

The history of nuclear medicine in the Republic of Slovenia II – spread of the new medical speciality into peripheral hospitals from 1960 to 1974

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*The second part of this historic overview describes the establishment of five hospital departments of nuclear medicine in the regional hospitals of Slovenj Gradec (1960), Celje (1968), Maribor (1973), Šempeter near Gorica and Ankaran (1974). The Basic Laboratory for Work with Radionuclides in Ljubljana, which represented the origin of all nuclear medical activity in Slovenia in its earliest pioneering era, gave rise to the following two units: Department of Nuclear Medicine at the Institute of Oncology, and the Clinic of Nuclear Medicine at the University Clinical Center in Ljubljana. For nuclear medicine, the 70's meant a period of rapid development induced by the introduction of radioimmune tests into the diagnostics *in vitro*, whereas the diagnostics *in vivo* was boosted by new devices such as gamma cameras, computers and Tc-generator. The number of new investigations has rapidly increased, and also the frequency of all investigations showed a trend of sharp increase all until 1980 when this progress slowed down. At that time diagnostics *in vivo* were implemented by ultrasonography and computerised tomography, whereas in the diagnostics *in vitro* radioimmune assays were gradually replaced by tests based on immunofluorescence and by other techniques which did not require radioactive labelling.*

*In the 80's, some investigations such as e.g. liver and kidney scintiscan were gradually abandoned in order to give place to some new ones (e.g. radionuclide ventriculography). The frequency of investigations after having reached its peak became stable, and annual frequency of investigations remained basically the same. A recapitulation from 1984 for the whole Slovenia with its population of 2,000,000 showed that a total of 44,215 investigations *in vivo*, 185,175 *in vitro* and 504 therapeutic applications of radiopharmaceuticals had been performed in that year in all seven Slovenian units of nuclear medicine.*

Key words: nuclear medicine – history; Slovenia

Introduction

In the first part of this historic overview the development of nuclear medicine in the capital

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of Slovenia since its beginnings at the Clinic of Internal Medicine in Ljubljana (1954), through the period of their joint work under the shared roof of the Basic Laboratory for Work with Radionuclides (1960–1968), up to the moment when the internistic and oncological nuclear medicine have finally separated, is presented.

The second part of this historic overview

describes the establishment of five hospital departments of nuclear medicine in the regional hospitals of Slovenj Gradec (1960), Celje (1968), Maribor (1973), Šempeter near Gorica and Ankaran (1974).

The article also gives information on staff situation and work performed in 1984; these data were collected by means of a questionnaire for the needs of the 4th Austrian-Hungarian-Slovenian Scientific Meeting on Nuclear Medicine, which was held on May 1985 in Ljubljana, on the occasion of the 30th anniversary of nuclear medicine in Slovenia.

1960 – Slovenj Gradec: General Hospital Slovenj Gradec, Unit of Nuclear Medicine

The first attempts to spread nuclear medicine outside Ljubljana can be attributed to I. Raišp from the General Hospital in Slovenj Gradec who introduced investigations of the thyroid with radioactive Iodine. The uptake of radioactive Iodine (131-I) in the thyroid was measured 2, 8 and 48 hours after the patient had ingested a test dose of 50 µ Ci 131-I-Naiodide; the activity in urine excreted during 0–8 hrs, 8–24 hrs and 24–48 hrs following test dose intake was also measured (Raišp and Burnik 1964).

As to the equipment, their working conditions were worse than of their colleagues in Ljubljana. In 1964, Simoniti et al.³ reported that using radioactive iodine, toxic adenomas of the goiter were discovered in 6 patients treated at the General Hospital in Slovenj Gradec. The author pointed out that owing to the lack of a scintiscanner, the hot thyroid nodes were localized manually using a Geiger-Müller's tube. The article of Raišp from 1968⁴ comprises a scintigram of a thyroid node imaged by the help of radioactive iodine, thus proving that a scintiscan facility had already been available in Slovenj Gradec at that time.

