gave impetus to international medical research by testing new drugs and new forms of treatment. Close cooperation between hospitals both domestically and abroad has proven to be very useful for rapid progress and mutual information. With international cooperation, more and better results are produced faster. The Radium Hospital has participated in numerous collaborative projects. This expansive period for cancer treatment from the 1970s was well taken care of by the heads of the clinical departments and laboratories. This started during Professor Herman Høst's time as head of the Department of Oncology and Professor Per Kolstad at the Department of Gynecological Medicine, continued by Professor Claes Tropé. It must be emphasized that such medical development is a team effort in which the entire hospital with all laboratories and departments is happy to participate.



Figure 11. Professor Herman Høst (middle) in conversation with head nurse Brynhild Bakken and oncologist Olbjørn Klepp in 1978.

The expansion of the surgical department with orthopedics, urology, gastrointestinal surgery, lung and chest surgery and plastic surgery in the 1980-90s became an important part of this. The department became an important participant in the scientific projects. Professor Carl Erik Giercksky was central to this process.

The best treatment results were often achieved with a combination of surgery, radiation therapy and drugs (chemotherapy, hormones or different variants of immunotherapy).

Radiation therapy was adopted in the early 1900s before these principles were established. The drug cancer treatment with chemotherapy started after World War 2 and gained momentum in the 1960s-70s. By that time, the scientific methods had begun to be substantially better secured. Medical science is international, but it requires national drivers to build up the national communities. Cooperation between several treatment institutions, both nationally and internationally, is often a prerequisite for obtaining sufficient data to draw firm conclusions.

Visionary leaders

Severin A. Heyerdahl and his initiative for the appointment of physicist A. H. Moxnes was the start of the Radium Hospital's long line of good managers. Both of these recognized the need for strengthening knowledge in radiation physics and the effect of radiation on various organ systems, radiation biology. One must also emphasize the clinic heads responsible and the laboratories' commitment to research in the departments. An important engine in this was the establishment of the research institute. The hospital's development and history must be seen in the context of the history of the research institute. Director Reidar Eker and Director Jan Vincents Johannessen are central here. Headmistress Ingeborg B. O. Totland was head of the nursing service and established special training in cancer nursing.



Figure 12. Directors Reidar Eker and Jan Vincents Johannessen and headmistress Ingeborg B. O. Totland

Expansions of the hospital after WW2

During the World War 2, the development of new radiation machines accelerated, mainly because it was believed that various radiation machines could have military significance. New high-energy machines, such as betatrons and linear accelerators, were introduced, which would eventually outcompete X-ray machines.

The earlier X-ray machines had a relatively low energy and required less shielding of the radiation. The radiation from an X-ray machine is weakened to a low level by, for example, a lead apron. A radiation machine built for cancer treatment is designed to provide higher energy X-ray radiation and needs much better shielding. The new type of radiation machines, the linear accelerators (abbreviated linac), require a special room with concrete walls up to two meters thick for shielding to be sufficient. Due to less need for shielding, the low-energy X-ray machines could be used in several hospitals around the country, but switching to linear accelerators would entail specially designed beam bunkers with thick concrete walls. This issue came up after the war. The Radium Hospital's buildings at the time were unsuitable. Thus, there was a new controversv in the air regarding the centralization of radiation therapy. The new technology was resource-intensive, and there was probably also a certain status involved for hospitals that received such modern treatment options. Installing linear accelerators required both medical and technical staff, as well as the high cost of building special radiation bunkers.



Figure 13. New beam machines required large radiation bunkers with thick concrete walls. The image shows betatron (top) and linear accelerator.

In the early 1950s, a public committee was appointed with a mandate to consider whether the Radium Hospital should be expanded with new linacs. Such an expansion would greatly increase the size of the hospital and make it possible to treat many types of cancer that could not previously be treated. The alternative was to establish "more special units elsewhere in the country." The work of the committee was slow, and the controversy intensified. The Radium Hospital still had significant disadvantages. We also recognize the debate from our own time about centralization versus spreading advanced treatment services thinly throughout the country. Representatives from Rikshospitalet opposed both «monopoly» and «gigantomania». But the environment at the Radium Hospital had its way in the end. The director of the Radium Hospital, Reidar Eker (1903-1996). worked very purposefully, and finally it was recommended that the hospital should be expanded with the new type of radiation therapy and the accompanying expansion to 300 beds. The problem, again, was a national economy that could not bear the costs. A new, nationwide fundraising campaign was initiated in the years 1951-52 in cooperation with the public radio station, NRK. In addition, the Storting was persuaded to pass a special law that provided tax exemption for contributions to the development of the Radium Hospital. Minister of Finance Trygve Bratteli, a man of peace, tried to calm the location dispute, which became very bitter. It served no one to continue the resistance or spoil the fundraiser campaign, he said. The end result was NOK 16,604,690, which was a very large amount at the time. This was the fourth time publicy raised money for the hospital. This time King Olay came to the opening, in 1958. Aftenposten printed an article about the event under the headline "The Radium Hospital - the Norwegian people's gift to themselves".



Figure 14. The opening of new buildings in 1958

Medicine developed very rapidly during this time. Already in the 1960s, it became clear that there was a further need for expansion of the hospital in terms of the number of beds, treatment capacity and modernization of the laboratories. This time it was possible to develop more predictable prognoses using the Cancer Registry's overview of the number of new annual cancer cases distributed by different diagnoses. This could be linked to Statistics Norway's calculations of population development and age composition for the period 1970-1990. The results were presented in 1968, and the Norwegian parliament decided that the hospital should be expanded to 440 beds. This time the development was paid for over the national budget; Norway had become richer. In 1978, the new part was used with operating theatres, a post-operative ward and bedside posts.

Establishment of the research institute

The idea of a research institute at the Radium Hospital was conceived and implemented by Director Reidar Eker. Just after World War 2, little was known about the mechanisms that drove the development of cancer, and how cancer cells could be attacked. Eker launched the idea of an interdisciplinary initiative, where knowledge in basic subjects such as biochemistry, biophysics and genetics would be utilized in parallel with pathology and clinical medicine. But funding was lacking. Director Eker consulted Norsk Hydro A/S Director General Bjarne Eriksen, who made funds available for the construction of new research areas next to the original clinic building. Norsk Hydro's Institute for Cancer Research was opened by King Haakon in 1954.



Figure 15. The research building (Norsk Hydro's Institute for Cancer Research) in the 1950s.

The success of the department meant that the activity increased, and it gradually became difficult to accommodate the desired research activity. Eventually, the researchers became very cramped and partially dispersed in various places around the hospital. The need for more space and a new research building emerged in the 1980s and 90s. Director Jan Vincents Johannessen worked long-term to expand the research institute. He worked for many years to buy up land between the Radium Hospital and the Ring Road with a view to building new research facilities on this site. The new research building was completed in 2009 and was opened by Queen Sonja. This time it was financed over the national budget and built after detailed input from the institute's employees. There was everything a modern cancer research environment needed, from safe research laboratories and good ventilation to suitable office spaces, meeting rooms and canteens. Finally, the entire institute was gathered in one building, with short lines of communication between the units.

Developments from the 1970s

From the end of the 1970s, a decentralization of treatment provision became relevant. Cancer treatment evolved with new treatment modalities. There were new, groundbreaking drugs in chemotherapy and hormones. These could be given at local hospitals, and patients thus avoided long journeys to the Radium Hospital. Gradually, there was a natural division of labor between the hospitals, where the most common cancer drugs could be administered at the local hospital, while more advanced treatment and radiotherapy still had to be performed at the Radium Hospital. The combination of surgery, drug therapy and radiation therapy gave better results for several types of cancer. For long-term treatment programs over many months, parts of the treatment could take place at the local hospital in collaboration with the Radium Hospital. This was advantageous both for the patients who avoided a few long journeys, and for the Radium Hospital, which reduced the burden somewhat. This development reinforced the need for formalized cooperation between the various hospitals in Norway. The number of patients benefiting from the treatment increased. The development of several small radiation departments around the country was probably viewed with mixed feelings in the professional environment at the Radium Hospital. There was a fear of poor quality in the radiation therapy. But here, too, a good division of labor gradually emerged according to the same principles as for drug treatment with chemotherapy and hormones. Reorganization in the health service is always problematic, what should be decisive when there are conflicting arguments between subjects, economics, geography and tradition?

Chemotherapy had a fantastic effect on several forms of cancer. We can mention blood cancer (leukemia), lymphoma and testicular cancer. New drugs came in turn. It was therefore not surprising that some thought in the direction that the importance of both surgery and radiotherapy would be replaced by chemotherapy at some point in the future. However, that hasn't happened until now, still in 2023, surgery and radiation are the most important treatments for cancer alongside drug therapy.

Over the past 70 years, there has been a major technical development regarding radiation machines. There has also been an increasing spread of radiation machines in Norway. In this way, more patients can receive radiation therapy, capacity is no longer limiting to provide the best treatment. Radiation therapy has now been established at the hospitals in Oslo (the Radium Hospital and Ullevål Hospital), Bergen, Trondheim, Tromsø, Stavanger,

Kristiansand, Gjøvik, Ålesund and Bodø, and more are under planning and construction. To this end, it is important to remember that the establishment of radiotherapy requires a significant support network in diagnostics, such as CT, MRI, pathology and, not least, personnel who can operate these complicated machines. A national protocol for the investigation and treatment of cancer diseases has now been developed. These protocols function both as a "cookbook" for how each cancer should be treated and a means of task allocation between local hospitals and regional hospitals, such as the Radium Hospital. The protocols are updated regularly in line with international developments. It is important that this national cooperation, which also has strong ties to academic communities in the other Nordic countries, is followed up regularly.

The buildings of the Radium Hospital

Radiotherapy was the premise for the establishment of the Radium Hospital in 1932 and the expansion of the buildings in the 1950s and 60s. The nature of cancer treatment changed somewhat when new pharmacological treatment principles were introduced. At the same time, there was also a major development in the surgical professions, which opened for new and improved treatment methods. It also led to a need for more operating theatres and other specially designed areas. This was the argument for the large increase in beds in the 1970s and 80s. This created debate: Should the Radium Hospital be a radiation hospital or a complete cancer hospital? The different treatment modalities are not competitors, they are used together in common programs for the best possible outcome for the patients. This integrated treatment is a strong argument for the unification of all the professional communities in cancer treatment. The complexity of diagnostics and treatment has increased dramatically in recent years, which pulls in the same direction. Tissue diagnostics now includes many types of advanced special examinations. Also, of molecular structures. The X-ray department no longer only deals with X-rays, but also has adapted other technologies that presents disease processes in a completely new way. This development led to a need for formalization of competence, and new occupational groups emerged. Surgery gained more subspecialties, physicists and engineers gained further specialization, radiographers further trained as radiation therapists and nurses for cancer nurses, etc. Doctors became not only cancer specialists, but specialists in particular cancers. Medical opportunities have expanded faster than health budgets can bear. The answer for the Radium Hospital was piecemeal developments with emergency solutions, provisions and budget overruns.









Figure 16. The building mass at The Radium Hospital in different time periods (1932, 1958, 1980 and 2015)



Figure 17. Sketch of the buildings at The Radium Hospital with year of start of operation. A jumble that shows how a lack of longterm planning from central health authorities results in poor conditions for patients and staff. The figure shows the hospital in 2015 before the major expansion in 2020-24.

Financing the activity

When the Radium Hospital was established, the money for the new building had to be provided through gifts and fundraisers. Money was also raised for the purchase of radioactive radium by establishing the so-called "Radium Fund". It was discontinued only in 1992. Today, funds are allocated to hospital operations through the South-Eastern Norway Regional Health Authority, as for other hospitals in the region.

The many expansions at the hospital are due to the need for increased capacity. In addition to funding through the nationwide fundraisers, patients had to contribute "cure money" in the first years Eventually, it became impossible to base the hospital's operations and investments on volunteerism and donations. State appropriations were needed. From 1960, operations were covered by the national budget. But large and small gifts to the Radium Hospital are still the basis for both research and good patient measures that fall outside the state's allocations.



Figure 18. From the beginning, the operation of the hospital was financed by fundraising campaigns, but eventually decisions on appropriations were made by the Storting.

The Radium Hospital Foundation

The foundation was established in 1929 when it bought the land where the Radium Hospital is located today. The big fundraisers gave it the financial foundation. Its purpose was to run a national hospital for the treatment of cancer, i.e. the Radium Hospital. After a few years, the state increasingly had to cover hospital deficits, and from 1960 the Radium Hospital was included in the national budget.

with its own chapter. The foundation's articles of association were amended in 1963 so that the board was hereafter appointed by the Ministry of Social Affairs. It was now the ministry that controlled the foundation and later lost both governance and oversight as described below. This became obvious to everyone in connection with the reorganization of hospitals from the 1990s onwards. In the Ministry of Health and Social Affairs' "Report on the transformation of the Radium Hospital, Rikshospitalet and the National Center for Epilepsy into state-owned enterprises" from November 2000, the relationship is formulated as follows: "In summary, since 1959/1960 the hospital has gradually been drawn into the state sphere through a number of individual decisions in the area of finance and budget, personnel and management arrangements. A review in 1997 found no documentation that the state has formally taken over ownership of the Foundation or that the enterprise has been incorporated into the state as a legal person". One gets the impression that the government-appointed board of the Foundation has been so passive over the years that it was finally questioned whether the Foundation even existed! With the major health enterprise reform in 2002, ownership of the Radium Hospital was again brought into focus. The state did not know who owned what at the Radium Hospital and the Ministry of Justice had to establish that the foundation was not actually closed down but had only slept! The foundation therefore still had a responsibility regarding properties at the Radium Hospital.

