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Proton Therapy of Tumours and the Possibilities of Its Introduction in the Slovak Republic

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Abstrakt: V liečbe onkologických ochorení sa okrem iného uplatňuje aj ožarovanie nádorov zväzkom ionizujúcich častíc. V súčasnosti je vo svete aj u nás štandardom liečba zväzkom fotónov a elektrónov. Tieto častice vykazujú exponenciálny pokles dávky v tkanive. To má za následok ožarovanie velkého objemu zdravých tkanív, ktoré sa nachádzajú "v ceste" zväzku. Práve rádiotoxicita zdravých tkanív je limitujúcim faktorom v rádioterapii. Protóny sa vyznačujú tým, že najviac energie strácajú na konci svojej dráhy. Dolet protónov je pritom možné regulovat vhodnou voľbou ich počiatocnej energie. Vďaka týmto vlastnostiam je možné pri ožarovaní zväzkom protónov dosiahnut menšiu dávku v zdravých tkanivách, čo vytvára priestor pre zvyšovanie dávky v nádore. Platí, že čím väčšia je dávka v nádore, tým vyššia je úspešnost liečby. Protónová terapia predstavuje moderný a velmi efektívny nástroj v boji proti onkologickým ochoreniam. Doterajšie klinické výsledky v zahraničí jednoznačne poukazujú na prínos protónovej terapie vo zvyšovaní úspešnosti liečby. Slovensko má v súčasnosti vytvorené podmienky na zavedenie hĺbkovej protónovej terapie v rámci projektu Cyklotrónové centrum SR v pomerne krátkej dobe.

Abstract: Besides other modalities, irradiation of tumours with a beam of ionizing particles is applied in the treatment of cancer. Currently, treatment with photon and electron beams is a standard worldwide and in Slovakia as well. These particles exhibit exponential falloff in tissues. This results in the irradiation of large volume of healthy tissues, which are located in the beam's path. Radiotoxicity of normal tissues is the limiting factor in radiotherapy. Protons are characterized by loosing the most of their energy at the end of their path. The range of protons can be controlled by the proper selection of their initial energy. These properties of protons make it possible to achieve lower doses to the healthy tissues, thereby allowing escalation of dose to the tumour. Higher doses to the tumour result in higher effectivity of the treatment. Proton therapy represents a modern and highly effective tool in the struggle against cancer. The present clinical outcomes have proved the benefit of the proton therapy for the improvement of the treatment successfullness. Slovakia has created conditions allowing implementation of the depth proton therapy within the frame of the Cyclotron Centre of the SR project in a relatively short period of time.

More than 20 000 new cases of malignant diseases are diagnosed anually in Slovakia. Cancer is the second most frequent cause of death in Slovakia and in the developed countries just after cardiovascular diseases. Furthermore, the incidence of cancer constantly increases as a result of civilization factors and better quality of diagnostics. Due to modern diagnostic equipment, it is possible to detect cancer at an stage, thereby increasing the chance for cure.

Besides surgery, chemotherapy and other treatment modalities, radiotherapy plays an important role in the treatment of cancer. It is based on the fact that cancer cells are more sensitive to ionizing radiation than the cells of healthy tissues. The aim of radiotherapy is

Devoted to Prof. Pavel Povinec 65-th anniversary to apply lethal dose on the tumour while sparing the normal tissues. Doses that exceed the tolerance of healthy tissues can cause severe and irreversible damage. Therefore, attention should be paid to the treatment planning. Nowadays the planning of radiotherapy is based on computers, which make it possible to calculate the dose of ionizing radiation in any point of a patient's body accurately. This is used to prepare the optimal irradiation plan.

At present photons and electrons with energy of several MeV produced by commercially available linear accelerators are used for radiotherapy. The accelerators are constructed to comply with the medical requirements. Photons and electrons have exponential dose-depth dependence. This means that for tumours located in a certain depth the maximum dose is not in the tumour. Moreover, the organs lying behind the tumour will also receive some radiation. This often leads to the irradiation of large volumes of normal tissues. In other words the integral dose outside the tumour is high.

