

An outline of the development of radiotherapy in Slovenia*

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The historical data on the development of radiotherapy (RT) in Slovenia are presented from its first use in this country in 1902 till present. The Institute of Oncology in Ljubljana (IO) was established in 1938 with the intention to provide a sound development of radium and roentgen cancer treatment. After the World War II the development of RT at IO was rather dynamic, which is evident from the data on new radiation sources in external beam therapy (accelerators, telecobalt units), in brachytherapy (various sealed radioisotopes) as well as in therapy with unsealed radioisotopes being introduced. In 1947 a Chair of Oncology and Radiotherapy was instituted at the Medical Faculty of the University of Ljubljana (with the seat at the IO). In 1955 radiotherapy and oncology was officially recognized as a separate branch of medicine, requiring a special, obligatory postgraduate residency training. Considering the size of population of Slovenia (near 2 million), it was reasonable that by the time RT became almost completely concentrated in one central institution i.e. in the IO, representing its core and cohesive activity in the multidisciplinary cancer treatment approach.

Key words: radiotherapy-history; Slovenia

Introduction

As an old-timer in radiotherapy (RT), engaged at the Institute of Oncology, Ljubljana (IO) since 1946, the data given below on the development of RT in Slovenia in the following decades have been recorded by my own knowledge. For the previous period I collected the information from our predecessors in this field, out of their dispersely published or unpublished papers or by personal communications of some of them.

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For better understanding the topic, following are some relevant data on Slovenia. It is situated in the north-west part of the former Yugoslavia, covering a territory of 20 256 km,² and at present comprising near to 2 million population. Ljubljana is its capital (286 681 inhabitants) and the next largest city is Maribor (105 431 inhabitants). According to the data of the population-based Cancer Registry of Slovenia, the number of new cancer cases in the year 1950 was 1 795 (130 per 100 000 population),¹ whereas in the year 1987 it was 5 736 (288 per 100 000 population).² As noted since 1950, about 50% of cancer patients are, sooner or later in the course of their disease, treated by radiation. In the last decade around 3 000 have been treated yearly in the IO.

History

Soon after the World War I, the interest of our physicians for RT was on the one hand enhanced by its already commonly recognised effectiveness in the treatment of cancer and also of various benign diseases, and on the other, by the increasing cancer morbidity in our population.

Roentgenotherapy of cancer and benign diseases was introduced at the Roentgen Department of the General Hospital in Ljubljana, headed by Dr. Alojzij Kunst, in 1923, two years later it was started in Maribor in a private sanatorium by a gynecologist Benjamin Ipavic³ and presumably some years later in the General Hospital in Brežice by its chief-surgeon Josip Cholewa in frame of the activity of the Oncological Laboratory he established there in 1920.⁴ In the '30s this therapy was carried out also in some other public or private roentgen stations in Ljubljana and some other towns. At that time, mainly the Siemens universal roentgen apparatus was used for both diagnostics and therapy.³

Before World War II, the few specialised rentgenologists that were there (altogether 6), as well as two gynecologists interested in RT, received their knowledge in this therapy mainly in the Viennese Central Roentgen Institute (headed by Dr. Guido Holzknecht), and also by visiting the relevant institutions in Prague, Berlin, Frankfurt-upon-Main, Munich and Paris.³

As to the *radium therapy*, it is of historic interest that in Ljubljana it was used for the first time in the years 1902-16 by Dr. Emil Bock, the then chief of Ophthalmology Department of the General Hospital, for treating skin cancer in eye region.³ For this purpose he used a special applicator (Figure 1) containing but 4 microcuries of radium (according to present measurements). Further, from 1929 on, in the above mentioned Oncological Laboratory in Brežice a pair of »radium-points« (alloy of radium with platinum – unfiltered), containing 1 and 1.5 mg of radium respectively, were used for interstitial application in cancer treatment.⁴ However, a year before the then Head of Otorhinolaryngologic Department of the Ljubljana General Hospital Dr. Josip Pogačnik provided for cancer treatment purposes 49 mg of radium in needles and tubes at his own expense, since he could not get the means from the government.⁵ Bought from him, these were in fact the first radium sources available for the treatment in our Institute.^{5,6}

For more than ten years, the physicians of various specialities, interested in cancer research and its radiation treatment, devoted strong endeavours to establishing an institution intended exclusively for cancer, and in which RT, specially radium therapy would be concentrated. Finally they succeeded, and in 1938 by the order of Slovenian government such an institution was