After discussions within the Ministry of Health and Care Services, it was naturally decided in 2007 to appoint a new board for the Foundation *"in order to create consistency between the actual and formal conditions in the management of the hospital".* The new board had a great deal of documentation work ahead of it, and many formalities were brought in order according to today's requirements. One of the main tasks was to identify what land and buildings the foundation actually owned. The hospital had been developed in many small and large projects, and the funding was partly public and partly from donations given to the foundation.

After two years of searching old archives, previous state budgets, parliamentary propositions, minutes and basic book documents, the board submitted a comprehensive real estate report to the Ministry in October 2009. The report described which properties and buildings the Foundation owned, including the land on which the Radium Hospital stands. In addition to the Radium Hospital's site and parts of the buildings, this included staff accommodation (79 apartments) and two kindergartens.

After the report was presented to the Ministry of Health and Care Services in 2009, a lengthy process between the State and the Foundation began. In 2012, the parties agreed that the foundation should eventually be closed down and that hospital land and buildings should be transferred free of charge to the state. Staff housing and kindergartens were to be sold.

The sale sums were to be deposited in blocked bank account for future investments in the Radium Hospital. In 2017, a formal agreement was made between the state and the foundation. All funds in the foundation were to be transferred to the state, but in such a way that the money was spent on the development of the Radium Hospital: *«The hospital property is transferred on the condition that it or its value will also be used for the future as a cancer center for treatment and research for the fight against cancer diseases for 30 years after the conclusion of the Agreement. The parties agree that funds released from the sale of Apartments etc., and which are deposited in an bloked account pursuant to the Management Agreement (of 2012), shall be used in their entirety for the purposes referred to in clause 2 of the Agreement, i.e. for treatment and research to fight cancer."*

With this, the foundation made a cash contribution of NOK 220 million for the planned new building at the Radium Hospital, and that the state transferred the building site free of charge. The money was to be used as part funding for a new breast cancer center in the new building.

In 2024, the new hospital building will open with a modern breast cancer center at the Radium Hospital. The Foundation's contribution to the financing and transfer of the land have been important pieces in enabling this major project to be carried out. The foundation will formally be dissolved in 2024 when the new hospital building with a breast cancer center is put into use. All the foundation's assets and assets will then be transferred to the Radium Hospital – Oslo University Hospital. This ensures the continuation of the Radium Hospital as a national cancer center.



Figure 19. Aerial view of the Radium Hospital and the research institute (bottom right) in 1953

Collaboration with Rikshospitalet (the National Hospital)

As previously mentioned, radiation therapy started in Norway at Rikshospitalet in 1912. Radiation therapy continued there even after the opening of the Radium Hospital in 1932. However, Rikshospitalet never installed modern, powerful radiation machines, but only had X-ray machines for radiation therapy.

However, the installation of a so-called cobalt machine, a forerunner of modern linacs, was planned. The Norwegian Association to Fight Cancer had allocated money for this machine. The plans were stopped after opposition from the Radium Hospital, which believed that it was both professionally and organizationally better to gather all radiation treatment in one place in the Oslo region. At that time, there were two cancer societies in Norway that probably competed more than they cooperated. One had a strong connection to Rikshospitalet, the other to the Radium Hospital (see later about «The Norwegian Cancer Society(s)»).

Something important happened in the relationship between the Radium Hospital and Rikshospitalet at the end of the 1970s. The driving force was the academic leadership of the oncology department at the Radium Hospital and the ear-nose-throat (ENT) department at Rikshospitalet, respectively. Professor Høst and Professor Winter. They saw the need for closer cooperation. The professional communities at the two hospitals supported this. Special mention can be made of Chief Physician Halvor Vermund at the Radium Hospital. After several years as a professor at various universities in the United States, he returned to Norway in 1978 and was appointed head of department. The combination of surgery at Rikshospitalet and radiotherapy and chemotherapy at the Radium Hospital gave good results for patients with cancer in the ENT area. This collaboration was a paradigm shift and has undoubtedly saved many lives! The departments still work closely together. The treatment with surgery at Rikshospitalet and radiation and possibly chemotherapy at the Radium Hospital are planned and carried out together. This also became the prerequisite for international research collaboration that has further improved treatment outcomes.

The staff at Rikshospitalet who worked with radiotherapy were transferred to the Radium Hospital in 1991. The medical communities within cancer treatment, both in Norway and internationally, were at this time in the process of becoming subspecialized. This means that employees are becoming increasingly specialized in cancer treatment and types of treatment. Direct contact between these specialized professional environments was therefore a necessity.

Cancer Registry of Norway

In 1952, farsighted professionals saw the need for a registry of cancer cases and the results of cancer treatment in a national perspective. The Cancer Registry of Norway was established, but formally it was the "National Association against Cancer" that was behind it. The registry was located at the Radium Hospital, but "belongs to the Director of Health", as they put it. It was a national register.



Figure 20. Minister of Health Karl Evang and Director General Reidar Eker (right) were key players in connection with the establishment of the Cancer Registry of Norway

The Cancer Registry of Norway had its own board. Accurate statistics are key to getting an overview of cancer incidence and preparing forecasts. Among other things, it provides the opportunity to calculate and substantiate future needs for specially trained personnel and treatment capacity. When the Cancer Registry of Norway was established, a statutory registration of all cancer cases in Norway was also adopted. The registry captures all new cases of cancer and publishes annual statistics on *incidence* (number of new cases per year) distributed by the different types of cancer. Municipalities, gender and age are also registered. Also recorded is *Prevalence*, a figure for the occurrence at a specific time of current or former cancer patients who are still alive. The prevalence has increased markedly because more people are cured, and many non-cured people live for a long time with the disease due to life-prolonging treatment. Central to the registration is the pathology departments' responses to the tissue samples as an important key for correct registration.

Many countries now have cancer registries. The registers make it possible to compare prevalence in different countries and in different parts of the country. Occupational cancer risk has been identified. Examples include the association between nickel exposure and sinus cancer in Falconbridge staff and between asbestos exposure and lung cancer. The registry also provides information about the results of smoking cessation and other preventive measures. Sometimes unrest arises in a local community if there are more people affected by cancer. The Cancer Registry can then see whether this is a statistical coincidence or whether there may be a special reason behind it, as at Falconbridge. The Cancer Registry's databases will also form the basis for quality registries, where patient pathways can be followed over time. The effect of treatment and side effects and the risk of harm can be assessed. We can quantify the risk of complications associated with various therapies and outcomes for disease control and preservation of functions. As mentioned, the Cancer Registry of Norway is also an important source for calculating future needs for treatment places and treatment capacity. The registry has been crucial in the preparation of national cancer plans.

The Cancer Registry of Norway currently works within three main fields – cancer statistics, research and screening. Cancer statistics include the registration of cancer cases as a continuation of the original task from 1952. The Cancer Registry of Norway publishes an annual overview of cancer in Norway that is available to all interested parties. The Cancer Registry of Norway has a number of research projects to map the prevalence and consequences of cancer for different patient groups, and many employees at the Radium Hospital have completed their doctoral degrees there. The Cancer Registry of Norway is also responsible for screening programs for various cancer diagnoses – the mammography program, the cervical screening program and the bowel screening program. It is correct to say that the cancer registry enjoys a high international recognition and is much of the reason why for many clinical trials are performed in Norway.





Activities at the hospital

The activities at the hospital can be divided into examinations, treatment and care. The examinations consist of the activities that are performed before the patient is treated and include pathology, diagnostic imaging and blood sampling. The treatment is radiation therapy, surgery or drug therapy. Care includes the services performed by the nursing staff before, during, and after treatment.

1 Examinations

The poor treatment results in the early 1900s are due not least to the fact that cancer cases were discovered very late in the course of the disease. It is still the case that small tumors are easier to treat with good results than large ones. How can cancer be diagnosed? The brief description is symptoms that lead to a clinical examination. The patient's account of symptoms and the doctor's clinical examinations with hands and stethoscopes are the same today as they were 90 years ago. What is new are the tools that technological development has given us. X-ray examination and other diagnostic imaging are particularly important to reveal the presence of a tumor and any distant metastasis. Other forms of examination are tissue samples and blood tests.

Benign tumors can usually be surgically removed because the boundary to healthy tissue is sharp. Precancerous lesions are often called "in situ". They can also usually be removed smoothly but can develop into cancerous tumors if they are allowed to grow in peace. The most well-known examples of precancerous lesions are seen in the cervix and breast tissue. They must either be treated or followed very carefully.

Cancer is characterized by the tumor growing with little control and often into neighboring organs. They also have the ability to spread to other places in the body. The most common is spread via the lymphatic system to lymph nodes near the tumor (regional spread) or via the blood vessels to organs elsewhere in the body (distant metastases or systemic disease).

1a Pathology. The key to diagnosis

From its inception in 1932, the Radium Hospital had a laboratory for pathology. This was well equipped by the standards of the time. The staff was also very well qualified, so the laboratory had a very good reputation from day one. The department had its own small building next to the main building. The task at the department's start-up was fourfold: microscopic examination of

tumors and cancer cells, examination of deceased patients, teaching (medical students, doctors who will become specialists, technicians and other professions) and research. The department experienced a sharp increase in activity right from the start. The unmet need for the department's services was enormous, and development was rapid. Then, as now, correct treatment depended entirely on a definite and accurate diagnosis. This resulted in both an increase in the number of samples and ever greater demands for special examinations of each individual sample. The number of examinations of tissue samples (biopsies) increased from 1,500 annually before WW2 to 45,000 in 1972! For Pap smears (cytology) there was an even greater increase. Such surveys were started in 1951 and 500 samples were assessed in the first year. Already 20 years later, the number of samples had grown to 137,000. Many of the department's tasks are imposed from the outside. As a service unit for the patient departments, the workload cannot be controlled to any great extent. The increased demands have resulted in a need for more space, larger staff and more equipment. Research has also increased tremendously since its inception. Many types of research require pathology experts to be involved in conducting investigations of tumor tissue and cancer cells. Since its inception, the Department of Pathology at the Radium Hospital has been the most important Norway for cancer investigations. With this position also comes the need to train new doctors, specialists and technicians for the whole Norway. By the 1990s, the staff had increased to over 100 employees. The greatest workload has always been to use the microscope to look at pieces of tumors and cancer cells. Most of the samples have come from patients at the Radium Hospital, but difficult samples from other hospitals have also been examined. The department has naturally become a national center for diagnosis of special cancers that require a great deal of experience and special equipment.

As activity in the department has increased, there has also been a need for division into sections within this subject area, each with its own specialist expertise. At the merger with Rikshospitalet, Aker and Ullevål in 2009, the department at the Radium Hospital had six sections: Biopsy and autopsy with responsibility for autopsies and microscopic examinations of tumor tissue (30 000 annual examinations), cytology with partially computerized, automated solutions, electron microscopy (very resource-intensive), digital pathology with the use of artificial intelligence, molecular pathology (cancer cells at the molecular level) and experimental pathology (research).

After the merger in 2009, the pathology activities at the Radium Hospital has been part of the large pathology department at Oslo University Hospital (OUH), which has pathology activities at the Radium Hospital, Ullevål and Rikshospitalet. The Radium Hospital is still a center for examination of cancerous tumors from all over OUS, in some cases also from other hospitals in the region and occasionally from other regions in Norway. A correct and detailed pathology diagnosis is crucial for the treatment of the individual patient. If the pathologist makes the wrong diagnosis, the result can be disastrous for the patient because the wrong treatment is then given. Since 2015, the department has been located in the modern premises in the OCCI building right next to the Radium Hospital.

Microscopic examination of the tissue was crucial for making a cancer diagnosis 90 years ago. The same is true today. One must extract a piece of tissue (biopsy) or cells from the tumor (cytology). The procedures for sampling are today far simpler and safer than before, since we

can get help from diagnostic imaging to locate the tumor better and thus take tissue samples in a safer way. The tissue sample is sent to the pathology department, which normally needs several days to prepare the samples and make assessments under the microscope. Sometimes special examinations of the cancer cells need to be carried out.

Today's techniques provide much safer and far more precise answers than old-fashioned surveys. The examination techniques at the pathology laboratories have in many ways been at the forefront of modern treatment with specialized medicine, where the detection of molecular changes in the cancer cells is the basis. This mapping can take time, sometimes over a week. The choice of treatment is governed by the nature of the sample. The waiting time for an answer can feel long and uncomfortable for the patient, their next of kin and the healthcare personnel. But we are completely dependent on a correct answer with all the details needed to choose the right treatment. It is important to know as much as possible of the cancer cells' "weak" points.

Modern treatment has used "specially designed molecules" – so-called monoclonal antibodies (MAB). These can bind to the surface of the cancer cells or penetrate the cancer cells and attach to the inner parts there. The work in pathology departments is crucial for modern patient-adapted treatment. These are very laborious procedures, and the field of pathology is therefore in a «subclassification phase». The subject is in an exciting development where artificial intelligence can become an important tool. The staff at the pathology laboratories have close contact with the clinical departments and are often in formal, interdisciplinary meetings where pathologists, X-ray doctors and clinicians gather the threads and provide a forum for ensuring the correct diagnosis. The technical procedures depend on specialist expertise laboratory personnel.