The situation is different for the proton therapy. Due to the physical properties of these particles, a substantial increase in the conformity of radiotherapy can be achieved. This means that the protons are able to focus the dose on the tumour more precisely. This property of protons can be explained by the phenomenon called Bragg's peak. The dose deposited by the protons rises steeply in the end of their range, which is a function of the initial energy. By selecting the proper energy the Bragg's peak can be moved directly to the tumour. It is proved that the integral dose in the healthy tissues is 2 to 3 times lower with protons than with photons. This enables dose escalation in the tumour without breaking the tolerance limits of normal tissues.

Proton therapy represents a big step in the treatment of oncological patients. Its benefit in the form of higher successfulness of treatment and considerably lower incidence of complications connected with irradiation is definitely proved. Over the last years there is a “boom“ of proton therapy in the world. It is expected that this kind of treatment could gradually replace the conventional radiotherapy. The number of hospitals with proton therapy abroad is growing every year. Mass development is, so far, limited by high costs of the construction of such centres. Russian scientists proposed and built a simplified and much cheaper proton therapy complex, which is a fully operational tool in the fight with tumour diseases. Proton therapy became accessible to small countries such as Slovakia.

Radiotherapy planning

Before the treatment of the patient starts, it is necessary to prepare an individual irradiation plan. It is a proccess consisting of several steps. Firstly, the radiation oncologist has to decide whether the patient is indicated for radiotherapy. If yes, the dose of radiation, the type and energy of radiation, irradiation technique and, of course, the treated site have to be determined. The irradiation technique is defined by the number and spatial orientation of the beams which are called fields in radiotherapy. There are some widely used standard techniques, e.g. two opposite fields or “box“ technique (two front–back and two side fields). The reason for the use of more than one field is the effort to achieve homogeneous dose distribution in the target volume and to ensure that the radiation tolerance of healthy tissues will not be exceeded. The modern linear accelerators (Fig. 1), which are used in the conventional radiotherapy, allow irradiation with electrons and photons with different energies. Electrons are used for the irradiation of superficial sites (skin, chestwall after breast surgery ...). Tumours located more deeply are treated with photons. The most frequently used photon energies are 6 MV and 18 MV. The label "6 MV" describes the maximal energy of photons. The spectrum of the bremstrahlung photons is continuous and its maximum is approximately in the third of the maximal energy.

After accepting the patient for radiotherapy he/she is sent to the so-called simulator – machine simulating the irradiation conditions. The simulator is equipped with an X-ray tube attached to a gantry. It can be used to visualize patient's anatomy. During the simulation the patient stays in the position in which he/she will be irradiated (the simulator itself is not intended for irradiation). The radiation oncologist draws lines on the patient's skin which will be used for repositioning of the patient. The correct positioning is crucial in radiotherapy. It is not a simple task because a patient is not a "solid body". His body is in a constant motion. There is a respiratory motion and the internal organs motions (e.g. peristaltic motion). Moreover the patient can loose weight during the course of radiotherapy or the radiation can lead to the tumour shrinkage. All the mentioned motions and changes influence the accuracy of hitting the target volume.

The next step in the process of radiotherapy planning is CT (computer tomography) of the treated site. CT examination is used for both – to localize the tumour and to obtain relative electron density of the tissues, which is then used for the dose calculations. Fig. 2 represents a transversal CT slice in the pelvic region with a computed dose distribution in the form of isodose curves – lines connecting points with the same dose. The task of the radiation oncologist is to delineate the so-called target volume on the transversal CT slices. The CTV (clinical target volume) consists of the gross tumour (visible or palpable tumour) and the adjacent region with microscopic disease. The so-called critical organs like spinal cord, kidneys, lungs etc. have to be delineated as well. Besides CT other diagnostic modalities are often used for radiotherapy planning, especially MRI (magnetic resonance imaging) and PET (positron emission tomography). Use of several diagnostic tools increases the accuracy of the disease localization thereby increasing the treatment effectivity.

According to the delineated target volume and the requests of the radiation oncologist the physicist prepares the irradiation plan. The physicist has to set up the field parameters (field size, gantry angle, collimator angle, field weight,..) to achieve a homogeneous dose distribution in the CTV with the prescribed dose and the dose in the critical organs as low as possible. At present the conformal radiotherapy is considered a standard. It uses shielding blocks or multi-leaf collimator (MLC, Fig. 3) to adapt the shape of the field to the CTV. The shape of blocks or the position of the leaves of MLC is adjusted in the treatment planning system in the BEV (beam's eye view) mode, which is a view of the patient from the beam direction. This function is a standard component of the modern planning systems (Fig. 4).

