



**„Frédéric Joliot-Curie”
National Research Institute
for Radiobiology and Radiohygiene
of the National Public Health and
Medical Officer Service,
Hungary**



**Brief information on its past and achievements,
present role, structure and ongoing tasks**

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Brief history of the Institute

Following the decision of the Hungarian Government taken in 1954, the Institute was founded by the Ministry of Health, supported by the Ministry of Defense, under the name of *Central Research Institute for Radiobiology* on **January 1, 1957**. It has been located in the Törley Castle on Budafok hillside (South part of Budapest) since its foundation. Its first director was *Vilmos Várterész, MD, PhD* leading the Institute for 15 years. The Government set as a basic task for the Institute to "study the radiation-induced diseases and their healing that could arise in some persons or groups of people in the course of peaceful utilisation of nuclear energy or its use for military purposes, and through an extensive application of radioactive isotopes".

By virtue of the Government decision, the Minister of Health renamed the Institute to "*Frédéric Joliot-Curie*" *Central Research Institute for Radiobiology* as of January 1, 1959.

As a consequence of changes in international and domestic circumstances, and mainly the launch of the home nuclear energy programme, the sphere of tasks of the Institute continued to expand. First with the national coordination and implementation of radiohygiene research and practical activities, including workplace and environmental radiohygiene sectors, and later by research and development of radioactive diagnostic and therapeutic preparations. In the interests of performing the newer tasks and clarifying the profile of public health institutes, Department of Radiation Hygiene of the National Institute for Occupational Medicine, the Radiation Physics Department of National Institute of Roentgen and Radiation Physics and the Radiation Hygiene Laboratory of the National Institute of Public Health were attached to the Institute.

The Institute thus expanded was renamed by the Minister of Health as "*Frédéric Joliot-Curie*" *National Research Institute for*

Radiobiology and Radiohygiene (NRIRR). This name is being used since January 1, 1963.

The Institute has become the professional centre of the country for radiation health. It was directed by *Tibor Predmerszky, MD, PhD* in 1972-74. In line with the new tasks, the third director of the Institute *László B. Sztanyik, MD, PhD*, Director General (who led NRIRR for over 23 years) reorganized the Institute from 1974 onwards. He established three professional departments: the Department of Radiation Biology, Department of Radiation Hygiene, and the Department of Application of Radiation and Isotopes. From the middle of the eighties an autonomous Laboratory of Non-ionizing Radiations has been functioning as a fourth unit. In 1998 it became the 4th department of the Institute.

On February 1, 1984 the Postgraduate Medical School has established the ***Chair of Radiation Hygiene*** at the basis of the Institute. Its first leader was Prof. Dr. L.B. Sztanyik, followed by Prof. Dr. G.J. Köteles since June 1995.

NRIRR headed by *Prof. György Köteles, MD, DSc, Director*, became a part of the "Fodor József" National Centre for Public Health (NCPH) on January 1, 1998. The Institute has preserved its professional independence, but in financial and legal aspects it became a partially independent entity. At that time the Accredited Radiohygiene Laboratory has been established by the National Accreditation Council. It includes both Departments of Radiohygiene and it involves all methods used by their staff members to assess the radiation exposure levels and conditions at the workplaces and in the environment. From September 2004 by April 2007 the Institute was directed by *Sándor Pellet, MD, PhD*.

NRIRR has been designated by the World Health Organization in October 2004 as a WHO Collaborating Centre for Radiation

Emergency Medical Preparedness and Radiation Health. NRIRR has become the 5th WHO Collaborating Centre in Hungary. Activities of NRIRR related to its tasks within the WHO Radiation Emergency Medical Preparedness and Assistance Network (WHO/REMPAN) are headed by Assoc.Prof. István Turai, Head, Division of Radiation Medicine and Biodosimetry.

NCPH was terminated by the Government at the end of 2006 and – according to its new Statute enforced on January 1, 2007 - NRIRR has become a partially independent national institution within the National Public Health and Medical Officer Service. Reorganizations have been continued, the former Department of Application of Radiation and Isotopes was merged with Department of Radiobiology. The Chief Medical Officer of Hungary has designated *István Turai, MD, PhD, MPH* as Acting Director General of NRIRR on May 1, 2007.