Figure 22. Pathologist. From the left, work can be seen by a microscope, which is the pathologist's main instrument, a tissue sample and a cell sample seen in the microscope

The pathology departments also take care of autopsies. Much has been learned through these surveys. It both was and is a procedure "at the service of life." It is checked whether the correct conclusion has been reached and whether the examinations have captured all aspects of the disease process. This is still an important quality assurance procedure, even though modern diagnostics can reveal far more details than we could 20-30 years ago.

1b X-ray diagnostics, later expanded to "diagnostic imaging"

When the Radium Hospital was opened in 1932, there was no separate X-ray department. It was part of the Department of Clinical Medicine, later called the General Department. The X-ray service consisted of three different X-ray machines, each for its own use. The devices could provide images on film or be used for fluoroscopy. There were also contrast agents that could be drunk to get a closer look at the stomach and intestines. Fat-soluble, iodine-containing contrast agents came after the war and made it possible for the Radium Hospital to become a leader in Norway in examinations of lymph nodes. This was important in detecting the spread of cancer to the lymphatic system (lymphography). This examination has now been replaced by CT and MRI.

It was not until 1957 that a separate radiology department was established. Proper working conditions were also established, and more doctors and nurses were hired. The Radium Hospital received its first CT in 1979, ultrasound scanner in 1981 and MRI in 1987. Gradually, the Radium Hospital has become a national leader in taking tissue samples under the guidance of ultrasound, CT or MRI.

When money was raised for the Radium Hospital, there was great interest in the X-ray machine's possibilities. The fascination of being able to see the skeleton in the pictures was great. The development leading up to today's CT (computed tomography) and MRI (magnetic resonance) is simply miraculous. But there were several steps along the way, some of which were very unpleasant and risky for the patient. Today, when we read about the examination techniques used by X-ray 40-50 years ago, our first thoughts turn to the patients and the discomfort and painful procedures they had to go through. The risk of complications could also be greater than we would accept today. What we call conventional X-rays or "ordinary" X-rays distinguish skeleton and lime very clearly from soft tissue. For example, X-rays of the head show the skeleton, but it is not possible to see details in the brain. In the brain there are some fluid-filled cavities. To see the brain better on X-rays, the fluid was drained and replaced with air. Then it was possible to identify some contours and possible asymmetry in the brain. However, the procedure was painful for the patient, and the result often uncertain with questionable conclusions.

A very good aid was provided when X-ray contrast agents were used. In the early years, this development also had some unpleasant aspects for the patients. Later, more gentle contrast agents were introduced. Blood vessels, musculature and internal organs are difficult to identify without contrast agents. By injecting a liquid into the blood with elements of "heavy substances" such as iodine, the blood vessels will draw very clearly. The blood vessels in a cancerous tumor do not develop like other blood vessels and often appear as abnormal, tangled skeins. The contrast agent is excreted in the kidneys, and we can therefore also see these and the drainage down to the urinary bladder. Later came

contrast agents that were far more gentle to use than the first ones, so that patients risked less side effects and a lower risk of complications. Contrast agents are still in use, both in conventional X-ray, CT, ultrasound and MRI.

The Radium Hospital played a key role in the development of examination methods for the lymphatic system, including both lymphatic pathways and lymph nodes. Contrast was injected into the lymphatic pathways, e.g. on the back of the foot. This made it possible to map the lymphatic pathways all the way up to the neck, where the lymph is emptied into the veins. The day after injection, cells in the lymph nodes had "eaten" contrast agent and were visible on the X-rays. It was then often possible to see which lymph nodes were affected by disease. The contrast remained for several months and could thus also show an effect of the treatment. This study was an important contribution to the development of lymphoma treatment.



Figure 23. An X-ray of a head and an image from lymphography using contrast agent are shown here



The major advances came with CT, MRI, ultrasound and PET/CT. For the patients, this has become an0 enormous advantage with less pain and discomfort during the examination. These methods provide a far more precise information about the disease process, which provides a better adapted treatment. CT, MRI and ultrasound provide a three-dimensional image of the internal organs of the body. Semiconductor technology and faster computer systems became available in the 1960s and 1970s. This made it possible to gather information from the rotating X-ray tube by CT and from the radio signals that powerful radio frequency pulses induce in the nuclei of hydrogen atoms by MRI. The images of the body's internal organs are constructed by a computer connected to the CT, MRI, ultrasound or PET machine itself. Some people feel uncomfortable lying in a narrow tube with a lot of noise during the MRI scans, but the procedures are virtually painless, and patients are very well monitored along the way. Tissue samples can be taken while guiding the needle to the correct location by the CT or ultrasound machine. One can now take tissue samples from almost anywhere in the body.


Figure 24. CT and MRI machine

An X-ray doctor (radiologist) must evaluate all the images. This involves assessments that can be very difficult. Sometimes the radiologist cannot give a definite conclusion. Diagnostic imaging is like pathology, we don't always get an answer with two lines underneath.

These imaging techniques are also utilized in the planning phase of radiation therapy. We obtain better knowledge about the delimitation of the tumor and can thus also adapt the dose distributions better.



Figure 25. Old X-ray machine. Dictation of X-ray answers

1c Nuclear medicine - diagnosis and treatment with radioactive isotopes

Nuclear medicine is a field of study that includes treatment and diagnostics using radioactive isotopes, also called radionuclides. Nuclear medicine activity at the Radium Hospital started in the 1950s and was initially organised under the central laboratory. Gradually, imaging systems and image processing became a more important part of the business, especially after PET/CT scanners were introduced. In the 2000s, nuclear medicine became part of the Department of Medical Imaging.

Gamma cameras came on the market in the 1950s. These record gamma radiation from radioactive substances injected into the patient. The injected substances are absorbed into the cells. The formation of bone tissue is much faster in case of injury or disease than in normal bone tissue, and one therefore obtains a weak picture of the normal skeleton and a clear picture of the diseased areas. Newer gamma cameras have a CT scan attached to provide an accurate location of the disease. The gamma camera's most important function at the Radium Hospital has been early detection of the spread of cancer to the skeleton, especially in breast and prostate cancer, so-called skeletal scintigraphy.

After a long struggle from the mid-1990s, Norway, as the second last country in Europe, received a PET/CT scanner at the Radium Hospital in 2006.

In the most common PET / CT examination, the radioactive substance ¹⁸F FDG (18 fluorodeoxyglucose) is used as a tracer. It is this radiation that is registered in the PET scanner. PET images function in the form of sugar metabolism in the tissue but provides little anatomical information. Anatomical information is obtained by combining a CT scanner with the PET scanner, so-called PET/CT. The PET / CT scanner at the Radium Hospital has been very important for the follow-up of lymphoma patients. It is also important in the assessment of lung cancer, among other things as a useful tool for selecting possible operable patients.



Figure 26. Gamma camera and PET/CT machine

Radioactive substances for injection are also used in the treatment of cancer. The mechanisms are the same as in diagnostic use. This is called theragnostic (therapy + diagnostics). The method is far from new and was developed more than 75 years ago using radioactive iodine (¹³¹I) for diagnostic imaging and treatment of thyroid cancer. Development of the method gained momentum in the 1980s and 90s and is now used for some types of cancer. The success of this type of diagnostics and treatment has stimulated the further development of theragnostic, including for diagnosis and treatment of prostate cancer. To avoid radiation damage to healthy organs, radioactive substances must be used that have short-range radiation in the tissue. The tissue where the radioactive substance accumulates thus receives a lot of radiation, while all other areas of the body receive little radiation. The most important radioactive substances used at the Radium Hospital have so far been radioactive iodine for thyroid cancer and radioactive monoclonal antibodies (MAB) for lymphoma.



Figure 27. Radioactive isotopes are used in conjunction with diagnostic examinations and radiation therapy

And then the word *radium* reappears, but in a quite different form from the needles as described from Marie Curie's time. The new one is dissolved radioactive ²²³Ra which is given intravenously. The isotope ²²³Ra like calcium, targets bone (skeleton) and is concentrated especially in cancerous tumors. The isotope emits alpha radiation that has a very short range, corresponding to a few cell diameters. The range of the radiation is thus on a microscopic level. The drug is used for prostate cancer with spread to the skeleton, and it will be exciting to follow the further development of this treatment principle.

1d Central Laboratory - blood tests

Right from the start of the Radium Hospital in 1932, the Central Laboratory had its humble roots in a small laboratory in the oldest part of the hospital. Laboratory nurses performed simple blood analyses of the time. In 1951, a senior consultant was appointed head of the Clinical Laboratory, as it was then called. This was a combined position between laboratory service and cancer research. Already at that time, the hospital invested heavily in cancer research. In any case, the appointment represented a significant professional upgrade of the discipline and the laboratory.

In 1956, the hospital was expanded substantially with a new block. Here the Clinical Laboratory had large premises by the standards of that time, 260 m². In 1977, the clinical laboratory received a formidable expansion to 2,000 m². Upon move-in, the Clinical Laboratory was formally upgraded to department status and changed its name to the Central Laboratory. This name was chosen because the business would now include both microbiology, clinical chemistry and transfusion medicine. In the 2000s, the Central Laboratory entered into a merger process with the Department of Medical Biochemistry at Rikshospitalet. This merger was successful because a sensible distribution of analyses with economies of scale was reached. Later, this cooperation was further expanded after the merger with Ullevål and Aker to form Oslo University Hospital.

Previously, needles and syringe tips that had been sterilized over and over again were used. They could get lethargic eventually. Now there are disposable equipment in which syringes and needles for blood tests are completely clean and sharp. Puncture becomes less uncomfortable. Blood count and sedimentation rate were previously two key tests. The repertoire today is completely different. The blood tests can provide answers to how the body maintains its internal environment. Samples must be taken before an operation, many times during surgery and the days after. Before chemotherapy can be given, we need to know if the bone marrow is ready for new treatment, is the salt balance normal, is liver function satisfactory, is the body getting enough oxygen, etc.? Some cancers produce certain tumor markers that can provide answers to whether treatment is effective. They may also indicate a relapse if the values increase at subsequent check-ups. The drug concentration can also be monitored in some cases. One of the challenges of drug cancer treatment is that the breakdown of therapeutically active drugs varies from individual to individual. The blood tests are one of several necessary elements in the cancer treatment's safety net. Manual procedures have been replaced by machines that can perform many analyses and provide answers within minutes, and the dissemination of answers is provided electronically. At the same time, one gets informed answers to previous tests, and one does not have to search through old papers.

A much-discussed tumor marker in the blood tests is PSA, Prostate Specific Antigen. PSA is an enzyme that is produced on the prostate gland. The enzyme is secreted into the fluid from the prostate and prevents the sperm from clumping. Normally, very low levels of PSA are found in the blood, but in various conditions affecting the prostate, an increase in the amount of PSA in the blood can be observed. This can be explained by the fact that the various conditions cause PSA to leak from the prostate. Elevated PSA can be found in both inflammation and cancer of the prostate. It is also found in benign growth of glandular tissue in the prostate,

which is more common in older men. The measured value must therefore be related to age. Values that exceed certain limits do not mean that something is wrong. Nor is it the case that a value within the age level excludes cancer. It is important to be aware that one cannot draw any certainty conclusions on the basis of such a measurement. However, the higher the PSA level, the higher the risk of prostate cancer. After treatment of prostate cancer, e.g. surgery, the PSA level will hardly be measurable. A later increase in the value indicates relapse of the disease.



Figure 28. Work on the analysis of blood samples now and in the old days.

1e Digitization

Digitization has also reached the healthcare sector. Major problems have arisen when computer systems have failed, and treatment has not been provided because patient records have been inaccessible. The hospitals have more or less come to a halt, and there have been major stories in the national news. It didn't make the news if a patient paper journal "was on the move" and could not be tracked down when needed, but it could be a major problem for the patient. Digitization of the records created problems in the initial phase, but it is now a more stable system, and no one wants the paper records back. Previously, the records were easily accessible at the wards with the breaches of privacy this could entail. Digital journal systems ensure that privacy is safeguarded in a new and better way by allowing it to be traced who has recorded the journal information.

Analyses of blood samples are currently performed by automated machines, and the results are sent electronically to those who shall have access to them. Today, this is very fast and comparable to previous responses since they are readily available. Other test results are sent out in the same way. Previously, test results were sent by mail. This took longer time and could mean that patients started treatment and follow-up of treatment later.

Diagnostic imaging based on film has been replaced by images on screen. Film archive has been replaced by a digital archive (PACS). Images can now be sent digitally from hospital to hospital in seconds, and one does not have to search for old photos in a film archive that may have been in another hospital. Another advantage is the possibility of adjusting parameters such as brightness and contrast in the images as needed afterwards. Fewer images must therefore be retaken, and the radiation burden for patients is reduced.

For radiation therapy, the introduction of computer technology has also been of great importance. The planning of radiation therapy, which until the 1970s was a manual process, is now done by advanced computer systems using digital images from CT and MRI to obtain anatomical information. The treatment machines are controlled by their own digital systems to ensure that the patient is treated according to plan at each individual appointment. CT images are also taken on the treatment machine before and during treatment to ensure patient position and that radiation is delivered correctly.