After the preparation of the treatment plan – often more variations, the radiation oncologist has to choose the plan which he/she considers to be optimal taking into account the dose homogeneity in the target volume and the dose distribution in the critical organs. After completing this last step the patient is ready for the first irradiation fraction.

From the conventional radiotherapy to protons

The use of protons for the treatment of oncological diseases was first proposed by Robert R. Wilson in 1946. This idea was realised a couple of years later, in 1954, more than half a century ago, in Berkeley. In 1957 the proton therapy was introduced in Uppsala (Sweden) and other physical laboratories in Russia, USA, Japan and other countries joined gradually. Only horizontal beams were used for the treatment because there were no proton gantries available in that period of time. The first proton centres were dedicated to the treatment of specific diseases like diseases of the pituitary gland, arteriovenal malformations, ocular melanomas and Parkinson disease.

Eye tumours are irradiated with protons with energy of about 70 MeV. The treatment method was developed in the laboratories in Berkeley and Harvard and transferred later to Europe (PSI, Switzerland). The progress in the field of diagnostics in medicine (introduction of CT, MRI and PET) enabled precise localization of tumours and treatment planning. This allowed the proton therapy to be extended to other sites of the body.

Despite the relatively long history of proton therapy the number of patients treated with protons so far is only of the order of ten thousands worldwide. The reason for that is the long-term absence of dedicated proton centres. The proton therapy was available only in physical laboratories for the past decades and it was only in the 1990's when the first hospital-based proton centres appeared. The first decade of the 21st century is characterised by a flourishing of proton therapy. In the USA, Western Europe, Japan and other countries the number of proton centres grows each year. Recently the number of patients treated with proton therapy worldwide has exceeded 50 000. Proton therapy is no more a domain of laboratories – it becomes commercially available.

Physical properties of protons and their interaction with matter

Protons are electrically charged particles with a positive charge equal to 1. From the point of view of chemistry protons are positive ions of hydrogen, which is logically the source of protons. When passing through the matter the protons steadily loose their energy until they are almost stopped. The distance travelled by protons until being stopped is called range. This quantity depends on the initial energy of the protons. The range-energy dependence of protons in water is illustrated in Fig. 5. It is clear from the graph that the range of protons increases with energy faster than linearly.

The energy loss of heavy charged particles such as protons is caused by their interaction with electrons bound in atoms and molecules (excitation, ionization), nuclear reactions and bremstrahlung. The most relevant of these mechanisms are the collisions of protons with electrons. These collisions cause the gradual loss of energy of protons along their path. The energy losses can be described by the Bethe-Bloch formula, according to which the specific energy loss is proportional to the square of particle's charge (z), atomic number of matter (Z), number of atoms per volume unit (N) and indirectly proportional to the square of particle's velocity (v):

$$dE/dx \sim z^2.Z.N / v^2$$

Some important implications can be made from this formula:

1. heavier ions with higher charge have higher specific energy loss
2. in a medium with higher density the specific energy loss is higher (e.g. in bones it will be higher than in soft tissues)
3. the specific energy loss increases with decreasing velocity of a particle

Nuclear reactions also have a considerable impact on the character of a proton beam. When passing a 20 cm thick layer of tissue 25 % of the protons will interact with nuclei of the medium. Inelastic nuclear reactons result in a lower number of primary protons in the beam and in release of secondary particles (neutrons, ions, radioactive nuclei). Energy loss caused by bremstrahlung is negligible for the energies typical for proton therapy.

Advantages of proton therapy

The aim of radiotherapy is to apply a lethal dose of ionizing radiation to the tumour while keeping the damage of healthy tissues at an acceptable level. Ideally we would like to irradiate the tumour with a high dose and to have a zero dose outside the tumour. Unfortunately, this is technically impossible. The experts working in radiotherapy try to approach this ideal state as close as possible.