In respect of the 50th anniversary of foundation of the Institute a detailed review has been compiled - ***50 years of the “Frédéric Joliot-Curie” National Research Institute for Radiobiology and Radiohygiene*** (in Hungarian, ed. Dr. I Turai, pp.187, Budapest 2007) – to summarize the main achievements of the collective of NRIRR in a half century time. Here are some extracts from this book just to brief the reader about the nature, national role, results and recent tasks of this - unique for our country – Institute. The Institute started in 1957 with 16 staff members, steadily growing to 260 workers to the early 90ies and having only 80 researchers and assistants in the last two years.

Despite the significant reduction of the manpower and the financial support from the state budget, the Institute has been doing continuous efforts to meet all requirements defined by its new Statute from 2007 and other decrees of the Government and Minister of Health. Recent tasks and scientific cooperation at international and national levels

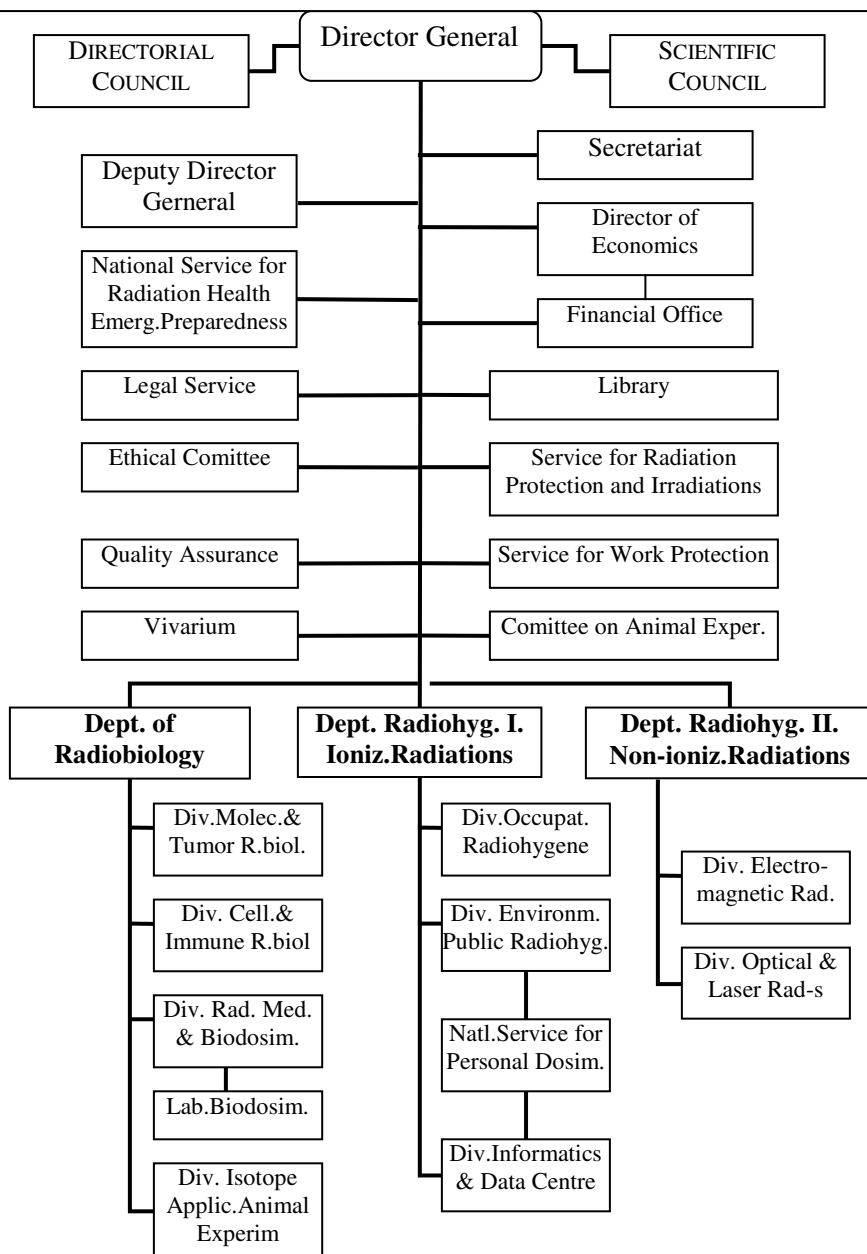
are described in the introductions of the current three departments and ten divisions of NRIRR (a few pages later).

During its 51-year activity the Institute served Ministry of Health as its single national body for radiobiology and radiohygiene research, training, consulting, advising, radiation monitoring and radiation protection against ionizing and non-ionizing radiation exposures at workplaces, in the environment or during medical applications. NRIRR maintains the unique National Service for Radiation Health Emergency Preparedness in 24h/365day non-stop duty shifts and also the National Personal Dosimetry Service for over 30 years.