2 Methods of treatment of cancer

As discussed earlier, the treatment of cancer has developed from 1932, when radiotherapy was most important, to today where surgery and drug therapy are of great importance. Surgery and radiotherapy are performed in cases of localized and regionally limited disease, while distant spreading must in principle be treated with drugs, either as tablets or by injection. Locally symptomatic spread can be treated with radiation.

2a Radiation therapy

Radiation therapy has had a tremendous development from the establishment of the Radium Hospital until today. Initially, the treatment was carried out with radium and with X-ray machines with low energies. After the war, new therapy devices such as betatrons and linear accelerators appeared, which provided new possibilities. At the Radium Hospital, the first betatron came into use in 1953, while the first linear accelerator came in 1969. By 1970, the hospital had three betatrons, one cobalt apparatus and a linear accelerator in use. The linear accelerators gradually took over, and after the new radiation therapy building was completed in 2006, the hospital had eleven accelerators in operation. After Oslo University Hospital was established in 2009, there are now ten radiation therapy rooms at the Radium Hospital, but usually only nine accelerators are in operation due to the fact that a new accelerator is almost always under installation in one of the rooms. Evening shifts are then established to maintain radiation therapy capacity.

Although there have occasionally been problems obtaining funding for the replacement of linear accelerators, the Radium Hospital has been an early adopter of new technology. Computer-based planning of treatment plans was adopted in the 1970s with proprietary systems. At the hospital, control and information systems for radiation therapy were also developed, the KOR system in 1982 and Visor in 1993. Visors were commercialized in 1994 and sold to radiation therapy centers around the world.

Quality control – ensuring that treatment is delivered as planned – has changed character as technology has evolved. Initially, quality control consisted of checking that the machines were delivering the radiation dose that was expected. Eventually, X-rays were taken that showed how the radiation fields fit with the patient's anatomy. When film was replaced with digital imaging plates in the 1990s, these were also introduced in quality control in radiation therapy. Physicists at the Radium Hospital were among the first to make use of the new possibilities for image verification. In recent years, three-dimensional control has been introduced by comparing CT images on therapy devices with images taken in the planning process.

Collaboration between doctors (oncologists) and medical physicists has led to many advanced treatment techniques being introduced at the Radium Hospital. *Intraoperative radiotherapy* (IORT), in which irradiation was administered into the abdominal cavity while the surgical wound was open, was tested in the 1990s. *Stereotactic treatment* is a form of radiation therapy that is given at high doses from many angles. This treatment provides precise treatment for small tumors in the head and lungs and initially required customized treatment equipment. *Total body irradiation* (TBI) represents an extreme variant of radiation therapy in which the entire body constitutes the treatment area. It is an advanced and resource-intensive treatment that is used, for example, to knock out bone marrow function in connection with stem cell transplantation.

Radiation therapy can be given in several ways. Radiation that has high enough energy to damage atoms and molecules in cells is called ionizing because they knock electrons loose or do other damage to the molecule. The healthy cells repair the damage in DNA more efficiently than the sick cancer cells. Cells that divide rapidly are generally the most sensitive to radiation. Cells that have not repaired the radiation damage can die when they try to divide again. It may therefore take some time before we see the final effect of radiation therapy.

External irradiation using a device that emits radiation from a source that has a certain distance from the patient is the most used form of treatment. Examples include the so-called X-ray therapy machines that were first introduced at the beginning of the 1900s. Then came the radium cannon (radiation source ²²⁶Ra) and later the cobalt machine (⁶⁰Co radiation source) where the radioactive source was placed in a chamber in the machine. In the radium cannon and the cobalt apparatus, the rays are released in a controlled manner by opening the chamber where the radiation source is located. Later came the betatron and linear accelerator, in which electrons with the help of microwaves are accelerated in a tube (waveguide) when the machine is turned on. The radiation can be used directly as electron radiation or to generate X-rays when the electrons hit a heavy metal "target" (tungsten) (see figure below).



Figure 29. Principle for generating radiation with a linear accelerator

In brachytherapy, or "short distance radiation", radium was originally encapsulated in hollow, rigid needles. They could either be placed on the skin surface or inserted into the tumor or attached to prostheses. Previously, radiation treatment of cervical cancer was carried out with a prosthesis that was loaded with radium needles and then placed in the vagina. The treatment staff had to manipulate the radioactive sources into treatment positions daily, and the nursing staff also came into close contact with the patients with the radium needles install. Radium has now been replaced by radioactive iridium (192 Ir).

Brachytherapy is radically improved both for the benefit of the patient and the staff. So-called afterloading machines are now used, where non-radioactive applicators are placed in the patient's natural cavity in the body. The applicators are connected to flexible hoses, and the afterloading machine then leads the radioactive source from a shielded chamber inside the machine out to the applicators. This is done while the patient is lying alone in the treatment room, under monitoring. The staff thus performs the job without being exposed to radiation. The desired dose is calculated in advance, where the number of source positions is determined based on the volume to be treated. The plan also includes the number of seconds the sources should be in the processing position, and the whole thing is programmed and controlled by a computer.

Figure 30. Work on an afterloading unit for brachytherapy. The patient lies on the left in the picture under green cover. Hoses from the radiation machine enter the patient.

Radiotherapy may also be given by intravenous injection of radioactive isotopes, as discussed earlier in the section on nuclear medicine.

The development of the radiation machines goes far back in time, where the Norwegian Rolf Widerøe (1902-1996) was involved, among others. Widerøe came up with the idea of using a transformer to accelerate electrons, and in 1923 he made a sketch for this. He called it a beam transformer,

which later became known as a betatron. However, Widerøe did not succeed in getting the beam transformer to work. In 1927, Widerøe also designed the first linear accelerator for positively charged particles (ions), but he is best known for the construction of the betatron. This was eventually improved and mass-produced at Widerøe's workplace in Switzerland, Brown Boweri & Cie (BBC). This was a radiation machine that could emit high-energy radiation that went far into the body and was therefore a major advance. Widerøe had contact with the physicist community at the Radium Hospital, and the Radium Hospital was the second hospital in Europe to have a betatron installed (1953).

Betatron from the 1960s

Cobalt machine from the 1970s

Linac from the 1980s

Modern linac from the 2000s

Figure 31. Radiation therapy machines in different time periods

The effect of using different radiation energies in irradiation can be seen by comparing the so-called *depth dose curves* that show how the radiation energy is distributed inwards into the tissue. The X-ray machines deliver high doses into the skin and tissue just inside, but do not reach deep enough to radiate tumors deeper inside the body. The machines are therefore best suited for treating superficial tumors, such as skin and subcutaneous tissue. The linear accelerators, on the other hand, provide a relatively low radiation dose to the skin while providing a higher radiation dose to the tissues deep inside the body. The curves in the figure below show how the radiation effect is inwards into the tissue. The rays from linac penetrate deeper while there is less radiation effect in the skin.

Figure 32. Virtue dose curves

The bottom curve (designated 3.0 mm Cu HVL) shows how low-energy X-ray radiation delivers the most radiation dose to the skin, but does not reach as far down into the tissue before the effect is gone. The other 4 curves show radiation with different radiation energies (megavolts, MV) from linac. Here, the rays reach much further into the body.

Since the 1960s, linear accelerators have been the workhorses of radiation therapy in many countries. They can be constructed with several energy choices, the most common being from 4 MV to 16 MV. The linear accelerators are very flexible and can rotate 360 degrees around the patient, while the table the patient is lying on can also be rotated and moved in six directions. The linear accelerator has undergone several technical improvements and is controlled by advanced computer programs. All movements are controlled with millimeter precision. A betatron, on the other hand, does not have such properties and is therefore no longer in use. At the Radium Hospital, all radiation machines are now linear accelerators, except for an X-ray machine with "soft" (50-150 kV) radiation for completely superficial skin disorders. In 2024, a facility for proton therapy will be installed at the Radium Hospital, discussed in more detail below.

The practical implementation of radiation therapy today is entirely dependent on diagnostic images, especially CT and MRI. They provide a three-dimensional image of the body with its internal organs, and the tumor tissue can also most often be identified. This is the starting point for planning radiation therapy. We can determine in advance the radiation dose both to the tumor and the areas of the body that must be spared from radiation. The images become a form of test model for how radiation therapy should be administered. In practice, the radiation machine is controlled by computer programs, but the patient must still be put in place and in the right position manually. Radiation therapists with their own training for radiation therapy manage these procedures.

A problem with all forms of cancer treatment is the damage one inevitably inflicts on the healthy tissue located near the tumor. It is expressed both during and after treatment. When treating cancer, one wants to inflict as much damage as possible on the cancerous tissue, in the healthy tissue the least possible damage. Radiation therapy has become more and more targeted with technological advances, and the radiation is now delivered with millimeter precision in the body. New treatment algorithms and equipment for radiation therapy are constantly being developed, and it is mainly the rapid development of computer technology that contributes to this development. We can mention treatment methods such as intensity-modulated treatment (IMRT) and volume modulated arc therapy (VMAT) as examples of this, as well as laser-based surface scanning of the patient for position determination and placement on the table.

With the new Radium Hospital in 2024 comes a proton center, a billion kroner investment that we have high hopes for. Proton therapy is a type of radiation therapy in which charged particles in the form of protons are used instead of X-rays. The purpose is to increase precision further and thereby reduce the harmful effect on healthy tissue. It is made possible by the so-called "Bragg Peak." The energy deposition is relatively constant until it increases sharply when the proton slows down and eventually stops.

Thus, there is no dose load of healthy tissue on the back of the Bragg top. In addition, protons have less laterally scattered radiation. This means that the proton radiation is better delineated than the conventional X-ray radiation. It is more possible to treat tumors with high radiation doses even if the tumors are located close to tissues that cannot tolerate much radiation. The range of protons in the body is energy dependent, and by using protons with different energy, the Bragg peaks can cover a desired processing area, see figure on the next page.

Figure 33. Model of a room for proton therapy

Figure 34. The figure on the left shows the depth dose for X-rays (blue) versus protons (red). Protons provide maximum dose deposition at a certain depth corresponding to the Bragg peak in contrast to X-ray radiation where the dose maximum is close to the surface. The figure on the right shows how protons can cover a larger area of steady energy deposition by using more proton energies and thus placing the Bragg peaks at different depths (blue).

With proton therapy, large doses of radiation can be administered to a limited area, and it is then very important that the radiation hits the right area. The importance of good tools to ensure that the radiation hits correctly is therefore even greater with proton therapy than with conventional radiation therapy. Follow-up with CT images during treatment is therefore important for registering changes in the patient's anatomy.

Protons have been used with varying success over the years, often in association with particle physics laboratories with access to accelerators. In recent decades, however, dedicated proton facilities for cancer treatment have become commercially available, and there are now about 40 proton centers globally. Sweden got theirs in 2015, Denmark established proton radiation in 2018, and Norway will have proton systems in Oslo and Bergen in 2024-2025. However, the costs of a proton plant are very high both in terms of acquisition and operation.

Proton irradiation is also used, especially for cancer in children and patients with cancer of the head/neck region. Other forms of cancer may also benefit from proton radiation, both in healing and palliative terms, and a number of studies and follow-up of the effect of this form of treatment are planned.

How is radiation therapy dosed?

Less than a year after the discovery of the X-rays, they were used in the treatment of cancer. One problem that was encountered early on was: How do you measure the "amount" of radiation? It was noted early on that irradiated skin turned red. Initially, the degree of skin flushing was therefore used as a measure of radiation dose. It goes without saying that this was a relatively subjective and unreliable measure of dose, and the first objective measure of radiation dose based on physics came in 1928. In the years that followed,

the measurement methods were further developed, and in 1977 Gray (Gy) was introduced as a unit for absorbed dose. When we measure 1 Gy, it means that 1 kg of the irradiated substance has absorbed 1 J (joules) of radiant energy.

How can radiation best be given to the patient? Can the entire dose be given at once or does it need to be divided into smaller units? Initially, not surprisingly, there was a lot of trial and error. After decades of experimentation and theoretical deliberation, the conclusion was that daily treatments over a certain period of time were best. Nevertheless, many questions remained; There were many variables. How large a total dose could be given? The limiting factor was the healthy tissue that also received radiation. Posterity has shown that the radiation tolerance of the different organs is very different and depends on how the radiation is given. Moreover, cancerous diseases are different, not everyone needs the same amount of radiation.

The goal was to find a mathematical formula that included all variables and could predict the biological effect of a given radiation regime. The model that is currently the best we have for predicting the effect of different radiation schemes is the so-called *"linear-quadratic model"*. Depending on which cancer is treated, it is common today, with healing as the goal, to give 2 Gy daily 5 or 6 days a week for a total of 40-70 Gy. For palliative purposes, 3 Gy is often given daily to a total of 30 Gy. If the goal alone is to relieve pain, 8 Gy as a one-time treatment may suffice.

The radiation risk for staff was very high when using radium. For shielding, 13.5 cm thick lead plates were used where the radioactive needles were stored. Staff were often exposed to high doses of radiation since they were in daily contact with the radiation sources. Some could suffer permanent injuries, especially to their hands and fingers. Radiation is used in cancer treatment, but radiation can also be carcinogenic and lead to other tissue damage. The technical development of new radiation equipment has been of great benefit to the patients, but also to the highest degree to those who work with this form of treatment. Today's working environment for those who work with radiation therapy is safeguarded in a far safer way than before. Personnel who may come into contact with radiation wear personal dosimeters that register any radiation exposure. The statistics show a near radiation-free environment over the past 30 years after manual machine tuning and treatment of radiation sources were replaced by remote-controlled systems.