Introduction of IMRT (Intensity Modulated RadioTherapy) in the conventional radiotherapy has resulted in a higher conformity. This method allows decreasing of the dose in critical organs located very close to the target volume. Thanks to this the dose to the tumour can be higher, thereby improving the perspective of patients. However, the introduction of IMRT the possibilities of conventional radiotherapy are practically exhausted. Further progress in radiotherapy can be achieved only by switching to a new type of particles. At present the research is focused on particles like protons, neutrons, heavy ions and antiprotons. Each particle has its own dose-depth distribution.

The benefit of proton therapy in comparison with conventional radiotherapy can be derived from a different mechanism of energy transfer to the medium. The protons deliver most of their energy at the end of their range. This is known as Bragg's peak (Fig. 6). The dose beyond the Bragg's peak falls rapidly to zero. Unlike this the dose for photons decreases exponentially with depth. Therefore, when comparing protons with photons, it is often said that the protons have an inverse dose-depth distribution. The position of the Bragg's peak depends on the energy of protons. With appropriate selection of energy the maximum of dose can be delivered to the tumour. Beyond the tumour the dose is equal to zero (in fact, not exactly zero but negligible). This advantage can be fully utilized in the cases when a critical organ is very close to the tumour. Furthermore, the integral dose in normal tissues is 2 to 3 times lower for protons than for photons. This results in a reduction of radiotoxicity of the treatment and allows dose escalation in the tumour. Increase of the dose in tumour of 10 % can lead to a TCP (tumour control probability) increase by 15–20 %.

Another advantage of protons is that they are electrically charged particles and, therefore, can be controlled by magnetic field. This fact is used for tumour scanning with a thin proton beam, which will be described later. The possibility of controlling the proton beam is used also for the transport of the beam from the accelerator to the treatment rooms. One accelerator can produce a beam for several treatment rooms.

Protons exhibit a smaller lateral scattering and, therefore, also sharper beam boundaries than photons. Interactions of protons with a medium can result in nuclear reactions in which neutrons are released. However, the contribution of neutrons to the overall dose is negligible. One of the products of nuclear reactions caused by protons in a human body are also radionuclides with a short half-life. They can be utilized to check the dose distribution in the body in a PET examination. Radionuclides do not represent any risk for the patient.

The best way to consider advantages of proton therapy is to compare particular irradiation plans. Fig. 7 shows an IMRT plan with 9 fields at the left and a proton therapy plan with 4 fields at the right. The target volume is the delineated yellow and the critical organs are red. In both cases the maximal dose is delivered to the target volume with a high accuracy but in the case of protons the integral dose outside the target volume is substantially lower than for IMRT.

Accelerators for proton therapy

A suitable accelerator is essential for preparation of a therapeutic proton beam. Basic requirements for these accelerators are the following:

1. *Energy of protons adjustable in the range of 70–230 MeV.* This energy interval allows irradiation of tumours localised in all parts of the body. However, if the accelerator is intended only for a specific localization of tumours, e.g. eye tumours, it is sufficient to have only energy that covers that specific localization (in the case of eye tumours 70 MeV is sufficient). If the accelerator produces a proton beam with energy above 300 MeV then the proton tomography can be introduced.

2. *The current of protons in the order of tens to hundreds of nA*.This requirement is derived from the typical time for one fraction which is a few minutes. Too long irradiation times are uncomfortable for the patients and too short times do not allow the staff to respond in the case of a mistake.

3. *High reliability, simple operation and availability*. A medical accelerator should have a simple maintanance. Accelerator is usually operated by people who do not have detailed information about the function of individual components. Therefore the operation of it should be as simple as possible.

The most common accelerators for the proton therapy are cyclotrons and synchrotrons. Current linear accelerators are too large and too expensive for medical purposes. However, in USA researchers proposed only 2 m long linear accelerator for proton therapy which could be mounted to a gantry. The price of this system should be acceptable.

The main advantage of a cyclotron is its compactness. As a result of a massive electromagnet, which is a part of cyclotrons, these accelerators are rather heavy – their weight is several hundreds of tons. The core of a cyclotron is a cylindrical vacuum chamber situated in a sectoral magnetic field oriented in the direction of vacuum axis (usually vertical direction). The magnetic field is produced by two poles situated above and under the chamber. Accelerated particles (protons) follow a helical path from the middle of the chamber to its edge. The cyclotrons are divided into two groups – isochronous cyclotrons and synchrocyclotrons. Moreover, a cyclotron can be equipped with a superconducting magnet, which results in the reduction of the size of cyclotron.