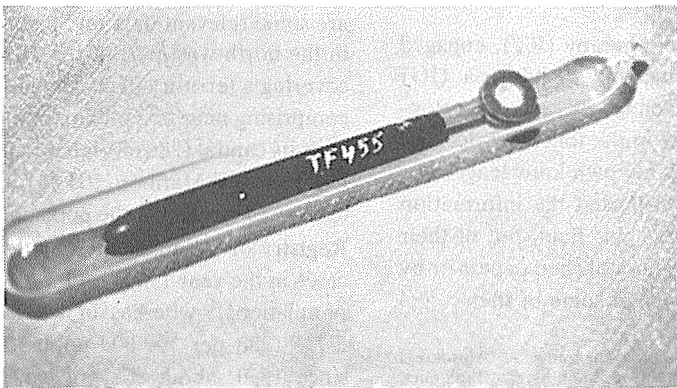


Figure 1. Applicator with ^{226}Ra ($4 \mu\text{Ci}$) purchased by Dr. Emil Bock in 1902 for treatment of skin cancer in eye region at the Ophthalmology Department of the General Hospital in Ljubljana. Length 18 cm.

established in Ljubljana.^{6,7} It was the embryo of our present IO. Its original name was: *Institute for Research and Treatment of Neoplasms*, and the concept of its activity as a comprehensive cancer center was already outlined, although its starting space, equipment and personnel capacities were very modest. It was situated in an adapted part of an almost 200-year old building (previously barracks) where some of its units have remained till present time. There were only 28 patient beds.⁷

The RT equipment comprised three roentgen units: one orthovoltage (Siemens Stabilivolt 180-200 kV) for deep therapy, one (according to Schaefer & Witte – 90-100 kV) for intravaginal irradiation, and one (according to Chaoul – 50-60 kV) for »contact« irradiation of superficial lesions.^{6,7} Besides, a stock of altogether 410 mg of radium encapsulated in tubes and needles was available.⁷

The initial Institute's staff of 5 physicians consisted of 1 surgeon (director Josip Cholewa), 2 gynecologists, and 2 general practitioners.⁷ Only 4 years later one specialized roentgenologist was engaged. In fact at that time modern radiation treatment methods of cancer and benign disease were introduced by the chief gynecologist Leo Šavnik, who had been already before, mainly at his own initiative, trained in the radiotherapy in several European (mainly German) radiotherapy centers.^{3,6} Among the initial staff of the Institute there was also an electroengineer engaged part time for maintenance of roentgen equipment, and radiation planning dosimetry.^{6,7}

Immediately after the World War II, during which the activity of the Institute was severely impeded, it was joined with the Roentgen Institute of the newly formed University Hospitals (from the previous General Hospital in Ljubljana), into a common *Institute of Roentgenology and Radiology*. Fortunately, this had lasted only for 8 months, as it soon became evident that such a symbiosis was unreasonable. Thus, these two institutions were separated, ours getting the present name: *Institute of Oncology*, and which in 1961 became autonomous like it had been before

the World War II. Moreover, by December 1947 the *Chair of Oncology and Radiotherapy* was instituted at the Medical Faculty of the University of Ljubljana, the seat of which was entrusted to our Institute. Thus, an adequate education in this subject has been provided for the undergraduate medical students in the last terms of the curriculum.

During the first post-war decade, when the possibility to engage more physicians in the IO was opened, our endeavours were devoted mainly to catching up with the development of RT as achieved in respective institutions abroad, e.g. in Stockholm, Paris, Manchester, New York. This was enabled by ensuring adequate conditions, i. e. on the one hand in RT trained physicians, radiophysicists, and technicians, and on the other, by updating the treatment and dosimetric equipment. It is worth mentioning that by year 1955 in Slovenia *RT together with oncology was officially recognised as a special branch of medicine*, i.e. apart from roentgen diagnostics, with which it had been joined previously. From then on, for obtaining the title of specialist in this branch, a special program of residency has been required, lasting for 3 years until 1978 and for 4 years afterwards. From 1955 till now, i.e. in the last 35 years, 31 physicians have passed board examination in this branch; 8 of them have also reached doctor of science degree.