2b Surgery

The Radium Hospital was started as a hospital for radiotherapy with the radioactive element radium and with X-rays. Originally, the hospital was not planned for operations at all, and the Radium Hospital had no surgeons. Surgeons from other hospitals came to examine patients as needed. Eventually, a permanent agreement was made with surgeons at Rikshospitalet. But all operations had to take place at other hospitals, primarily Rikshospitalet. In 1958, the first surgeon was hired at the Radium Hospital. The main task was to assess whether patients should have surgery in addition to radiation and chemotherapy. Cooperation across disciplines was introduced very early, but operations still had to be carried out elsewhere. The surgical department at the Radium Hospital was established in 1965, when operating theatres with postoperative and intensive care units were first established. This was the starting shot for an impressive development of cancer surgery at the Radium Hospital. The hospital gradually became a regional and national center in several types of surgical cancer treatment.

In 1976, the A-block was built with a significant expansion of the surgical business. As the surgical department increased its activity, the surgical offer became further specialized with the establishment of several subspecialties: Urology, Thoracic Surgery, Orthopedics, Gastrointestinal Surgery, Endocrine, Breast and Plastic Surgery. Several of these became important for the development of cancer surgery at the national level. Gradually, close collaboration with other hospitals was 0developed, especially Rikshospitalet. In 2023, there will be a total of seven operating theatres with associated wards, a post-operative and intensive care unit. In the new building, which opens in 2024, there will be ten operating theatres. The trend at both the Radium Hospital and other hospitals has been towards more gentle procedures with shorter hospitalization periods. The use of surgical robots and other endoscopic techniques, as well as better anesthesia, have enabled both safer and more gentle surgery. While you were previously hospitalized 10-12 days after surgery, you can now be discharged 2-3 days after the procedure.

Collaboration is very important in all cancer treatment. Here, the surgical department at the Radium Hospital has been a leader in Norway. Interdisciplinary teams were established at an early stage to consider complex treatment. That is, the surgery was part of a comprehensive plan for the patient. Such a plan may include chemotherapy, radiation therapy, hormone therapy and surgery. This has gradually become common in other hospitals as well. It has been shown that such complex treatment provides both better survival and less adverse effects for patients.

The Department of Surgery at the Radium Hospital has contributed to the education of health personnel. Many doctors have worked here for a while to specialize in different types of cancer surgery. The department has for many years taught students in both medicine and nursing. Research has also been an important task in the department. Since 2009, the department is part of the large surgical community at Oslo University Hospital (OUS). The division of labor between the individual parts of this large hospital is a dynamic process. The new building, which opens in 2024, is planned for a further increase in capacity for surgery.

Surgery has a central place in cancer treatment. It was the only form of treatment before the 1900s. At that time, the possibility of detecting disease and mapping the extent of the disease was very limited. To compensate for this uncertainty, it was decided to remove as much tissue as possible around the tumor. Seen with today's knowledge, some interventions were far too extensive. Many patients suffered major ailments for the rest of their lives. Today, cancerous tumors are usually detected at a much earlier stage.

In breast cancer, breast-conserving surgery has now been introduced, in which only the tumor itself together with the sentinel lymph node is removed. The sentinel lymph node for the chest often sits in the armpit. It picks up early spread from the breast. The limited procedure may be sufficient if combined with radiation and possibly chemotherapy and/or hormones. This is a great benefit for patients because the side effects are dramatically less and the quality of life correspondingly better.

Figure 36. Surgical activity

Plastic surgery is often associated with cosmetic surgery, but in this context this is done to correct defects after cancer treatment, both previous surgery and radiation therapy. In major procedures, there is sometimes "not enough skin" to close the wound. Plastic surgery techniques can then retrieve skin with blood supply from nearby places on the body. Orthopedic procedures with new prosthetic techniques have had an almost miraculous development. It is utilized for skeletal cancer. In some cases, amputation can be avoided by using so-called extremity-preserving surgery. The use of prostheses for joint replacement is largely used in cancer treatment of cancer in or near joints.

By using chemotherapy or radiation therapy prior to surgery, tumors that are sensitive to this treatment may shrink so that the procedure can be reduced in scope. This illustrates the collaboration that has been developed between the various medical specialties.

Developments in the fields of anaesthesia (anaesthesia) and intensive care medicine mean that more people can tolerate major procedures. Extensive and major interventions may still be the best chance of controlling the disease. The age limits for many procedures have been greatly expanded, so that older patients can now tolerate extensive treatment programs.

Developments in surgery, anaesthesiology and intensive care medicine must be seen in conjunction with each other. This has paved the way for giving many patient groups better and often more gentle treatment. In addition, the diagnostic subjects provide more precise information about disease status and prevalence.

One of the major breakthroughs in surgery is the so-called keyhole surgery (laparoscopy), which was developed in the 1980-1990s. The technique was first used for investigations, later also as a surgical method for diseases of the stomach, including cancer. The advantages of laparoscopic surgery compared to a regular abdominal operation are several; Less scars and pain as well as faster rehabilitation. It also reduces the risk of subsequent complications due to adhesions in the surgical area. Keyhole surgery can now be used in many places in the body, although the abdominal cavity is still the main area.

A continuation of keyhole surgery is robotic surgery. The robotic platform DaVinci was installed at the Radium Hospital in December 2004. This was the start of a new surgical era in urology at the Radium Hospital. From being a department with large, open operations, keyhole operations are now mostly performed with the DaVinci robot. The method is particularly used for prostate cancer, and thousands of patients have undergone surgery in this way. The patient can often be discharged only a couple of days after surgery.

2c Medicinal treatment.

The chemotherapy came after World War 2. The first drug was based on mustard gas, which was a feared poison gas from World War 1. This was used at the Radium Hospital in the early 1950s. At about the same time, hormone therapy for prostate cancer was started. The patients were then given the female hormone oestrogen. This did not heal but could slow the progression of the disease.

Towards the end of the 1950s, more modern chemotherapy came on the market, and the Radium Hospital was among the first to use these new chemotherapeutics. The first of these was cyclophosphamide (Sendoxan) which is still in common use!

During the 1970s, there was also a major development in chemotherapy. The hospital adopted new types, which dramatically improved the life expectancy of some patients. Testicular cancer and lymphoma were among the groups that had a significantly better prognosis. Unfortunately, there were no similarly good effects on some other types of cancer. In recent years, new treatment principles, such as immunotherapy, have been adopted. It is a constant development, which provides better and more gentle treatment to patients.

Several of the most important chemotherapy products have their origins in plant extracts. Many have since been industrially manufactured. Some have been modified, and one has succeeded in improving the effect. Many of these chemotherapy drugs are still in use. The chemotherapy affects both healthy cells and cancer cells. A positive treatment effect is achieved by the healthy cells repairing the damage better than the cancer cells. Chemotherapy courses are usually given at certain intervals, e.g. every three weeks over several months. The principle is that then the healthy cells will have time to repair themselves between each course, while the cancer cells have not yet had time to do so. Thus, cancer cells are hit harder than healthy cells by chemotherapy.

Figure 37. The flower in the picture is of Vinca Rosea which is the origin of the vinca alkaloids. The best known preparation names are "Oncovin" and "Velbe".

Many chemotherapy drugs have led to major treatment gains. Many forms of leukemia and lymphoma and almost all with testicular cancer can be cured today thanks to these medications. The list of diagnoses that benefit from chemotherapy is very long. Chemotherapy also has an important place in the context of surgery and radiotherapy in that the interventions and radiation treatment may be less extensive. Some chemotherapy drugs can increase the effect of the radiation and can also be given preventively to prevent later recurrence or spread. Knowledge about side effects and how they can be treated and reduced is constantly improving.

Many patients suffer from side effects during the treatment period, and this can take a heavy toll on their strength. Some struggle to get back to normal, even though the treatment was successful. Fatigue - chronic exhaustion - is a term many cancer patients are familiar with.

One of the things patients fear most about chemotherapy is nausea and hair loss. Nausea and vomiting of a few hours' duration are common after most cytostatics. In some cases, these side effects may last for several days. Interview studies have shown that nausea and vomiting are the side effects that patients feel most burdersome. There are currently several effective treatment regimens for nausea. The greatest advances came with serotonin antagonists, and the selective serotonin receptor antagonists constitute the largest and most important group of antiemetic drugs.

Hair loss of varying degrees can be seen after treatment with a variety of cytostatics. Hair growth usually picks up again a few weeks after the end of treatment and is usually returned to the same character as before. In some cases, the development of frizzy hair or pigment changes is seen in the initial period after treatment. The benefit of cooling of the scalp (ice cap) during administration can be demonstrated by some chemotherapy regimens, but this method is controversial.

The effect of hormone therapy on certain cancers has long been known, and sometimes the effect is very good. The main diagnoses are breast cancer and prostate cancer. The mammary gland is stimulated by estrogen. Blocking stimuli from oestrogen can have a striking effect on disease where cancer cells are hormone-sensitive. Castration by irradiating the ovaries has been replaced by drugs that more specifically prevent the adverse effects of oestrogen in breast cancer. Prostate tissue is affected by testosterone, and it is utilized in the treatment of prostate cancer. Previously, estrogen was used for treatment of prostate cancer with metastasis. It had several unpleasant side effects, including feminization. New drugs have now been developed that block the testosterone effect on cancer cells. These are examples of the usefulness of new biological knowledge. The benefit for patients is a simpler treatment with limited side effects.

Figure 38. Drug therapy

In recent years, more details have been mapped in molecular structures on or inside the cancer cells. This is utilized in treatment. One can design and produce substances, monoclonal antibodies, that can bind specifically to these structures by using techniques similar to those used in the manufacture of vaccines. Then the attack becomes more targeted towards the cancer cells, and they are used today against many forms of cancers. Powerful weapons, such as a radioactive substance or chemotherapy, can also be coupled to monoclonal antibodies, MABs. Then a targeted radiation treatment or chemotherapy of the cancer cells is achieved.

Immunotherapy is an exciting treatment concept that has contributed to significant progress. Here, MABs are used against surface structures on the most important of the body's own immune cells – the T-lymphocytes. In order for the immune system not to overreact in the fight against bacteria and viruses, brake structures have been developed on the T-lymphocytes. The cancer cells can activate such braking structures so that the immune system does not work.

By using monoclonal antibodies against the brake structures, the brake is released and the immune system (T-lymphocytes) kills the cancer cells more efficiently.

Another form of targeted or tailored treatment is to use substances that penetrate the cell membrane and bind to the altered signaling molecules inside the cancer cells. Examples of the use of such drugs are imatinib in the treatment of chronic myeloid leukemia over the past 20 years, and gastrointestinal stromal tumor (GIST) in the last ten years. Such substances are also of great help to patients with other types of cancer, such as lung cancer.

A relatively new form of cancer treatment is photodynamic therapy (PDT). This is a type of treatment that has largely been developed at the Radium Hospital. In contrast to conventional radiation therapy, non-ionizing radiation is used, i.e. light. However, light alone is not sufficient. In the early 1900s, it became known that some substances could inactivate microorganisms when activated with light, they are phototoxic. Porphyrins are such substances. In addition, porphyrins have two other properties, they accumulate and remain in cancerous tissue when administered intravenously, and they fluoresce by illumination. This has been used in both diagnosis and treatment of cancer. The discovery was patented, and this was the basis for the establishment of the company PhotoCure. The company develops and sells pharmaceutical products and medical devices for photodynamic treatment, cancer diagnosis and selected dermatological indications.

2d Gynecology

The three most common locations of gynecological cancer are in the uterus, cervix and ovaries.

Gynecological cancer treatment uses surgery, radiation, chemotherapy and hormone therapy, as well as the new types of drug therapy. The field therefore has no separate treatment type, but it has used many types of cancer treatment right from the start, often in combination. The gynecological department at the Radium Hospital was established already at the hospital's inception in 1932 as the first specialized department. Since the start, the treatment of gynecological cancer in women in Norway has been closely linked to the gynecological department at the Radium Hospital. Still in 2023, the department is the national "engine" for treating gynecological cancer in women. The department is still Norway's foremost place for the education of doctors and other health personnel in gynecological cancer treatment. Internationally, the department has also been at the forefront, both by virtue of its size and its excellent treatment results.

3 Nursing

The nursing service was central already when the Radium Hospital was opened in 1932. Helene Larsen was the hospital's first headmistress and the leader of about 20 nurses. She was part of the management team and was involved in the planning and construction of the new hospital. The subsequent headmistresses were also part of the management team for the hospital and were important contributors to projects for the development of the hospital.

As it is today, it was difficult in the post-war period to recruit qualified nurses. In the early 1950s, therefore, a nurse residence was built north of the main building from 1932, where it was possible to live for nurses and other hospital employees. The two buildings have now been demolished to make room for new hospital buildings.

In the 1960s, the visiting service/patient friends at the hospital were established. The visiting service had hostess service at the outpatient clinic and in the reception. From 1972, the title of headmistress disappeared, and the head of the nurses was called chief nurse. The chief nurse was a member of the management team and was responsible for the entire nursing service, which also included radiation therapists, radiographers and bioengineers. The nursing service had overall responsibility for the operation of the wards, outpatient clinics, reception department and sterile center, which also included food, waste management and goods purchases.