Isochronous cyclotron compensates for the relativistic increase of the mass of the accelerated protons by constantly increasing the magnetic induction from the middle to the edge. The frequency of the electric field is kept constant allowing a continous regime of acceleration. A synchrocyclotron has a constant magnetic field and the frequency of the electric field changes. It works in an impulse regime. The disadvantage of cyclotron is the fixed energy of the extracted protons (equal to the maximal energy for the particular accelerator). Therefore, it is necessary to use absorber with a variable thickness to reduce the energy of protons. In the case of applying a scanning technique the speed of scanning is limited by the speed of mechanical motion of the absrober. Furthermore, the presence of absorber results in undesirable activation of material.

Synchrotron has a toroidal shape and the magnetic field is present only in the ring. A typical diameter of medical proton synchrotrons is 6–8 m. Synchrotron consists of an injector (usually a small linear accelerator), magnetic dipols and quadrupoles, a high-frequency system and a system for extraction of the beam. Magnetic dipoles are used to bend the trajectory of protons and the quadrupoles ensure beam focusing. Between two dipoles the beam propagates straightforward. Unlike in cyclotron the particles in a synchrotron do not travel along a spiral but in an approximately circular path with a constant radius. The magnetic induction in the ring increases proportionally to the momentum of accelerated particles. This fact results in an impulse character of acceleration in a synchrotron. For the scanning technique a slow beam extraction is used because, it can solve problems connected with impulse regime of synchrotrons. The principle of slow extraction is that during every revolution of particles in the ring only a small fraction of particles are extracted and therefore, the beam seems to be almost continuos. A typical duration of slow extraction is in the order of tenths of seconds which is milion times more than the duration of one revolution. An important advantage of synchrotrons is their ability to change the energy of protons during irradiation. This feature is utilized when applying the scanning technique.

Transport of proton beam from accelerator to the patient

Linear accelerators used in the conventional radiotherapy are situated directly in the treatment room. Each treatment room has its own accelerator. In the case of proton therapy only one accelerator located outside the treatment rooms is needed because it can supply the beam sequentially to all the treatment rooms. Transport of the beam from accelerator to the treatment rooms is performed via transport channel. The beam is either fixed (usually horizontal) or it can pass through a gantry. Large proton therapy centres in the world are commonly equipped with one to three gantries. These devices allow irradiation of a tumour from different directions without moving the patient during the treatment. However, proton gantries are much bigger and heavier in comparison with electron gantries used in conventional radiotherapy. Their radius of rotation can be up to 5 m in contrast to 1 m typical for conventional radiotherapy. The mass of a proton gantry is typically 100 tons and its price is comparable to the price of the accelerator itself. Fig. 8 shows a proton gantry with an unusually small radius of rotation (only 2 m) in PSI, Switzerland. The patient can see merely a part of the gantry. The rest is hidden behind the panel. A cheaper alternative to a gantry is a fixed horizontal beam in combination with a rotary chair.

Modification of a proton beam

The beam from the accelerator is usually very thin and almost monoenergetic. Such a beam is not suitable for radiotherapy. Two basic techniques of beam modification are used – active (scanning technique) and passive (scattering technique).

If a scattering technique is used, the beam will pass at first through a range modulator (Fig. 9), which will spread the Bragg's peak to cover the entire tumour. This is called the „Spread-Out Bragg's peak“ (SOBP). Fig. 10 shows a SOBP, which is a superpostition of proton impulses of different range and relative weight. These parameters were chosen in order to achieve a homogeneous dose distribution in the target volume. A range modulator can be a wheel with leaves of various thicknesses. If a beam passes through a modulator it will contain particles with a variety of energies. For lateral expanding of the beam scatter foils are used. They are made of a material with high atomic number (e.g. lead), where multiple coulomb scattering takes place. If only one foil is applied, the beam profile will be gaussian. Addition of a second foil will ensure almost uniform fluence of particles. Finally, the beam passes through a collimator and compensator, which will adapt the beam to the shape of the tumour. The compensator and collimator are produced individually for each patient and that is, of course, time-consuming.