In 1984, six-member staff of the unit for nuclear medicine headed by I. Raišp performed 1446 *in vivo* and 7212 *in vitro* investigations, and applied therapeutic doses of radioiodine in 10 patients.⁵

1968 – Celje: Health Center Celje, Center of Therapy of Internal, Contagious and Dermatologic Diseases, Department of Nuclear-Medicine

The Laboratory of Nuclear Medicine in Celje was built and equipped already in 1967, whereas regular work there started a year later; F. Fazarinc, specialist in internal medicine, became the head of the unit. Two of the staff members obtained their basic knowledge at the Institute "Boris Kidrič" by attending a course on the use of radionuclides in medicine. Additional practical and theoretical upgrading of their knowledge was accomplished later on at the Institute of Nuclear Medicine in Ljubljana.⁶

According to F. Fazarinc, further development of their laboratory and all advances in the quality of work occurred as a result of new equipment purchase. Thus the initial facilities were enhanced by kinetograph with analogous subtractor which was developed by the Institute Jožef Stefan; from that machine later on the team of J. Šnajder in collaboration with F. Fazarinc from Celje and M. Erjavc from the Institute of Oncology in Ljubljana developed a renograph. This has become a constituent part of equipment in numerous laboratories of nuclear medicine in former Yugoslavia. The purchase of a gamma camera DYNA 11/4 (Picker) with a computer PDP 11/34 (Digital) in 1978 denotes the next important mile stone in the development of nuclear medicine in Celje.

In 1984, 15 professionals headed by F. Fazarinc performed 5995 *in vivo* and 43,669 *in vitro* examinations, and applied therapeutic doses of radionuclides in 17 patients.⁶

1968 – Ljubljana: Clinic of Internal Medicine, Department for Nuclear Medicine

The year 1968 means the end of the mutual work of specialist in internal medicine and oncologists in the Basic Laboratory which was situated in the former St. Peter's Military Barracks. The former moved into the Clinic of Internal Medicine, where upon the Laboratory of nuclear medicine changed its name and became a Department for Nuclear Medicine of

the Internal Clinic. In 1970 there were 7500 measurings performed in that department comprising 2 chemical laboratories, 3 measure rooms, one outpatient facility and one hematologic laboratory.^{7, 10}

The Department, however, occupied that place only for a short period of time. Already in 1971 it moved in the 5th floor of the newly built Clinical Center in Ljubljana, though the construction works had not been completed yet. After having gained its organizational independence, the department became the **Institute of Nuclear Medicine**. This was the first institution in Slovenia to have a gamma camera PhoGamma III Nuclear Chicago with scintigraphic data analyser (computer) which was a prerequisite for introducing of new techniques in nuclear medicine.⁷

Further promotion of the Institute took place with completion of the Clinical Center in 1973, when it was allocated its permanent place in the groundfloor of the new building. Having obtained also suitable hospital ward capacities, the Institute finally became the **Clinic for Nuclear Medicine**. The staff consisted of 9 specialists in internal medicine, 9 graduated biotechnologists and 16 technical assistants. The Clinic functioned in three radiochemical laboratories with annual capacity of 20,000 competitive radiochemical examinations, and 5 rooms for *in vivo* measurements with annual turn over of 10,000 investigations. The data obtained by static and dynamic scintigraphy were quantitatively analysed by means of an electronic computer.⁷

Clinic for Nuclear Medicine was also a teaching base for two-term postgraduate study in nuclear medicine;⁸ in 1974 the first ten students successfully completed their studies within the frame of this program. In the same year, a Section for Nuclear Medicine at the Slovenian Medical Society was established in Celje.⁹ The Clinic became the seat of the Executive Board of the Section, as well as the seat of the Executive Board of the Yugoslav Society of Nuclear Medicine.