In 1997, the nursing service was reorganized once again. The service was previously organized as a dual management. With the introduction of unified management, the field of nursing was given responsibility for nursing to all patients, both inpatient and outpatient. The most important responsibilities of the nursing service were coordination of patient treatment and hospital operations. In 1997, there were approximately 450 employees in the nursing service.

After the Radium Hospital was merged with Rikshospitalet, the value and importance of the nursing service had to be argued for in practice, and strategies had to be drawn up to make an impact in a complex reality. A merger with Rikshospitalet led to the chief nurse becoming clinic head nurse. The number of nurses employed at the Radium Hospital was approximately 500.

Figure 39. Nurses in party uniform

The development of cancer treatment linked the patients more and more closely to the care services. Many treatment programs, such as extensive surgery, long-term chemotherapy and high-dose radiotherapy, could be a major burden. Bothersome side effects needed relief. Several new chemotherapy drugs were launched in the 1960s-1990s. Some could cause serious complications if recommended procedures were not followed. Treatment had to be monitored, and procedures could be complicated. Symptom-relieving treatment also progressed rapidly. More and more effective pain-relieving drugs with new forms of administration that required closer follow-up were developed. Unfortunately, it was not uncommon for pain management to be managed by strict rules right up until the 1960s-70s. The pain injection with morphine preparation should not be given more often than every four hours, it was believed. Some of the patients asked desperately for the next injection because of excruciating pain. The answer could be: "In half an hour. The superior has decided that." Here, great progress has been made in that pain management is managed according to the patient's symptoms. The new forms of administration require better monitoring than the stopwatch, the strong pain-relieving drugs are potent agents.

The need for special expertise became increasingly pressing. Ingeborg B. Totland initiated a very important initiative: *Further education in cancer nursing*. The goal was to provide nurses with specialist expertise to improve and safeguard patient care. Good experience had been gained with specially trained nurses in several other areas. Examples include midwives, surgical nurses and intensive care nurses. The modern health service is completely dependent on this competence building of nurses.

The oncology nurses' meeting with academia faces the same challenges as for doctors. Medicine as a field of study can be called a craft that requires academic competence in the theoretical basis of the activity. Both are in continuous development and require constant professional development. The engine of the patient-oriented, practical part is the employees in hospitals and in the primary health service. The practical skills are learned through the work of the departments. The special education also requires the acquisition of theoretical knowledge, including continuous updating. The engine of academia is the university employees and research institutions. It is assumed that there is an organised interaction between these. The teaching and research communities also need contact with practical life, and the "craftsmen" need contact with academia. The academic positions at the universities now also include nursing and general medicine.

Figure 40. Bed ward.

The specialist training of nurses has undoubtedly contributed to changing the structure of the health service in the direction of a collaborative team. The responsibility is still defined, but the team must collectively arrive at the safest possible treatment. What used to be two separate divisions, doctors and nurses, with completely different cultures, have merged more into a community. Of course, nurses still handle traditional nursing tasks, such as traditional care.

We have heard many times the stories about the doctor's visits 50-60 years ago. A delegation that rushed in to the patients in strict order. First the highest-ranking doctor, then other doctors by rank and position, nurses in the same rank order. The patients lay neatly arranged in their beds. The head physician led the discussion. The discussion perhaps literally went over the patients' heads. This signaled distance and authority. We can only imagine how anxious patients felt. This way of working has changed, and communication between patients and healthcare workers has become more open. The impetus for that is probably complex. Hospitals are influenced by developments in society in general. The nurses have played a major role in improving communication and contact between patients and the health services. Nurses and assistant nurses have close and often long-term contact with patients. They get closer to the patient's complaints and see the need for symptom relief from hour to hour. Headmistresses and chief nurses were powerful individuals, but they were also role models. They have undoubtedly contributed to opening up for the good patient care that became a hallmark of the Radium Hospital a few years after its opening. At that time, most of the patients were hospitalized during radiotherapy, and there was much better time and peace for contact than today.

Nursing is included in all treatment, and the patient's need for nursing and care is essentially the same today as it was 90 years ago. However, this does not mean that the field of nursing is unchanged. The subject is drawn into the treatment processes and in the monitoring of complicated procedures. Nursing is now an academic subject, as the many special tasks assigned to nurses require additional education. Some things are unchanged, where qualities such as empathy, ethics and patience remain. The possibilities for relief have improved with new knowledge and new medications. The nurses are involved in the treatment procedures and play a key role in both treatment and care. They represent an important continuity in the patient's treatment process.

When the result is not as planned and desired

The cancerous tumor grows into the normal tissue that we want to preserve. The tolerance limits of healthy tissue are therefore an important control factor for treatment. For radiation therapy, after much trial and error, it was decided that splitting into smaller daily doses was best.

In 1969, a mathematical formula was introduced to calculate effect and side effect. Before the major expansion of radiation machines in the 2000s, treatment capacity was a major challenge in Norway. Long waiting lists and rejection of applications were the consequences for the patients. An obvious question was whether national capacity could be increased by simplifying treatment. Sometimes the formula was pushed too hard, and there were injuries and side effects that were more severe than expected. It was understood that the formula did not fit with the radiation biological realities. The purpose was thus to help more people with a simpler treatment that should be equivalent, but also ended up with more radiation injuries. Now we have new and safer models for calculating radiation doses.

New and improved examination methods are an important reason for the medical progress patients enjoy today. As described earlier in the chapter on diagnostic imaging, the road to get there has presented several challenges before the methods were fully incorporated. X-rays, ultrasound examinations and MRI findings must be interpreted. In the initial phase, some findings were misinterpreted, for example a benign tumor could be interpreted as spread from cancer. The consequences for the patients were that they received a treatment they should not have had.

Figure 41. The Radium Hospital in the 1970s. The main entrance and the hall in the entrance hall.

Fortunately, we can conclude that injuries after treatment have been significantly reduced in recent years. However, we must emphasize that cancer is sometimes so severe that the treatment is close to the tolerance limits. There are large variations in what the individual tolerates of cancer treatment, which makes the treatment difficult to implement for everyone. This requires a culture of openness in the health services, and patients must be informed about the consequences of the treatment in the short and long term. If there is an increased risk of late side effects, the patient must be informed in advance.

Treatment can cause acute injuries such as "burns" to the skin and mucous membranes. These will usually be healed, but months to years after treatment, late damage may occur. An example could be the connective tissue in the body that becomes thickened and firm. This can cause serious, chronic side effects. With the use of combined radiotherapy and chemotherapy, very good results were achieved in the 1960s and -70s. Many patients who previously died recovered. But the late damage was not apparent until 10-15 years later. Some of these patients struggled with sequelae for the rest of their lives. The dilemma is the same today: If a new drug with a good effect on patients with a fatal disease is introduced, treatment will also be started today instead of waiting 10-20 years to assess any long-term effects. In 2005, a competence center was established to investigate late side effects at the Radium Hospital. Knowledge about late side effects is important since many drugs are in use for many years. One must not only survive, but also have a good quality of life.

Everyone makes mistakes sometimes, it's human. The result can also be wrong without anyone making mistakes. Rare and unexpected side effects may occur, or it may be a matter of direct mishaps and bad luck. Sometimes staff reviews can turn out to be wrong. Openness about the risk of adverse effects has been an important change in attitudes over the past 20-30 years. The health services must learn from incidents that cause harm to the patient, and hospitals must have their own quality committees that assess all incidents that are reported. The most important goal is not to expose anyone in the staff, but to learn lessons. IT technology has provided good prerequisites for safer control routines for both radiation therapy and chemotherapy. The radiation physicists at the Radium Hospital were among the first to establish a quality assurance scheme in cooperation with the Norwegian Radiation Protection Authority, as it was called at the time. The deviation system that was established has become a model for identifying errors and routine deviations that can be an aid to ensure better treatment in the future.

The patient in focus

It was hard to be a patient 90 years ago. Despite all the progress, being a patient is still both demanding and uncomfortable. The patient at the center was a goal and a desire of healthcare personnel at the time as well, but they had much fewer alternatives.

When the Radium Hospital was planned in the early 1900s, the two public diseases tuberculosis and cancer were both taboo and partly shameful. Tuberculosis is contagious, and the poorest part of the population was hardest hit. The disease was silenced and kept hidden. Fear that cancer could also spread was probably why the neighbors of the Radium Hospital's building plans was met with protests that «cancer patients would travel in the area and cause untold violence...». Openness characterizes today's attitudes. Many people, both celebrities and others, have appeared in the mass media and written books about what it is like to live with cancer. They don't tell the same story and each individual tells their own unique story. The disease strikes very differently, with some being cured by a simple surgical procedure while others have to undergo extensive treatment with unpleasant side effects that can extend over months, perhaps years. Young people in education lose progress in schooling, and career choices may need to be reconsidered. Employed persons with dependency responsibilities may experience financial problems. It is of great value to our society that so many people come forward and talk about big and small problems, joys and sorrows. We learn from it and our national social safety net has been adjusted and improved. Mental reactions and social conditions affect patients differently, and different personalities cope with the stresses differently.

Most hospitals that provide chemotherapy have their own department or section where patients see the same staff every time they need treatment. Knowledge and accessibility is a good description of their function. It provides security and reduces uncertainty and anxiety for patients.

Psychologists and psychiatrists are a very important resource. It is not a defeat or sign of weakness to ask for help from a psychologist or psychiatrist. Painful thoughts, anxiety and depression are a natural consequence of illness, and it can hit hard. Some staff have as their primary task to help the patients who need it with this. Unfortunately, such support functions will often be cut back on when budgets are tight. Existential questions related to faith and beliefs can also feel difficult. Christian services is therefore available, and it is also possible to mediate contact with other religious communities.

Social workers help patients with the large paper mill that the social services (NAV) represents. Young people in education may need special advice that can adapt their study interruption or changed career choices. The study centers are probably the ones that can give the best advice in collaboration with the health service.

Figure 42. Physiotherapy is very important for rehabilitation after treatment.

Physiotherapists help with exercise programs and exercises. They also contribute to the adaptation of assistive devices, together with occupational therapists. Occupational the therapists guide patients who need changes in their homes in order to continue living there and create leisure facilities for ambulant patients who are hospitalized for a long time. For many years, the hospital also had a leisure contact who arranged trips around Oslo, had library and arranged concerts and performances. In recent years, such services have been reduced because patients are no longer hospitalized for weeks. Life as a current or former cancer patient is complex. The main task of the psychosocial team consisting of psychiatrist. psychologist, social worker. occupational therapist and priest is to ensure that patients can live their lives in the best way both in the hospital and at home after discharge. Nutritional physiology is a separate subject. Thei job is usually to guide obese people who want to slim down. But at the Radium Hospital, the problem is the opposite, how can weight loss be avoided?

The GP scheme can be regarded as a cornerstone of the Norwegian health service. It is the GP who will gather all the threads of our diverse health service and hold on to them for the individual patient both before and after treatment. It is therefore important that the hospital has good communication with the GP. Both patients and hospital staff should discuss with their GPs how collaboration can be organized. As a patient, it is an extra reassurance that the local health team is well informed about treatment and care needs.

The Montebello Center was established as a training center for cancer patients and their 1990. The families in academic and administrative anchoring is assigned to the Radium Hospital. In 1900, Mesnalien health resort outside Lillehammer was opened, as Norway's first private tuberculosis sanatorium. The health resort was closed in 1983. For year it was empty while public committees and councils deliberated. Director Jan V Johannessen of the Radium Hospital solved a political problem with creative input and established the Montebello Center as a health and rehabilitation center for cancer patients and their families in the old tuberculosis hospital.

Figure 43. Montebello Center

Art at the Radium Hospital

The original, monumental building from the 1930s can be called an architectural work of art. The patient reception was a great columned hall. The first years were characterized by a strained economy, and there was no money left over for artistic decoration. Over the years, the hospital has received a number of gifts, such as paintings and graphic magazines. Former director Jan Vincents Johannessen is very interested in art, and the corridors were gradually richly decorated. There was a lot that could distract from heavy thoughts for both patients and those who worked there.

Jakob Weidemann

Ferdinand Finne

Inger Sitter

Figure 44. Pictures exhibited at the Radium Hospital

Many musicians and actors have entertained the patients for free with various cultural elements. For many years there were weekly concerts in the main hall for patients and relatives. The patients have met many celebrities up close, and it warms when many of the artists keep coming back without any form of payment. For patients and relatives, this provides a good break from worries and heavy thoughts.

Research, development, aid and education

Research and development have been important to the Radium Hospital ever since its inception. Research can be divided into laboratory research that is mostly carried out in the research institute, and clinical research that is carried out in the hospital. The expertise gathered at the Radium Hospital has led to many occupational groups taking parts of their education there. Hospital staff have also played a key role in establishing aid projects in developing countries.

Laboratory research - The Research Institute

The research institute at the Radium Hospital was established in 1954 as Norsk Hydro's Institute for Cancer Research.

The department was organized with different departments that had their special interests and broad powers to conduct the research they thought was most relevant and that they mastered best. The field of research that characterized the Radium Hospital right from the start, namely treatment of cancer with ionizing radiation (radiation therapy), was supported by research that investigated how radiation interacts with living tissue and can best be used to stop the growth of cancer cells.