However, this traditional and widely-used technique has some disadvantages:

- Time-consuming production of compensators and collimators
- Loss of energy in the range of 10–20 MeV in the scatter foils
- Emission of secondary neutrons in the scatter foils
- This technique is not applicable for proton therapy with modulated intensity

Therefore active modification of the beam is more preferred. Protons posess an electric charge which allows control of their motion with magnetic field. A set of two orthogonal magnets is used to deflect a proton beam. If the target volume is virtually divided into small cells, than it is possible to irradiate each cell individually with a narrow beam (diameter of a few mm) focused on the actual cell. The focusing in the beam direction is achieved by the modulation of the beam energy. At first the cells lying in the plane with the highest depth are irradiated. Then the energy of protons is decreased and the next plane is irradiated. The process continues untill the entire target volume is irradiated. The principle of scattering technique is explained in Fig. 11.

The intensity of radiation in each cell is chosen independently. This resembles IMRT in the conventional radiotherapy with the difference that in the case of protons the scanning is three dimensional (in the “depth direction“ as well). Therefore, some of the authors propose the term RIMPT (Range-Intensity Modulated Proton Therapy) to emphasize the 3D character of proton therapy.

Proton therapeutic complex of the Cyclotron Centre of the Slovak Republic

Proton therapy represents a modern and effective tool in the campaigne against malignant diseases. It is proved by the increasing interest in this treatment modality and a growing number of proton centres worldwide. Proton therapy has moved from physical laboratories to hospitals and became commercially available. After the introduction of IMRT this is another big step in the development of radiotherapy. Clinical outcomes clearly prove higher successfullness of proton therapy in comparison with conventional radiotherapy.

At present the conditions in Slovakia allow to establish a proton therapy centre in a relatively short period of time of 2–3 years. Slovakia could become the first country among new member states of the European Union which will own and operate this hi-tech technology.

Cyclotron Centre of the Slovak Republic

The aim of the project "Cyclotron Centre of the Slovak Republic" is to implement modern global trends in the field of improving the quality of life and health of population via progressive technology – accelerator producing charged particle beams with high energies. Several organisations controlled by Ministry of Health of SR, Ministry of Economy of SR, Ministry of Defence of SR, Ministry of Education of SR, Ministry of Environment of SR, Ministry of Building and Regional Development of SR, Department of Nuclear Inspection of SR, Slovak Academy of Sciences and Department of Normalization, Metrology and Examination of SR have united their effort to achieve this aim.

Activity of the Cyclotron Centre of the Slovak Republic in the field of health service is considered a priority. It is concentrated on preparation of new opportunities for nuclear medicine and radiotherapy to ensure early diagnostics of oncological, brain and heart diseases and to create new ways of treating cancer.

Existing departments of the Cyclotron Centre of the Slovak Republic

Within the frame of the Cyclotron Centre of the SR project, which has a multidisciplinary character encompassing health service, industry, education and other branches, several important stages have been already completed. Other facilities with a broad impact in the health service are in the phase of preparation and planning. At present CCSR consists of these departments:

1. Department of Positron Emission Tomography at the Clinic of Nuclear Medicine in the Oncology Institute of St. Elizabeth and Faculty of Medicine of the Comenius University in Bratislava
2. Department of Nuclear Medicine at the Internal Clinic of Central Military Hospital in Ružomberok
3. Department of Micro-PET at the Institute of Experimental Endocrinology of the Slovak Academy of Sciences in Bratislava
4. PET Centre Bratislava

The above mentioned departments comply with all requirements from radiochemistry, radiopharmacy and radiohygiene and they are already integrated in the network of health facilities. They enable not only an early diagnostics of cancer, brain and heart diseases with modern methods of positron emission tomography but also own production of short-lived radionuclides and PET-radiopharmaceuticals for the nuclear medicine departments in Slovakia and neighboring countries. The research is provided as well. The establishment of the radiopharmaceuticals production allowed foundation of a private department of nuclear medicine in Nitra, which is equipped with a PET tomograph.

Further development of the Cyclotron Centre of the SR

The present stage of building up of the Cyclotron Centre of the SR is in the field of health service concentrated on creation of new possibilities for the treatment of cancer. CCSR allows implementation of new progressive methods of cancer treatment like proton therapy, neutron capture therapy and fast neutrons therapy.