In 1975 the clinic – then already named the **University Clinic for Nuclear Medicine** – had a

staff of 37 professionals. *In vivo* investigations were performed with two gamma cameras directly connected to two computers; a program computer was indirectly connected with a kine-tograph (for kinetic measurements of renal and cardiac function) as well as with an automatic system for measuring of radioactivity in liquids. Programs for kinetic studies of renal, cardiac and cerebral function (vascularization), and for the analysis of radioimmune and other competitive radionuclide examinations *in vitro* as well as programs for computerization of scintigrams were performed.

With rapid development of the Clinic, discrepancies associated with the lack of space were brought to attention. Therefore, on the occasion of the 20th anniversary in 1975, a sanation program was accepted according to which the annual number of *in vivo* investigations should be reduced from 10,000 to 8,100, and *in vitro* investigations from previous 20,000 to 10,000; thus reduced program would be operative all until the Clinic's capacities would have been enhanced by new room capacities for out-patient service outside the existing ward. As a result, the sanation program did not so much decrease the extent of services performed, but rather stimulated the establishment of a new department for diseases of the thyroid, which found place in the basin of the Outpatient Clinic in Ljubljana. With this reconstruction in 1978, the Clinic for Nuclear medicine obtained a dislocated unit with 14 rooms for their out-patient activity.

In 1984, 52-member staff of the Clinic, headed by B. Varl, performed 11,961 *in vivo* and 107,636 *in vitro* examinations; therapeutic doses of radiopharmaceuticals were applied in 362 patients.

1968 – Ljubljana: Institute of Oncology, Unit of Nuclear Medicine

After dislocation of nucl. med. services for the needs of internal medicine, the rooms and equipment of the former Basic Laboratory were inherited by the **Department of Brachyradiotherapy and Nuclear Medicine of the Institute of**

Oncology. Further reorganization in 1970 split this service into two separate units, i.e. Brachyradiotherapy and Unit of Nuclear Medicine (UNM).

UNM primarily covered the needs of the Institute of Oncology.^{10,11} Apart from nucl. med. examinations, radionuclides were applied also for therapeutic reasons in patients with carcinoma of the thyroid, painful skeletal metastases and in patients with carcinosis of the serous membranes. The scope of work was never extended by *in vitro* investigations as in other nucl. med. laboratories in Slovenia.

While in the 70's all other units and laboratories of nuclear medicine in Slovenia used the equipment and radiopharmaceuticals commercially available in the country and abroad, and performed investigations that had already become a part of routine work elsewhere, at UNM the pioneer period was protracted well into the late 70's, which was reflected in perpetual experimenting and innovative activity.

A speciality of this unit, headed by M. Erjavec, was the development of own radiopharmaceuticals such as e.g. radioactive Fluor (F-18) by the help of school reactor TRIGA in Podgorica; labelling of Bleomycin with radioactive Cobalt (Co-57) and Technetium (Tc-99m). Further activity of this kind included "rediscovering" of certain investigations (e.g. perfusion scintigraphy using a neoport valve), in-house development of measuring equipment (e.g. whole-body scanner, renograph), and homemade computer programs.

Own Equipment:

Among *in vivo* investigations, the first place was taken by bone scintigraphy, first with radioactive Strontium (Sr-85), and later on, around the year 1970, with radioactive F-18. High energy of the used radiopharmaceuticals required a modification of the scintigraphic equipment. Thus in the 60's the commercial scintigraph was adjusted for Sr-85 use by strengthening the collimator with lead. In collaboration with the Institute Jožef Stefan own whole-body scanner was developed and constructed by a local Railway workshop; the scanner proved very handy for fast bone imaging with F-18,

which was among the most pretentious examinations performed.

The importance of the described device for skeletal scintigraphy could not be diminished even by the use of Tc-99m labelled polyphosphates an gamma camera purchased in 1974. The whole-body scintiscan had been used in patients with radioactive Fluor-18 applications all until the middle of the 80's.

The third device which was developed in collaboration with the Institute Jožef Stefan and the colleagues from Celje was the already mentioned renograph.