The scientific staff of NRIRR has prepared **2226 articles** for peer-reviewed journals (65% of them in English, 5% in German and Russian), has written **70 books** and book chapters (half of them in English). They include basic textbooks of Radiobiology and Radiohygiene (in Hungarian) that have been used for postgraduate medical training for decades, such as: *Várterész V. ed: Radiobiology* (also in German), 1963; *Sztanyik B.L. ed.: Prevention and Treatment of Radiation Injuries*, 1989; *Turai I.: Basics of Radiohygiene*, 1993; *Köteles Gy. ed: Radiohygiene*, 2002.

Senior scientists of NRIRR have contributed to over 80 publications of international organizations and served as radiohygiene, radiation protection and radiobiology experts for over 100 missions conducted by the International Atomic Energy Agency, the European Commission, the NATO and the World Health Organization. Five staff members of NRIRR were employed for 4-7 years by the IAEA and 17 researchers received IAEA fellowships for 3-12 months abroad. NRIRR provided training for young scientists from 25 countries of four continents (but Australia) in a total of 52 months. There were prepared **86 theses for academic degrees** by NRIRR researchers: 10 DSc, 41 PhD and 35 MSc theses in 1957-2008.

Organizational structure of NRIRR since February 1, 2008



Department of Radiobiology

The Department of Radiobiology (Head: G. Sáfrány, MD, PhD, DSc) was established from the former Department of Radiobiology and Department of Application of Radiation and Isotopes in 2007. The department is composed of four divisions. These divisions are working on the basis of the traditions and achievements of the legal predecessors.

Division of Molecular and Tumor Radiobiology

The Division of Molecular and Tumor Radiobiology (Head: G. Sáfrány, MD, PhD, DSc) was established in 1998. Presently 5 persons with university degree and 3 technicians belong to the staff. Among the senior staff members one has the Doctor of Science, and another one the PhD degree. Two graduated students are in the final stages of getting the PhD degree. The basic mission of the Division is to investigate the biological effects of ionizing radiation on the molecular level. They apply up to date methodologies to investigate the effects of ionizing radiation on somatic and germ cells. They investigate the fundamental pathways contributing to *individual radiation sensitivity* both at the workplace and during radiation therapy. Using whole genome microarrays they identified 30 genes that respond to radiation in all (10) investigated primary human fibroblast cell. Recently they study low dose radiation induced *bystander effects* and *genome instability* in primary human fibroblast cells. This is the sole laboratory in Hungary which investigates the radiation biology of tumors and they establish unique combinations of radiotherapy and gene therapy protocols to treat brain tumors. They found that radiation therapy can be very efficiently combined by immune activating gene therapy and with gene directed enzyme pro-drug therapy (Figure 1). Since 1998, they have published 24 papers in international journals with high impact factors.

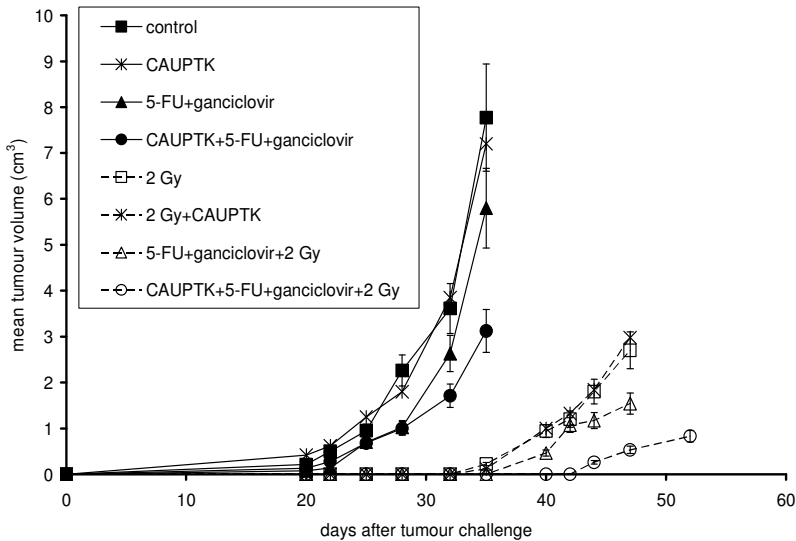


Figure 1. The anti-tumour effect of double-suicide gene therapy on established tumours. Subcutaneous tumours were established on mice by transplanting non-transduced GI261 cells into the right limb. Three and seven days later the tumour transplantation site was injected with Adex-CAUPTK (1×10^9 virus particles/mice) and animals were treated with 5-FU/GC. Half of the mice were irradiated with 2 Gy X-ray before the first and sixth 5-FU/GC treatments. P was < 0.008 , and $.0000$ for the virus + FU/GC treatment and for the irradiated group *versus* the untreated controls, respectively. P was < 0.0044 and $.0000$ for the radiation/FU/GC and for the virus/radiation/FU/GC groups *versus* radiation alone, respectively. The effect of other modalities was statistically insignificant.