The technical parameters of the basic facility of the CCSR – cyclotron DC-72 (Fig. 12) make it possible to implement all the above mentioned progressive treatment techniques. It was constructed in the Joint Institute for Nuclear Research in Dubna, Russian Federation and it will be transported and installed in Slovakia soon.

Proton therapy is planned to be put into operation as a priority. Slovak Republic will join developed countries, which already treat patients with proton therapy. Moreover, Slovakia has a chance to become a leader in this branche in the region of Central and Eastern Europe. However, the energy of protons accelerated in cyclotron DC-72 is sufficient only for proton therapy of tumours located in the depth of up to 3 cm. Therefore the CCSR will provide only proton therapy of eye tumours.

Proton Therapeutic Complex of the Physical and Technical Centre of the Institute of Physics of P. N. Lebedev of the Russian Academy of Sciences

The construction of proton therapy complex within the project of CCSR and putting it into operation will enable the extention of proton therapy to all the sites of a human body. The complex should become a part of the Military Hospital in Ružomberok. A new building is planned to house this complex.

Proton therapy centres built in the developed countries are expensive and require considerable space because of the huge gantries. Their price is in the range of 2–3 billion Slovak crowns. A much cheaper but fully operational alternative is the proton therapeutic complex on the basis of proton synchrotron developed in the Physical and Technical Centre of the Institute of Physics of P. N. Lebedev of the Russian Academy of Sciences (Fig. 13 and 14). It is a compact synchrotron with a diameter of less than 5 m built exclusively for medical purposes. The system is proposed to allow application of the scanning technique thereby utilizing the advantages of highly conformal proton therapy with modulated intensity. The parameters of the proposed synchrotron are as follows:

- Energy of protons in the range of 70–250 MeV ± 0.15 % with a possibility to change the energy during irradiation (the energy can be increased up to 330 MeV in the case of the introduction of proton tomography)
- Time needed to accelerate protons to the energy of 250 MeV – 1 s
- Slow extraction of the beam controlled by the computer. Duration of extraction – 0.1– 10 s
- Extraction effectivity ~90 %
- Beam diameter – 2– 20 mm
- Typical duration of one fraction – 1– 5 minutes
- Power consumption: maximal 100 kW, average 50 kW
- Overall weight – 15 t

Space requirements:

- Area with radiation protection – 8 13 m^2 (including the treatment room)
- Control room – 20 m^2
- Room for the refrigerating system and power sources – 30 m^2.

The sychrotron is equipped with a beam scanning system with a frequency of up to 200 Hz in the vertical direction and up to 1 Hz in the horizontal direction. Patients can be irradiated in the following positions: standing, sitting and lying. The positioning system allows the motion of patient in the vertical direction and also rotation around the vertical axis. If the patient is in the lying position only vertical motion will be available.

Components of the proposed complex

The facility also includes:

- operator console with computer and visual control (on the screen) of the irradiation process
- CT with a spatial resolution of 1–2 mm allowing vertical positioning of the patient. 3D image from the CT can be used also for treatment planning
- X-ray tube with a low intensity. The image appears on the screen of the computer and is automatically compared with the data stored in the database. If the images are significantly different, the operator will be warned and the irradiation can continue only after typing the password.
- Dosimetric devices for monitoring of the beam parameters – energy, intensity, position, dose, etc. If the deviation of these parameters from the plan exceeds the tolerance limits, the irradiation will be aborted. The information about the irradiation process is stored automatically thereby allowing resuming of the irradiation
- Devices for calibration and monitoring for calibration of the beam energy on a phantom, field-shaping system
- A set of spare parts
- Monitoring service via internet. The operators in the Institution will regularly connect to the control database of the proton complex, which contains specific information about the present state of the facility

The proton therapeutic complex is delivered with a 3-year full warranty. During this period all necessary service is free of charge. The planned lifetime of the complex is at least 25 years.