Figure 45. Institute in the 1960s

The country's foremost cancer research expertise was at the Radium Hospital. Due to their high level of expertise, the institute's researchers managed to secure external research grants, and they were eventually rewarded with research prizes that made the institute recognized. The allocations came primarily from the National Association against Cancer and the Norwegian Research Council, but also from international funds and contributors. The institute's employees received professorships in Oslo, Trondheim and Tromsø and thus attracted research talents from these universities. Students who were to take master's degrees and doctorates flocked to the institute, and many of them were engaged for further research at the institute.

As the years passed, several departments and several research fields were included, such as tissue cultivation, immunology and occupational cancer and, in later years, molecular biology. It became clear quite early on

that the idea of an interdisciplinary research environment on cancer issues and in close contact with the clinic was very good and proved to be very fruitful. The institute attracted outstanding researchers who gradually distinguished themselves among the foremost in Norway and abroad.

It should be mentioned that many medical doctors in the clinical departments gained experience with research methodology and technology from the Institute. They could work at the institute for longer periods, preferably as part of a doctoral degree. This promoted the exchange of expertise and knowledge between the basic research communities and the clinical researchers. The clinicians could discuss the challenges they faced during their work with patients, and the institute's expertise could contribute ideas on how to solve the problems.

The institute has developed several new treatment methods. Some of these have been patented and later developed into pharmaceuticals, which in turn have provided the basis for the establishment of companies with billions in value. This has become an important source of income for operations.

Figure 46. The Institute for Cancer Research today.

Science is a profession that must be learned. An important function for the clinic is to educate doctoral candidates who will later work and lead the activities of the clinical departments and laboratories. The knowledge base is constantly evolving. The elements that may be of significance for patient treatment must be captured. It is a demanding task. This is a prerequisite for the treatment programs, including the national recommendations, to always describe the best methods. Clinical research projects today set very strict requirements, and a basic scientific education is necessary.

In 1974, the Institute for cancer research was merged with the Radium Hospital. The funding of the Institute was mainly contributions from private businesses, private individuals, foundations and voluntary organizations in addition to basic support from national funds. Special mention must be made of the National Association against Cancer, which from 1988 was called the Norwegian Cancer Society.

Clinical Research – The Hospital

Clinical research, or experimental treatments, are studies that are conducted on humans. Here the effect of drugs or other treatment methods is examined. At the Radium Hospital, research activity has been central since its inception in 1932. Initially, clinical research was probably somewhat unstructured. Today, clinical trials of new drugs and treatment principles are conducted in accordance with strict and internationally accepted regulations. Most advances in medicine are the result of laborious and time-consuming work, where major breakthroughs are few and far between.

The introduction of new drugs in Norway takes place in four phases: Proposal, method assessment, decision and implementation. Norway has generally been slow to introduce new cancer drugs. On average, it takes almost two years from when a cancer drug receives market authorization until it can be used in Norwegian public hospitals. In 1978, things were different when one of the major breakthroughs in drug cancer treatment was the introduction of cisplatin. It was adopted in the summer of 1978 without much delay. Cisplatin revolutionized the treatment of lymphoma and testicular cancer and has also been of invaluable help in other cancers.

Clinical trials with radiation therapy have mostly focused on fractionation and dose. Both the total dose and how the individual radiation dose is given and possibly the addition of a drug.

In contrast to drug cancer treatment and radiotherapy, surgical interventions are more difficult to standardize. Experiments have been carried out comparing different types of operations. Experience from this study provides a basis for current practice.

Teaching and education

The Radium Hospital, like all other hospitals, is built and operated to provide both treatment and good information about illness and procedures related to this. The hospital also has two other very important and statutory tasks: research and teaching.

Research is done in many ways both within clinical and experimental disciplines and laboratory sciences. Academic competence is an important prerequisite for extracting relevant research results for use in the national treatment programs. They also have formalized contacts with Nordic and international academic communities. This was a tradition S.A. Heyerdahl introduced already when he attended the radiology congress in Stockholm in 1928.

Teaching and training in all health sciences is a duty related to hospitals. At the Radium Hospital, teaching is provided both through theoretical training and practical skills. This is done in cooperation with universities and university colleges.

<u>Nurses</u>

The Radium Hospital established special training for nurses in cancer. This started as a

In-house training where visionary nursing leaders at the hospital saw both the need and the solution. The education was later approved at the national level and is now incorporated into the college environment at master's level. This special education was started at the Radium Hospital in 1982. Oncology nurses have special expertise in cancer care. This education has contributed to a paradigm shift since knowledge has gradually come out well in the municipalities.

Figure 47. Old auditorium and staff training

Radiation Therapists

The same applies to radiation therapists where similar visionary leaders in the radiation therapy department saw the need as the demands on staff increased. Originally, it was nurses who controlled the radiation machines, but as the radiation machines became increasingly complicated, technical expertise was required. Today, radiation therapists control the machines. They have a background as radiographers but have also completed a one-year special education in radiation planning and radiotherapy. The Radium Hospital established such education in the late 1980s.

Midical doctors

Medical students have always been taught cancer at the Radium Hospital. This includes both lectures and practical training on the wards. Specialist training for oncologists in Norway has also largely taken place at the Radium Hospital. Here, doctors receive training in the treatment of the many different types of cancer. Many who are to be trained as other types of medical specialists will also work at the Radium Hospital for shorter periods for training purposes. Continuing education or special training of doctors who are already specialists largely takes place at the Radium Hospital. The hospital has the national expertise in key disciplines, and it is therefore natural that the hospital has been a driving force in spreading new knowledge in cancer treatment. Many doctors conduct research alongside their patient work, and a great many medical doctorates have emerged from the research environment at the Radium Hospital.

Physicists:

The technological development in radiotherapy in the 1970s led to a great need for medical physicists. In 1972, a separate line of study was established at NTH (University of Trondheim) for biomedical technology on the initiative of, among others, the Radium Hospital. Students from this line enjoyed periods of study at the Radium Hospital, and many took their M.Sc. thesis here. The training was important for the recruitment of medical physicists both to the Radium Hospital and the other radiation therapy centers. In recent years, there has also been a close collaboration with the University of Oslo (UiO). Many medical physicists have taken their education and doctoral degrees at the Department of Physics at UiO.

Aid to other countries

It is a very expensive and tedious process to start a completely new medical field in a country with limited resources. Ethiopia attempted to establish radiotherapy as a form of therapy. Doctors who were sent to other countries to specialize did not always return. Johan Tausjø, head of department at the Radium Hospital, acted on this problem. He grew up in Ethiopia and knows the culture, speaks the language and has contact with key people there. The idea was to send specialists from the Radium Hospital to Ethiopia to train the candidates in their home country. This included the training of medical specialists, physicists, radiation therapists, oncology nurses and other professionals in Ethiopia with teaching staff from Norway. This was well received in Ethiopia, a country of 100 million inhabitants.

Figure 48. Pictures from the relief project in Ethiopia

Over time, it has been possible to build up a modern cancer ward with well-educated employees and modern equipment at two hospitals in Addis Ababa. In addition, cancer centers have now been established in five other locations in Ethiopia. The goal was to create a professional environment that was eventually capable of its own recruitment of specialists. This has been very successful. There have been major contributions from the professional communities at the Radium Hospital since the practical program started in 2010. Since 2020, the hospitals they have managed to take care of the training themselves.

Important partners for the development of the Radium Hospital

It is costly to conduct research, and funding from the public sector is insufficient. It has therefore been very important to have other sources of funding.

The hospital and its patients have always benefited from gifts from donors. Without this, it would not have been possible to adopt new treatment methods or provide patients with good support. The public sector has provided little funding for the start-up of costly new treatment methods or welfare measures for patients and their families. Such initiatives are almost always funded by donations to the hospital. These donations have largely gone to the National Cancer Society and to local funds and grants that have played an important role in research at the institute and hospital.

1 Radium Hospital's Foundation When King Haakon VII opened the Radium Hospital in 1932, it was called "the Norwegian people's gift to themselves". The hospital was a foundation, and at that time money was raised for both construction and operation. Eventually, operations were paid for by the public sector, in the same way as for other hospitals.

Until today, the generosity of the Norwegian people has been great. Donations and testamentary gifts were kept in a separate account since the 1980s outside the hospital's operating accounts. In this way, the donors could be sure that the funds they provided to the hospital would not disappear into the large hospital budget. When the Norwegian hospitals were to be converted into health enterprises, and many of them were merged, the board of the Radium Hospital established in 2004, and with the approval of the Ministry of Health and Care Services, the Norwegian Radium Hospital's Foundation as a separate foundation **(radiumlegat.no)**.

The purpose of the foundation was, and still is, to provide funds to further develop the Radium Hospital as a complete cancer hospital in the foremost international range. The Foundation are not included in the national budget, nor are they receiving financial support from Oslo University Hospital. The activity is therefore completely dependent on donations and testamentary gifts. The Norwegian Radium Hospital's Foundation has been, and still is, a financial spearhead for the cancer center within diagnostics, treatment, research, innovation and care. The Foundation have been crucial in making the Radium Hospital "more than a hospital"

In addition to financing innovations in diagnostics, treatment and research, the grants have played a very important role when it comes to looking after patients, and their relatives, in an often critical phase of life. When you are affected by cancer, it is not just an organ or a patient that is affected, but an entire family.

This work has made Radium hospital an innovative cancer center, also internationally. The Foundation have played an absolutely crucial role in the establishment of the Montebello Center **(montebellosenteret.no)**, the Laurbærfondet, with free apartments for families affected by cancer, the construction of the world's only Wellness facility with swimming pool in a cancer hospital, training rooms, youth rooms, art library (Artotek), the establishment of Villa Ekebakken , an oasis just 5 minutes' walk from the hospital. This is just to name a few examples of the activity.

Not least, Radium Hospital's Foundation, together with Radium Hospital's Friends, and other good forces, fought in the front line when it came to saving Norway's only complete cancer hospital from being closed down. You can see the result now. A brand new hospital will be ready in the spring of 2024 to receive patients from all over the country. But the Foundation work in the fight against cancer is not finished. On the contrary. The Foundation will now increase their activities to ensure that in the future Norway has a cancer center that provides the best possible treatment for Norwegian cancer patients, regardless of their private finances.

Every year Radium hospital receives substantial funds from Radium Hospital's Foundation for research, patient measures, support for hospital operations and to strengthen the hospital's role as an international complete cancer center. The funds from Radium Hospital's Foundation have made it possible to establish completely new treatment methods and diagnostics that would otherwise not have been established and provide support to patients that the public sector cannot otherwise provide.

An important source for Radium Hospital's Foundation has been the many small amounts that come in from individuals and patients. Occasionally, large individual donations in the multi-million range are made which have made it possible to acquire expensive medical equipment for the hospital. Radium Hospital's Foundation have also contributed funds to the Norwegian Radium Hospital's history team. More about from Radium Hospital's Foundation can be found on the website www.radiumlegat.no.

2 The Norwegian Cancer Society(s)

The Norwegian Association for Fighting Cancer was established in 1938. The association put the spotlight on the prevention of cancer and in this connection placed great emphasis on diet. Vegetables were healthy and good for the body, they believed. Time has shown that they were correct in their recommendations. Others in the professional communities thought they placed too much emphasis on their diet and called them the Vegetable Society. One also had to try to find a biological explanation. They were right, too. The cancer cause had great appeal to people's generosity, and the Radium Hospital had also largely relied on donations and nationwide fundraising.

The "Vegetable Association" primarily supported the communities at Rikshospitalet. The relationship between the Radium Hospital and Rikshospitalet was still not good, and therefore the professional community with strong ties to the Radium Hospital established a new cancer society and called it the National Association against Cancer. Health Director Karl Evang assisted, and the director of Radium Hospital, Rolf Bull Engelstad, was first chairman. Director Reidar Eker later took over the chairmanship. The cooperation between the two associations probably didn't work well. The anniversary publication from 2015 (Brustad) states: "At the Radium Hospital, newly appointed researchers quickly became aware that the "Vegetable Society" had to be kept at a distance. If a researcher from here applied for support for his research from the "Vegetable Society", a taboo boundary was broken, and his travel pass from the Radium Hospital was thus almost guaranteed". We have until 1988 before the two associations chose to merge. Today, the merged association is called the Norwegian Cancer Society.

Voluntary work and private donations are still very important, especially for the research institutes and for research in the clinical departments. The Norwegian Cancer Society finances research projects with operating funds and salaries for PhD candidates. Part of the clinical research is paid for by the pharmaceutical industry when testing new drugs. The Norwegian Cancer Society is a key contributor to several different purposes related to cancer across the country. There are many examples that it can take time to get new positions into government budgets. The Norwegian Cancer Society has acted as a safety net and allocated money for positions and operating budgets on a temporary basis. In cases where new medical achievements require specialist expertise to be used, the Cancer Society has contributed. Other examples are various measures to improve patient welfare and direct financial support to disadvantaged cancer patients. The establishment of Varde centers is an example of measures to improve patients' and relatives' social and psychological well-being during treatment.

Today's major challenge with new and extremely expensive drugs for cancer treatment often has a cost framework that only the state can bear. But there is still a need for a safety net for social grants. There are good intentions in NAV's support schemes for patients, but sometimes someone my fall through the cracks. Then help from the Cancer Society can come in after an individual assessment. The state is often very slow in its decision-making processes. The Norwegian Cancer Society is therefore a very important player in establishing new initiatives. The Norwegian Cancer Society has undoubtedly led to both better treatment options for more patient groups and better conditions for patients.