Overcoming many obstacles, specially a constant shortage of space, the development of the IO as a multidisciplinary cancer treatment, research and education centre was rather dynamic during the whole post-war time, but still in the patient treatment RT remained its core activity.⁸ Although all other modalities of cancer treatment have been carried out, i.e. surgery, chemotherapy, endocrine-, and immunotherapy, they were and are mainly limited to those cancer sites in which they are mostly combined with RT. On the 50th anniversary of the IO, i.e. in 1988, the number of its patient beds was 365 of which 172 were assigned to patients treated by radiation. Among the total of 85 fulltime engaged physicians of various diagnostic and therapeutic disci-

plines, there were 25 radiotherapists, and among other 19 high degree professionals of other disciplines, there were 5 radiophysicists, and 2 radiobiologists; the number of radiotherapy technicians was 26. Until the end of 1990 these figures did not change essentially.

The development of RT might be evident from the *equipment and treatment techniques used*. Below, a brief review of the situation **from 1938-on** is presented with some comments.

External beam radiotherapy

Roentgen low-voltage, short source-skin distance («contact», superficial) therapy, as already mentioned above, has been used in the IO ever since its beginning, and is still performed, but to a limited extent (in cancer treatment being replaced either by applications of small sealed radioactive sources or by accelerators' electron irradiation). In around 1950 it was also introduced in the General Hospital in Maribor, and somewhat later in the Dermatology Department of the University Hospital in Ljubljana. In both instances, besides for the skin cancer it has been used to a great extent for the treatment of benign skin diseases. At the Dermatology Department in Ljubljana in the '60s even the *»telesuperficial«*, i.e. a total body surface roentgen irradiation by Siemens Dermopan for the treatment of generalised dermatoses was developed.⁹ Presently, the roentgen therapy of benign skin diseases has been almost completely omitted, since other effective means of their treatment are available.

Roentgen orthovoltage – deep therapy at the time when it was introduced in the IO, as also mentioned in the beginning, had already had some tradition in the Roentgen Department of the General Hospital in Ljubljana, and in that in Maribor. Since then, in the former institution it had still been carried out until 1959, mainly for benign diseases, whereas in Maribor it is still used in malignant diseases, mainly as palliative treatment, as well as in certain benign diseases, like also in the IO. In 1957 the latter obtained a new roentgen apparatus (Siemens Stabilipan)

which enabled *moving irradiation*, i.e. pendulant and convergent.¹⁰ However, we had not been using these techniques for a long time.

Supervoltage X-ray therapy we started to carry out in 1955 with a betatron 31 MeV (Brown Boveri), which was installed in the Institute of Physics »Jožef Stefan«. ¹¹ Despite the inconvenience that this Institute was located rather far from the buildings of the IO, this accelerator had been used for the radical treatment of deep seated cancers until 1978, when a *linear accelerator* (Philips MEL 75-20 with X-ray energy 8 and 16 MeV) was installed in a new building for teletherapy of our Institute, and by which also *electron beam therapy* (5-20 MeV) was possible. Two years ago another new linear accelerator (Philips SL 75-15, X-rays 6 and 10 MeV, electrons 5-15 MeV) was installed.

Telecobalt unit was first put into operation in IO by 1962 (Siemens' Gammatron I) with initial activity of source 1000 Ci. Later on it was replaced by two new ones (AECL Theratron 80 in 1968, and Philips Telecobalt in 1979) with rather higher initial activities of sources. In 1989 the second one was replaced by the fourth (AECL Theratron 780 with initial activity of source 10 000 Ci. In fact, for almost two decades the main deep therapy load was on the telecobalt units, and just to mention, along with them a *»mantle field«* technique, and the total-body (TBI) and half-body irradiation were introduced. TBI for immunosuppression at bone marrow transplantation in leukemia treatment in Ljubljana was first used in 1989.¹²

Finally, it should be mentioned that during the '70s adequate modern *facilities for radiation treatment planning and control* were provided. Among these were: the transversoaxial tomograph, two simulators, treatment planning computers, body outline tracing device, apparatus for formation of individual fixation masks, and other accessories for patient immobilisation during irradiation.

Brachytherapy with sealed radioactive sources

For this kind of treatment only *radium-226* in needles and tubes was used in the IO until 1956

(with total amount of the element being near 1 gram from 1947 on). By the end of '50s and in the following decades *radioisotopes* came into use. First, *cobalt-60* was purchased in form of globules, and grains in plastic mass (»plastobalt«), but it was used only for a few years, because of certain disadvantages of its application.