Their work is supported by various national grants coming from the Public Health Scientific Committee (ETT), The Hungarian Scientific Research Fund (OTKA), Economic Competitiveness Operative Program (GVOP), National Research Development Fund (NKFP), and the Science and Technology Fund. They are also supported by the European Union.

The Hungarian collaborative partners include the National Institute of Neurosurgery, the National Institute of Psychiatry and Neurology, the Department of Oncotherapy, University of Pécs and the Department of Genetics, Cell- and Immunobiology, Semmelweis University, Budapest. The most important international partners are Radiation Protection Research Unit, Centre D'Etude de L'Energie Nucleaire, Mol, Belgium; Radiation Biology Center, Kyoto University, Kyoto, Japan; Radiation and Nuclear Safety Authority, Helsinki, Finland and MRC Radiation and Genome Stability Unit, Oxford, UK.

Members of the Division effectively contribute to the educational activity of the Institute and they also participate in the under- and postgraduate educational programs of the Semmelweis University and the University of Pécs.

Division of Cell and Immune Radiobiology

The Division of Cell and Immune Radiobiology (Head: K. Lumniczky, MD, PhD) was established in 2007 on the basis of the former Laboratory of Cell Biology. Presently 4 persons with a university degree belong to the staff. Among the senior staff members two were awarded with the PhD degree. One graduated student is in the final stage of getting the PhD degree. The main scientific task of the Division is to investigate radiation effects on the immune system. Their most recent data shows that even low doses such as 10-50 mGy can seriously affect the various immunological pathways. They irradiated mice with gamma-rays and found that the number of splenocytes as well as their response to non-specific mitogen stimuli strongly depended on the applied dose. Regeneration processes were efficient only below 2 Gy. They also studied the quantitative and functional alterations of various lymphocyte subpopulations. They detected that B cells and CD8+ cells are the

most radiosensitive, while T-regs and NK cells showed a relative radioresistance.

Their work is supported by various national grants coming from the Public Health Scientific Committee (ETT), The Hungarian Scientific Research Fund (OTKA) and the Science and Technology Fund.

Their most important Hungarian and international scientific collaborative partner are the Department of Medical Chemistry, Molecular Biology and Pathobiochemistry and the Department of Radiotherapy / Radiooncology, University of Leipzig.

Members of the Division participate in the educational activity of the institute and they also contribute to the postgraduate educational programs of the Semmelweis University.

Division of Radiation Medicine and Biodosimetry

The Division of Radiation Medicine and Biodosimetry (Head: I. Turai, MD, PhD, MPH) was set up in 2007 by merging Division of Radiation Medicine and Division of Diagnostics of Radiation Effects. At present 5 permanent staff members belong to the Division (including two biologists and two technicians besides the Div. Head, who is dealing with his divisional duties in part time only due to his ongoing responsibilities as the Head of the Institute). There are also 4 external collaborators (retired senior researchers, two of them are DSc, an MD and an MSc in Biology) support performance of different tasks of this unit in a voluntary basis.

One of the predecessors of this Division was the Division of Pharmacology, that was originally established at the foundation of the Institute in January 1957, with the support of Ministry of Defense, to study radioprotectors and other modifiers of radiation effects due to high dose acute exposure. It was proved in animal experiments that ip. pre-treatment with Gammaphos (WR-2721) enables the survival of whole body exposed mice by a factor of two,

but it is less effective orally due to gastrointestinal factors. There is a need for future studies in experimental animals to define suitable chemicals and effective application methods for radioprotectors, and also for harmonizing chemical radioprotective efforts with the therapeutical means of ARS.

Applying morphological and also immune-histochemical methods, radiation induced membrane alterations were extensively studied. It was recently demonstrated that following even as low as 25 mGy X-ray exposure, both intracellular location and quantity of structural proteins (eg. occludin, β -catenin, catherines) have changed. It was found that concentration of these proteins had increased in the cytoplasm. Due to exposure to radiation bystander effect has been observed and typical cell junctions have changed, as is shown in Figure 2.