Homemade Computer Programs:

In the same way as the staff of the Unit headed by M. Erjavec developed their own measuring instruments, they also produced their own computer equipment. The beginnings reach back into late 60's when the first original digital amplifier for contrast scintigraphy was developed. Around the year 1968, with first computers coming into use, they developed a system of digital recording of information on a perforated band, which lead to the first system for computer processing and presentation of images. The top achievement was certainly their own program for hidden-lines isometric graphic presentation which was considered an advance even by the most developed centers in the world.

In 1972 the Unit obtained its own computer HP 2100 in virgin configuration. By the help of experts Jožef Stefan Institute, it was linked into a computer net connecting all the measuring devices in the laboratory. In 1974, the computer system was enhanced by inclusion of a gamma camera Nuclear Chicago Pho Gamma 4.

By breakdown of the computer in 1978, the programming work had been completely stagnating until 1984 when the Institute of Oncology obtained another gamma camera, produced by General Electrics, which comprised a computer Star and ready made programs that only needed to be adjusted to the specific needs of UNM

Radiopharmacy:

Around the year 1970, radiopharmacy mainly referred to in-house labelling of different ra-

diopharmaceuticals, in the beginning by means of Iodine-131 and later on with In-113. A major effort was devoted to the labelling of macroparticles for lung scintigraphy, and of microspheres for lymphography and scintigraphically guided intraarterial chemotherapy which has become widely recognized only 15 years later. All attempt to use intravasal applications of radionuclides with therapeutic intent have failed. Anyway, the therapeutic applications of radionuclides represented only 1 % of the Unit's routine.

Therapy:

Up to 1970, patients with sealed and open radioactive sources had been treated in this Department, whereas after the establishment of Brachyradiotherapy Department in that year, only open sources were applied in UNM.

After the introduction of intracavitary therapy with radioactive colloid gold 185, and metabolic therapy of thyroid tumors with Iodine 131 in the 50's, in the next decade the treatment for painful bone metastases by means of radioactive Phosphorus 32 and Strontium 89 came into use. As the therapeutic radiolymphography with iodised oils appeared quite promising, in 1967 own production of this radiopharmaceutical was started. The method, however, proved clinically irrelevant and was therefore abandoned. In the 80's, the above applications were enhanced by experimental use of therapeutic doses of 131-I-metaiodobenzylguanidine (131-I-MIGB).

In 1984, the team of 17 workers of DNM, headed by M. Erjavec, performed 9930 *in vivo* investigations and applied therapeutic doses of pharmaceuticals in 60 patients.¹¹

1973 – Maribor: General Hospital Maribor, Departments of Internal Medicine, Nuclear Medicine

In the appointed year, a Laboratory for Nuclear Medicine was allocated its room of 180 m² on the first floor of the building intended for these purposes. Nuclear Medicine in Maribor was started by R. Turk and five of his coworkers. The initial equipment comprised a scintiscanner Nuclear Chicago, a renaltron Nuclear Chicago,

a measuring device for Iodine uptake in the thyroid, and an automatic sample measuring device for *in vitro* investigations.

In 1984, the staff of 14 workers employed in the Dept. of Nuclear Medicine, headed by R. Turk and J. Šubic, performed 9731 *in vivo* examinations, and applied therapeutic doses of radiopharmaceuticals to 36 patients; they also carried out 16,978 *in vitro* investigations.¹²

1974 – Koper: Health Center Koper, General Hospital Izola, Unit for Nuclear Medicine Ankaran

This Unit started to work in July 1974. For the needs of NM service, 104 m² of place occupying 8 rooms were allocated in the Department of Internal Medicine of the hospital in Ankaran. This relatively small surface had to accommodate a common work room, hot laboratory, 2 measurement rooms for *in vivo* examinations, a room for application of radiopharmaceuticals, radiochemistry, waiting-room and an outpatient office with administration.

In the beginning, the staff consisted of a doctor – A. Malej, and an X-ray technician – M. Ogris with four technical coworkers; weekly consultancies were attended by the specialists M. Erjavec from Ljubljana, and F. Fazarinc from Celje. The Laboratory covered for the needs of the region including Koper, Izola, Piran, Sežana, partly Pivka and Postojna, and the Croatian part of Istria incl. Buje.