During the '60s the treatment of *superficial lesions* (specially in the eye region) was carried out also by *beta emitters* (*phosphorous-32* and *strontium-90* surface applicators), but not for a long time. However, since 1985, again a beta-ray eye plaques with *ruthenium-123* have been used in the treatment of chorioidal melanomas.

For the *interstitial* applications, in '60s also the *gold-198* seeds, *tantalum-182* wires (»hairpins«), and mainly *iridium-192* wires and seeds came into use. A relevant dosimetric system for implants was worked out in a cooperative study by one of our radiotherapists and radiophysicist.¹³

For *intrauterine irradiation*, in the '70s, Simon's afterload packing technique with *cesium-137* miniature sources was introduced, like it was previously performed according to Heyman with radium, and then with cobalt sources. As before, *cervical carcinoma* remains the main field of brachytherapy. Until 1953 it was performed according to so-called Paris (Regaud) technique, and since then according to Manchester (Paterson-Parker) technique. In the mid '70s, our own modified Henschke's manual after-loading application of cesium sources was developed. In 1985 a *unit for remote after-loading* (*CGR Curietron*) was purchased. Thus, in the last years cesium sources almost completely replaced the use of radium in the treatment of uterine cancers.

In other cancer sites the use of brachytherapy steeply decreased during the '70s. However, it seems that in the last years the interest, specially for interstitial therapy has been renewed. It is worth mentioning that in 1985 our radiotherapists introduced *interstitial hyperthermia* combined with RT, which has already shown favourable results.¹⁴

Radiotherapy with unsealed (fluid) radioisotopes

was first used at the Medical Department (later Department of Nuclear Medicine) of the University Hospitals in Ljubljana in the years 1954-59, i.e. by *iodine-131* in hyperthyroidism and thyroid cancer metastases, and by *phosphorous-32* in polycythemia vera and chronic leukemias.¹⁵ Later on, these kinds of treatment were introduced also in the IO, (*P-32* also for treatment of bone metastases). Besides that, already from 1956 on *intracavitary therapy* with gold-198 colloid has been used in the management of peritoneal and pleural cancerous effusions. Later also colloidal Yttrium-90 has been applied for this purpose.

By the end of '80s the computer assisted data processing for cancer patients treated by RT – was developed, linked with our population-based cancer registry, and in which the detailed clinical and technical data relevant to radiation treatment methods are noticed.¹⁶ Thus, it enables a continuous follow-up of the effectiveness of particular methods and treatment techniques in cancers of specific sites and stages.

Radiotherapists of the IO have been and are steadily fulfilling *their role in the necessary interdisciplinary approach in the treatment of cancer patients*, as since 1950 they have been regularly attending, by the IO initiated and organized *multidisciplinary joint clinics* for cancers of specific sites and separately for childhood cancers. In these joint clinics the specialists of other relevant branches, either from the IO and/or from other departments of the University Clinical Centre in Ljubljana take part. Most of these clinics have been taking place weekly in the IO. Besides, our radiotherapists have been paying *regular visits as consultants to the peripheral general hospitals* for many years already. Besides, they are *engaged in teaching radiation oncology* at undergraduate and postgraduate level of medical education, as well at the school for radiology technicians and at the school for nurses.

In connection with the above activities of our radiotherapists, I consider the problem derived

from the knowledge requirement for site specific cancer treatment worth mentioning. Accordingly, the radiotherapists have developed into subspecialists, loosing the broad knowledge and experience in radiation treatment of all malignant diseases. Actually, they are separately engaged in cancer treatment of the following site regions: 1. head and neck, 2. intrathoracic organs, 3. digestive, urinary and male genital organs, 4. female genital organs, 5. breast 6. lymphatic, haematopoietic, bone and soft tissues (including pediatric malignomas). In these fields they have been cooperating in some international clinical trials concerning the problems of combined modality treatment of patients with malignant diseases.

Conclusion

From this review of the development of radiotherapy in Slovenia it can be derived that with respect to the size of its population, there has been a sound tendency to concentrate it in the Institute of Oncology in Ljubljana, as the only such institution in this country. In fact, it is its nucleus in playing a cohesion role in the comprehensive multidisciplinary cancer treatment approach.

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