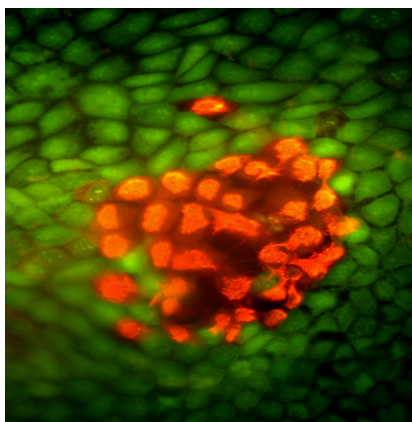


Fig 2. Bystander effect: 4 Gy exposed cells die in groups (red cells) losing their typical shape and having cytoplasmatic bridges.



Fig.3. Seven micronuclei in a dividing human lymphocyte following radiation exposure.

Laboratory of Biodosimetry was established in 1981 by Prof. G.J. Köteles and is being led by Dr. Gabriella Bognár since 1998. It is part of the Division of Radiation Medicine and Biodosimetry for over a year. All recently used methods for biological dose assessment in case of overexposure to ionizing radiation have been adapted and applied in the Laboratory: micronuclei technique (Fig.3) and chromosome aberration analysis for routine use, FISH (for retrospective cumulative dose assessment), PCC (to estimate the exposed part of the body) and Comet assay (to quantify double strand breaks). No stable chromosome aberrations were detected in nuclear power plant workers with cumulative dose exceeding 100 mGy. The cytogenetic changes have remained for a long time in uranium miners following termination of exposure to radon, indicating a higher risk for stochastic effects. Regular use of antioxidant vitamins (C and E) has reduced the frequency of cytogenetic changes. Recent task is to study cytogenetic effects of radon baths and high radon exposure in some dwellings. According to Decree No.16/2000 of Minister of Health, this Laboratory has been authorized to provide biodosimetry expertise in case of suspected radiation overexposure.

There are over 250 publications by the staff of the Division in peer-reviewed journals. Prof. G.J. Köteles and Dr. I. Turai are authors of IAEA and WHO textbooks in Radiation Medicine and Biodosimetry.

One of the most important recent task of the Division is *to train the staff* of nine university clinics and regional hospitals designated (by Decree No.64/2005 of Minister of Health) *to recognise and treat radiation injuries*. Annually postgraduate courses are conducted at NRIRR in Radiation Emergency Medicine, guides in this subject have been recently published and are prepared for physicians, nurses and rescue workers. The most important home collaborative partners are the State Health Care Centre (including the former Central Military Hospital since 2007); Faculty of Medicine of Semmelweis University, Universities of Debrecen, Pécs and Szeged, Regional

Hospitals in Miskolc, Szekszárd and Győr. Regional tasks are done by the Division within WHO/REMPAN since 2004 and EU/EPAL (Emergency Preparedness and Action Levels) since 2007.

Division of Isotope Applications and Animal Experiments

The Division of Isotope Applications and Animal Experiments (Head: L. Balogh, VD, PhD) was established in 2007 from the former Division of Nuclear Medicine and the Laboratory of Animal Experiments and Experimental Animal House. Presently, 4 people with university degree and 2 technicians belong to the staff members. Among the senior staff members one has the PhD degree. Two graduated student are in the final stages of getting this degree. The Division frequently receives foreign graduated students, who efficiently contribute to the scientific achievements. They also accepted two PhD students from the Szent István University. The main scientific task of the Division is the development and application of new nuclear medicine protocols for medical, veterinarian, agricultural, as well as experimental purposes.

In a very important new task they are going to find and spread alternative methodologies for the replacement of animal experiments: for instance they collect information from spontaneous diseases of animals (dog, cat, exotic animals) and try to apply these data for the development of new medical protocols.

The most important Hungarian collaborative partners are the Faculty of Veterinary, Szent István University, The Pannon University, Kaposvár, The Faculty of Health Science, Semmelweis University, the Faculty of Medicine, University of Debrecen; the Hungarian Society for Veterinary Oncology; the Foundation for Cancer-bearing Animals and the Hungarian Association for the Development of Alternative Methodologies.

The scientific work of the laboratory is supported by the International Atomic Energy Agency and by the European Union.