In 1984 the unit employed 8 workers headed by A. Malej, who performed 3110 *in vivo* and 6159 *in vitro* examinations, as well as 8 applications of therapeutic doses of radioiodine.¹³

1974 – Šempeter near Gorica: General Hospital, Department for Endocrinologic Diseases and Nuclear Medicine

The initiator of nuclear medicine in this part of Slovenia was B. Gornjak. In the school year 1973–74 he successfully completed the first post-graduate study of nuclear medicine in Ljubljana. Also both technicians underwent a 6 month training at the Institute of Nuclear Medicine in Ljubljana.

The 28th of October 1974 denotes the beginning of regular work in the Unit. On that day, the first renography was performed in a patient with suspected urolithiasis. When the 4-channel kinetograph (developed by Jožef Stefan Institute) produced its first renographic curve, the scarce staff of the unit including its head felt very proud of the achievement.¹⁴

The unit soon obtained additional equipment, i.e. semiautomatic sample measuring device AMES-Gammacord II, and in 1975 also a scintiscanner Nuclear Chicago. The number of investigations performed rapidly increased, and also the circle of users got wider. Apart from renographies, the Laboratory also performed scintiscans of the thyroid, kidneys and liver.

In 1984, the Department with the staff of 6 workers, headed by J. Burnik, performed 2042 *in vivo* and 3521 *in vitro* examinations, and 11 applications of therapeutic doses of radioiodine.¹⁴

Conclusion

The beginnings of seven different units of nuclear medicine in the hospitals of Slovenia with about 2 million population are presented. Each of these units was something special.

The most prominent advance was made by the Clinic in Ljubljana. Thanks to the endeavours of the pioneer of Slovenian nuclear medicine B. Varl, a simple laboratory at the Clinic of Internal Medicine has developed into a University Clinic for Nuclear Medicine with four departments: for *in vivo* and *in vitro* diagnostics and therapy, with a hospital ward and an outpatient department. This institution maintains the highest professional level of nuclear medicine in Slovenia, and represents a teaching basis for postgraduate studies in the appointed field of medicine. It also provides residency program for physicians – future specialists in nuclear medicine, and is the seat of the Section for Nuclear Medicine of the Slovenian Medical Society.

Opening of all seven Slovenian nuclear medicine units was promoted by rapid development; the 70's were the decade of great advances in nuclear medicine in the World as well as in Slovenia. The rapid development of this branch of medicine round the year 1970 could be attributed to the introduction of gamma camera, computer, Tc-generator, and radioimmune assays. Seemingly uncontrollable boom of nuclear medicine of the 70's by the end of the decade had to give way to new achievements in rentgenology and biochemistry. Hospitals tended to give preference to ultrasonographic and CT equipment over gamma cameras, whereas in *in vitro* diagnostics radioimmunoassays were replaced by enzyme and immunofluorescent tests which are devoid of radioactive materials. Thus, in the 80's, the new techniques developed in allied medical branches contributed to the advances in radiology, ultrasonography and biochemistry.

The expansion of nuclear medicine from Ljubljana into peripheral hospitals goes hand in hand with the period of rapid development of this new medical branch. With the establishing of seven Departments of nuclear medicine by 1974 the needs of Slovenia were fully covered. Further development was centred on the endeavours for obtaining most essential pieces of new equipment, improvement of room facilities, introducing of new investigation, establishing and maintenance of international collaboration etc.

The frequency of investigations reached its peak by the end of 70's, and annual number of investigations performed in the 80's remained basically unchanged. A review of the activity in 1984 for the whole Slovenia with the population of approx. 2,000,000, gives the following figures: 44,215 *in vivo* and 185,175 *in vitro* investigations, and 504 applications of therapeutic doses of radiopharmaceuticals were performed. By the 80's, nuclear medicine has finally reached its present stage when the quantitative development has been replaced by a qualitative one.

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