Figure 49. The logo of the Norwegian Cancer Society in 2023

3 Radforsk

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This is an investment foundation that commercializes research at the Radium Hospital. It was founded as an independent foundation in 1986 with the name Radium Hospital Research Foundation The portfolio consists of 15 commercial companies with a total value of more than NOK 2 billion. Through these companies, research activity has returned NOK 200 million to cancer research.

4 Oslo Cancer Cluster

Radforsk was involved in establishing Oslo Cancer Cluster (OCC), which is a non-profit research and industry cluster within cancer. The cluster aims to accelerate the development of new cancer treatments and diagnostics – for the benefit of cancer patients. Oslo Cancer Cluster was established in 2006. The cancer research community that Oslo Cancer Cluster is a part of has developed around Rikshospitalet, the Radium Hospital, the Oslo region's two universities, as well as companies and knowledge actors. In July 2008, the Oslo region and Oslo Cancer Cluster were appointed by the journal Genome Technology to be one of the world's best research environments in biotechnology. In 2019, Oslo Cancer Cluster had around 90 members representing the entire value chain from research to industry. One of the main priorities of the cluster members is to ensure that patients have quick access to new medicines and diagnostic tools during trials. Oslo Cancer Cluster arranges seminars and meetings to improve collaboration, build networks and share information, expertise and experience. Oslo Cancer Cluster is located next door to the Radium Hospital, along with the Cancer Registry of Norway and around 30 companies.

Figure 50. Oslo Cancer Cluster has premises in a new building next to the Radium Hospital in the same building complex as the Cancer Registry of Norway and Ullern Upper Secondary School

5 Norsk Hydro's fund for cancer research

A few years after the opening of Norsk Hydro's Institute for Cancer Research at the Radium Hospital, the institute realized that they lacked opportunities to travel abroad to learn. It was necessary to travel, especially abroad, to learn new technologies and to acquire modern knowledge in cancer research. Once again, Norsk Hydro came to the rescue. They allocated NOK 1 million to Norsk Hydro's Fund, whose purpose was to finance and promote research at the institute. The fund currently stands at more than NOK 100 million.

The allocations go towards participation in international research congresses and purchase of experimental equipment.
How does business work today?

Nurses, auxiliary nurses and doctors were a key occupational group when the Radium Hospital was established. These are, of course, still important occupational groups, but the activities at today's Radium Hospital are completely dependent on many other types of personnel, each with their own special education.

The list of occupational groups employed at the Norwegian Radium Hospital is long. Examples are bioengineers, radiation therapists, medical physicists, various engineers and technicians, IT staff, office employees, administration with different functions, porters with internal logistics, cleaning, kitchen employees, pharmacists with pharmacy services, etc.

A discussion about who is most important makes no sense. If only one group disappears, patient care will be reduced, and treatment will stop. It is the combined team of people working at the hospital that provides patients with today's treatment and care. The working habits has also changed. Previously, there was a sharp distinction between the tasks of doctors, nurses and auxiliary nurses. Specialist education in many fields has blurred the sharp distinctions. A good example is the collaboration between physicists, radiation therapists and doctors when providing radiation therapy. It is a united team that is behind the treatment program. The three groups come from different professional worlds, and they must work together and must understand a little of each other's subjects if the result for the patients is to be good.

The primary health service and local hospitals have been given increasing responsibility for following up cancer patients. They are therefore an important part of an overall treatment program. Health care is thus a chain that must be connected.

The relationship with Rikshospitalet has now been normalized for many years, and the two hospitals have developed a professional and constructive collaboration with a thoroughly discussed distribution of tasks. The hospitals have now been merged into Oslo University Hospital (OUS). One can speculate as to why a destructive controversy developed in the early history of the Radium Hospital. Gradually, the disputes have been settled without us being able to time it to a date or year. In the old days, the health service had a distinctly hierarchical management system, and Rikshospitalet did not want a competitor. The goal of cancer treatment is for everyone to have the same treatment, regardless of place of residence and which hospital they are admitted to. Increasing knowledge has had a very beneficial impact on hospital operations.

Future development plans for the Radium Hospital

We see it all over the country: Old hospital buildings are being rebuilt and expanded by "bud shooting". In the end, the hospital buildings as a whole will be unsuitable, a whole new start will have to be made. The Radium Hospital had also arrived there with a mishmash of dilapidated, old buildings.



Old buildings from the period 1950 - 80 were demolished due to both cumbersome operation and poor maintenance. Some of the buildings would probably soon demolish themselves if nothing was done. On the site of the demolished old buildings, a new large patient building, and proton center are now being built. The original building from 1932 was in very good condition and will be preserved further. They could build with good quality and a long-time perspective back then! Hopefully there will be a second stage of construction after this. As a result, all the old buildings, except the original building from 1932, will be demolished, and the hospital may appear as a new and completely modern cancer center.

Figure 51. The making spoon used before starting the building of a new patient building



Figure 52. This is what The Radium Hospital will look like when the current major expansion is completed in spring 2024



Afterword

RADHIST is an independent organization registered as an association in the Brønnøysund Register Center. The history team wishes to preserve the rich and exciting history of the Radium Hospital and is based on volunteer work there. RADHIST was established in 2021 by former and current employees of the hospital.

The duties of RADHIST are threefold:

- 1. Preserve and record objects that may be of historical interest.
- 2. Create and operate a website. The website (radhist.no) describes the history of the Radium Hospital and the activity that takes place at the hospital today.
- 3. Make a book about the history of the Radium Hospital for the opening of a new clinic building and proton facility in 2024 (this book).

Radium Hospital's Foundation have been the team's most important collaborator, and their support has been crucial for this book to be realized.

The book is based on a collection of contributions from many current and former employees at the Radium Hospital. Many of the members of the Board and Expert Council (see below) have been of crucial importance by finding material for the book and by making critical comments along the way. In addition to writing and collecting contributions, an editorial committee has ensured that the material is organized in a logical manner and to find relevant images. The editorial committee has also been responsible for the practical work of getting the book published.

Editorial Committee:

Jan Folkvard Evensen, Tor Green, Ole Nome, Gunnar Tanum, Kristin Øwre.

Board and Expert Council:

Hans Bjerke, Erik Boye, Janne Christoffersen, Jan Folkvard Evensen, Tor Green (web manager), Anne Grethe Ryen Hammerstad, Taran Paulsen Hellebust, Vidar Jetne, Ole Nome, Stein Kvaløy, Jan Rødal, Gunnar Tanum (leader), Turid Vetrhus, Kristin Øwre (secretary).

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Information is also taken from posts in Krepsen, DNRnytt, OnkoNytt and from presentations by former employees at the Radium Hospital.

Dictionary

Alpha particle: The atomic nucleus of the element helium (He) consisting of 2 protons and 2 neutrons.

Alpha particle emitter: Isotope (see this) that emits alpha particles.

Alpha radiation: Power of alpha particles.

Autopsy: An external and internal examination of a dead body.

Betatron: A machine that creates β radiation (beta radiation, electron radiation) in an electrodynamic accelerator, built on the principle of a transformer. The first betatron was built by the American physicist Donald William Kerst in 1940, but the principle it works by was previously described by the Norwegian Rolf Widerøe in 1928. Slowing down the electron beam generates X-ray radiation. A betatron can therefore deliver both electron and X-ray radiation.

Calibration: The comparison of an instrument against a normal one against a more accurate instrument or against a reference material.

Cobalt machine: Processing machine in which a radioactive source (⁶⁰Co-radiation source⁾ was placed in an isolated chamber. The radiation is emitted in a controlled manner by opening the chamber where the radiation source is located.

Cu HVL: Cu (copper) HVL (half value layer) - Half-value thickness is a quantity that indicates the ability of a substance to absorb X-rays, gamma rays, or neutron radiation. The half-value thickness of a homogeneous substance for a particular kind of radiation is the thickness of a layer of the substance that reduces the intensity of the radiation by half.

DNA: DNA (Deoxyribo-nucleic Acid) is our genetic material. In the individual's DNA, a unique, overarching recipe or working drawing is encoded.

Depth doses: Curves showing how radiation weakens as it penetrates tissues and other materials.

Endocrine surgery: Surgery that mainly treats diseases of the breast, thyroid, and parathyroid glands.

Ester: Chemical compound that occurs when an organic acid reacts with an alcohol during the splitting off of water.

Fatigue: Feeling of total exhaustion and lack of energy. Some describe it as a feeling of weakness, or constant tiredness.

Fluorescence: The emission (emission) of light (photons) from molecules immediately after they have absorbed higher-energy light radiation, that is, at a shorter wavelength than the emitted light.

Photons: A type of elementary particles that make up all light and other electromagnetic radiation.

Gamma radiation: Gamma radiation, which is also written γ radiation, is energetic electromagnetic radiation from radioactive atomic nuclei. Gamma radiation consists of photons (see this), similar to X-rays, but generally has a shorter wavelength and higher energy than what is called X-rays, although there is also an overlapping energy range.

GIST: An abbreviation for Gastrointestinal Stromal Tumors. It means tumors originating from the connective tissue of the gastrointestinal tract.

Imatinib: A so-called signal inhibitor, a drug that that interferes with the cells' signal-transmitting regulatory mechanisms. Imatinib is a tyrosine kinase inhibitor. These impede the activity of a protein called epidermal growth factor receptor (EGFR), a protein involved in the growth and spread of cancer cells.

IMRT: Intensity Modulated Radiation Therapy is a treatment methodology where one varies the shape of the radiation fields and treats from different angles and with different radiation intensities.

Immunotherapy: A new type of cancer treatment that activates the immune system to attack the cancer cells.

Ions: Atoms are usually neutral, containing as many electrons as protons. Ions are one or more atoms with a charge, as a result of which they have emitted or taken up electrons, respectively positive and negative ions.

Isotope: Variations of a particular chemical element with different numbers of neutrons. All isotopes of an element have the same number of protons.

Joule: A derived SI unit of energy (work or heat). The symbol for joule is J, named after the British physicist James Prescott Joule.

kV (kilo volts): (kilo=103) volts: unit of voltage.

Linac: is the same as linear accelerator, see below.

Linear accelerator: Machine for acceleration of charged particles. The acceleration occurs in a straight line unlike in other accelerators where the acceleration occurs circularly.

MAB: Monoclonal antibodies are antibodies that have the same reaction ability because they are produced by genetically identical cells, i.e. from one clone. Monoclonal antibodies therefore react against one and the same antigen.

MV (mega volts): (mega=106) volts: unit of voltage

NAV: Norwegian Labor and Welfare Administration

Pectoralis major: Musculus pectoralis major, large pectoral muscle located on the mammary gland

PACS: PACS (picture archiving and communication system) is an electronic system for digital storage, retrieval, viewing and transmission of images.

PET/CT: Positron Emission Tomography/Computer Tomography is an advanced nuclear medicine imaging method. The method is a well-documented, well-established and very useful tool in diagnostic imaging of cancer. A PET camera provides three-dimensional images of the entire body. Integrated CT allows the information from PET to be located anatomically accurately. PET / CT is helpful in detecting different diseases.

Pitchblende: A black and heavy mineral consisting of uranium oxide. The correct mineralogical name is uraninite, highly radioactive material.

Platinum needles: Hollow needles of platinum containing radium. Radium was encapsulated as it emits the toxic gas radon.

Radionuclide: An element with an unstable nucleus that emits radiation, be it alpha, beta or gamma radiation

Radioactive MAB: Radioactive element coupled with monoclonal antibody. This brings the radiation to a specific location like a magic bullet.

Radium cannon: Treatment machine in which a radioactive source (radiation source ²²⁶Ra⁾ was placed in a chamber of the machine. The rays are emitted controlled by opening the chamber where the radiation source is located.

Receptor: A receptor is a binding site for e.g. a neurotransmitter. Receptors are located on the outside of the cell membrane or inside a cell.

Screening: Examination of a group of people to detect early signs of a disease or increased risk of disease

Serotonin (antagonists): A neurotransmitter secreted by some nerve cells located in the brain and intestines. Antagonists counteract the effect of the neurotransmitter

Stem cell transplantation: A stem cell transplant (bone marrow transplant) involves destroying the body's own stem cells and then topping up with healthy stem cells from a donor. The donor can also be the patient himself. Cells can be extracted from one's own body and then reinserted after removing diseased cells.

Thoracic surgery: Thoracic surgery is surgery of the chest cavity extensive heart and lungs

T-lymphocytes: T-lymphocytes are a type of white blood cell that belongs to the lymphocytes. The T-lymphocytes are responsible for cellular immunity, i.e. the immunity mediated by the cells of the immune system.

VMAT: Volumetric Modulated Arc Therapy is a treatment methodology where irradiation is given while the therapy machine is rotated continuously around the patient while the shape of the radiation fields and radiation intensity are constantly varied.



The Radium Hospital after 2024

The Norwegian Radium Hospital history team (RADHIST) is an organization made up of volunteers who want to take care of all types of historical material from the Radium Hospital. Together with our website (radhist.no), this book wants to convey the main features of the hospital's history.

The book will be published in 2024 at the same time as the new clinic building and proton center are put into use.





Norwegian Radium Hospital's history team