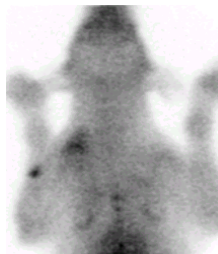
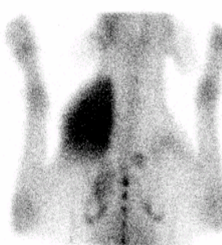


Figure 4. Scintigraphy of a dog (using gamma camera of NRIRR) before and 2 months after effective radiotherapy of the neck tumor

Department of Radiohygiene I. Ionizing Radiations

The Department (headed by Mr. Nándor Fülöp since February 1, 2008) deals with wide range of tasks in *radiohygiene* and *applied radioprotection* against all kind of ionizing radiation arising from both natural and artificial sources, which may cause potential radiation burden to the population and radiation workers, respectively. Especially, the Department is responsible to fulfill special tasks related to different radiological monitoring systems in Hungary, i.e.:

- Radiological Monitoring and Data Acquisition Network (RAMDAN), according to Decree of the Minister of Health No. 8/2002 (III.12.),
- National Environmental Radiological Monitoring System (NERMS) and
- Joint Environmental Radiation Monitoring System (JERMS), according to the Decree of the Government No. 275/2002 (XII.21.),

Tasks are distributed among four Divisions of the Department as follows:

Division of Occupational Radiohygiene

The tasks of the Division (headed by Dr. László Ballay including ten staff members, mainly physicists) cover the general radioprotection related to the workers, patients and the radiation safety of equipment and facilities applying/producing ionizing radiation, e.g. medical and industrial X-ray devices, accelerators, all kind of radioactive materials, radioactive waste disposals, nuclear reactors and the Paks Nuclear Power Plant, etc. Furthermore, the Division deals with the following additional administrative tasks supporting the different Hungarian authorities:

- compiling expert reports for registry, licensing and exemption processes,
- preparing legal regulations, standards, guidances related to the occupational radioprotection and radiation safety,
- court expert activities for legal actions,
- guidance and harmonization of the professional activity of seven Regional Radiohygiene Centres of NPHMOS in the field of occupational radiohygiene and protection,
- study of patients' and workers' doses in interventional radiography and interventional cardiology,
- operation of National Service for Radiation Health Emergency Preparedness (NSRHEP).

Division of Environmental and Public Radiohygiene

The main profile of the Division (headed by Mr. Gábor Kocsy, consisting of 16 staff members, including chemists, physicists and technicians) is to identify the ionizing radiation in the natural and human environment and assess radiation burden to the population. In relation, the tasks of the Division are:

- sampling from different media of environment (air, soil, drinking and surface waters, food- and feedstuffs etc.) for the purpose of regular radiological monitoring,

- determination of quality and quantity of radioactive materials in the human (using whole body counter – Fig.5) and the environment by on-site and laboratory measurements
- determination of radiation levels in the environment (Fig.6)
- determination of the radiation burden (dose) to the members of the public arising from natural and artificial sources of the environment
- determination of annual radiological sampling and measurement program of RAMDAN;
- processing and analysing measured data and determination of radiation burden to the population
- supervision and support of regional laboratories of RAMDAN
- preparation of annual reports of RAMDAN, NERMS and JERMS



Fig.5. Calibration of human Whole-Body Counter (gamma-spectrometer) using a "flask-phantom"

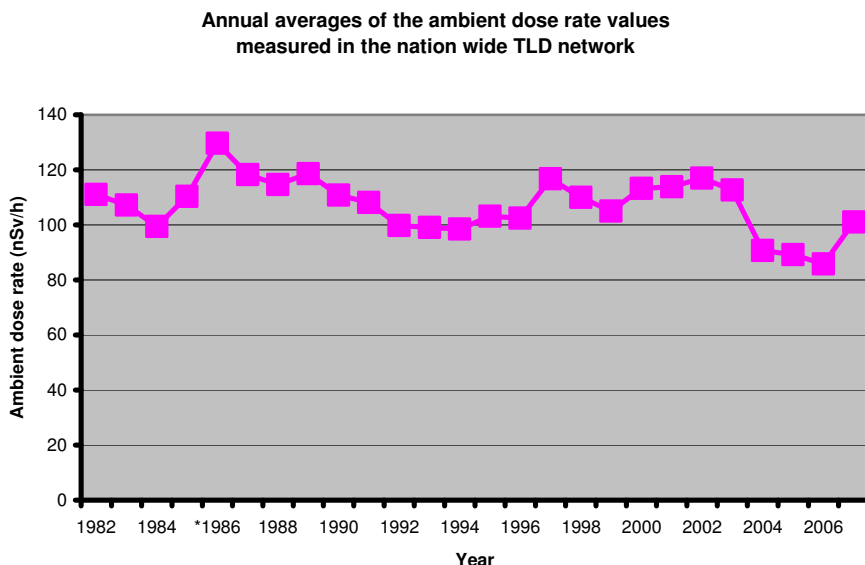


Fig.6. Annual average dose rate values in Hungary, 1982-2007

Division of Informatics and Data Centre

The primary task of the Division (headed by Mr. Balázs László, consisting of 4 staff members, including 3 informatics specialists and a data processing technician) is the operation of infrastructure of information centres collecting data and processing results measured by environmental radiological monitoring networks belonging to the Hungarian public health sector, i.e:

- RAMDAN Information Centre,
- JERMS Data Processing And Analyzing Centre and
- NERMS Information Centre.

Furthermore, this Division deals with the research and development of dispersion models to describe the environmental transport of

radioactive isotopes within different media, especially the atmosphere and terrestrial foodchains.

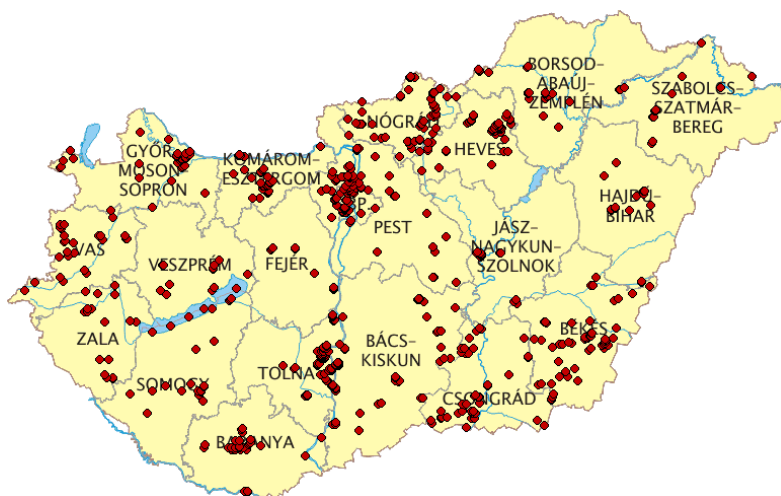


Fig.7. Geographical distribution of sampling locations of RAMDAN in 2006 operated by NRIRR and the laboratories of Regional Public Health Centres of NPHMOS (534 sites)

National Service for Personal Dosimetry

According to the Decree No. 16/2000 of the Minister of Health, the Service (Acting Head: Mr. Nándor Fülöp, consisting of 6 staff members) provides the regular control of occupational doses of all workers employed by all workplaces in Hungary applying ionizing radiation sources. The tasks of the Service include:

- registration of dosimetry data of individual radiation workers,
- tracking, administering and supervising the cumulative committed effective personal doses for 5 year long periods
- notification of workplaces and authorities for checkups in case of exceeding the occupational dose limits defined by the relevant Hungarian regulations

- providing film dosimeters and badges for the workers to control their whole-body photon-doses,
- administration and documentation for radiation workers in category A employed outside Hungary is in accordance with requirements of the Decree No. 30/2001 of the Minister of Health (consistently with the Directive 90/641/Euratom)
- archiving of all data recorded and film dosimeters for 30 year long period.

The Service analyses and administers about 95,000 film dosimeters per year for 16,000 radiation workers employed at 1200 workplaces..

Department of Radiohygiene I. - Ionizing Radiations has numerous official contacts abroad and at home (IAEA, EC, Regional Public Health Centres of NPHMOS, Hungarian Atomic Energy Authority, National Board for Protection in Catastrophy, Nuclear Power Plant Paks Ltd, Radioactive Waste Processing and Storing Facilities, etc).

Department of Radiohygiene II. Non-Ionizing Radiations

The tasks of the Department (headed by Dr. György Thuróczy, PhD, consisting of 10 staff members) relate to research work on the biological and health effects of non-ionizing radiation (NIR involves electromagnetic fields and radiations in the frequency range from 0 Hz to 10^{15} Hz) and NIR radiation protection measurement in the environment and at the workplaces in Hungary. It includes:

- exposure measurement and radiohygienic certification of the workplaces,
- certification of NIR sources and protection devices against NIR
- taking part in the elaboration of the NIR standards and regulations,
- helping different authorities in decision making by providing expert's opinions in the field of health effects of NIR.

The research results were published in international scientific journals (eg. in Bioelectromagnetics and Electro- and Magnetobiology) and more than 100 presentations were held in the Bioelectromagnetics Society (BEMS) and European Bioelectromagnetic Association (EBEA) Annual Meetings.

The Department is represented in the following EU and international scientific and decision making committees: **EU CENELEC** TC 106x: European Committee for Electrotechnical Standardisation; **IEC**: International Electrical Committee, TC 106; **WHO EMF Project, International Advisory Committee**; **COST 281**: Co-operation in Science and Technology: „Potential Health Implications from Mobile Communication Systems”; **EBEA** (European Bioelectromagnetic Association)

Division of Electromagnetic Radiations

This Division consists of 6 persons, Head: Dr. György Thuróczy, PhD.

Research topics:

- biological and health effects of mobile phone radiations in vitro, in vivo and on humans
- radiofrequency dosimetry in tissue equivalent liquid phantoms (Fig.8)
- biological and health effects of 50 Hz magnetic field in vitro, in vivo

Measurement methods in Accredited Laboratory:

- Radiation protection measurement of radiofrequency (RF) and microwave (MW) transmitters
- Radiation protection measurement of RF and MW equipments in work places
- Radiation protection measurement of 50 Hz in the environment

- Radiation protection measurement of electric and magnetic field in the frequency range from 0 Hz to 30 kHz in work places
- Specific absorption rate (SAR) measurement of human exposure to RF radiation (300 MHz - 3 GHz), Fig.9.

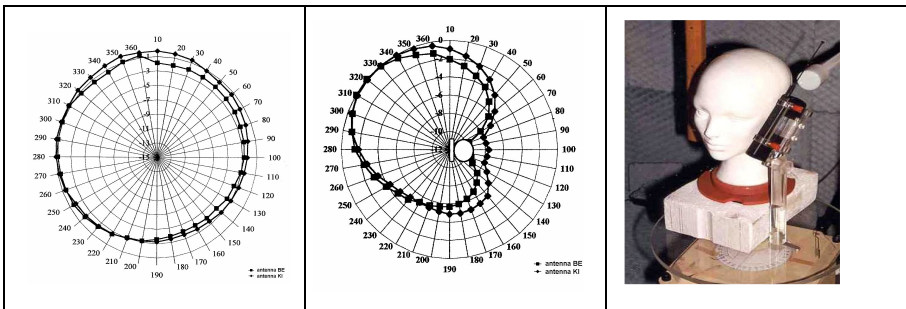


Figure 8: Measurement of radiation pattern of a mobile phone in the vicinity of empty human head shell phantom (left side) and when it was filled with tissue equivalent liquid (middle). The phantom head was turned around by a step motor driven carousel (right side), the power was set to 2 W. The radiation pattern of a mobile phone significantly altered in the vicinity of human head phantom. More than the half of the transmitted RF power was absorbed and the field became asymmetric.

Division of Optical and Laser Radiations

This Division consists of 4 persons, Head: Mr József Bakos.

Research topics:

- biological effects of optical radiations
- sunbed use by the public
- health effects of natural ultraviolet radiation from the Sun

Measurement methods in Accredited Laboratory:

- Radiation protection measurement of ultraviolet radiation in work places
- Radiation protection measurement of sun beds
- Certification measurement of protection devices against NIR
- Radiation protection measurement of laser radiation in work places.

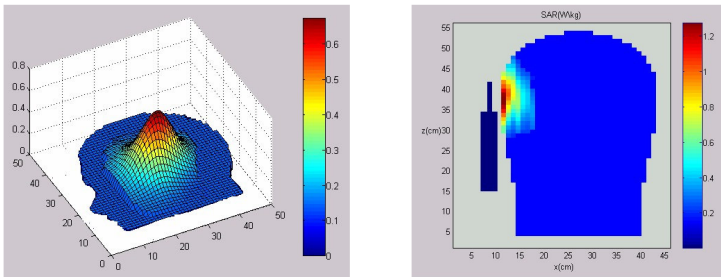


Figure 9. Specific absorption rate (SAR) distribution at 900 MHz frequency as the result of a measurement in human head shell phantom filled with tissue equivalent liquid (phone type: Nokia 6610i).

As it has been presented, NRIRR applies a broad variety of research methods and has gained an internationally and nationally recognised multidecade experience in studying radiation health effects, advising and consulting, teaching and training. NRIRR is open for further cooperation. Please, contact us: www.osski.hu & radbiol@osski.hu