Conclusion

Slovakia has gained a big advantage in the implementation of modern accelerator technologies, especially in the health service over the neighboring countries by realization of the “Cyclotron Centre of the SR” project (from the debt of the Russian Federation towards the Slovak Republic). Today we have a new opportunity to exploit this advantage. The current conditions in the Central Military Hospital of SNP in Ružomberok allow, in a relatively short period of time (2–3 years), building up and putting into operation the depth proton therapy of oncological diseases. In the case of a successfull and early realization of the project “Proton Therapeutic Complex of the Cyloctron Centre of the SR at the Central military hospital of SNP in Ružomberok” Slovakia can become not only the first of the new EU members performing the depth proton therapy but also one of a few countries in the world which will own and use this new modern technology (proton knife). It is time for the above mentioned discoveries (utilization of protons for cancer treatment and new highly sophisticated technical solution of proton beam application – “proton knife”) to find a place in the everyday life. To make the proton treatment of cancer available for everyone.

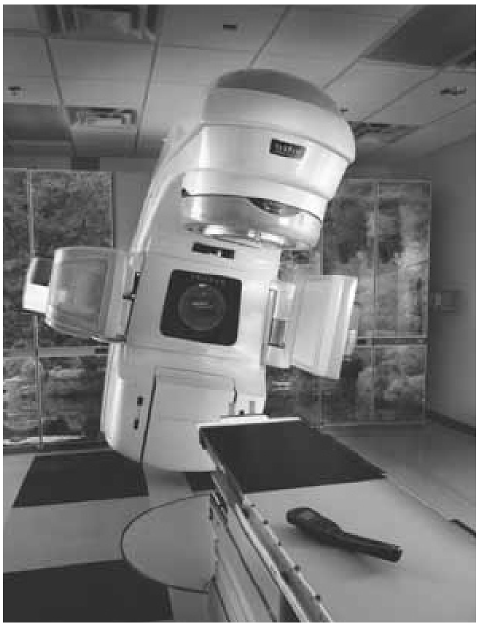

Fig. 1. Linear accelerator. In the foreground there is an irradiation table with manual controller.

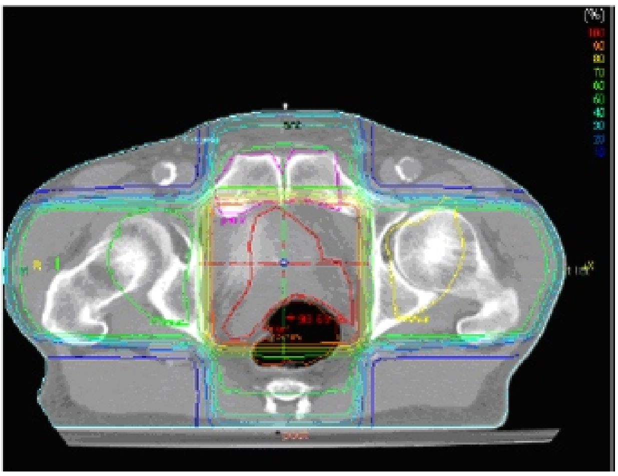

Fig. 2. CT slice in the pelvic region with isodose curves (curves connecting points with the same dose). Every colour represents a certain percentual dose. In the middle the target volume is delineated with a red contour.

Fig. 3. Multi-leaf collimator – the position of individual leaves defines the shape of the irradiation field.

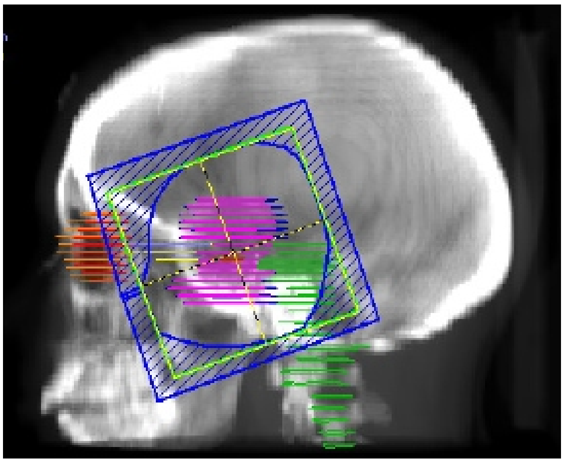

Fig. 4. Beam's eye view – the irradiation field in the temporal region is represented by the yellow rectangle, the blue stripped region is shielded with blocks.

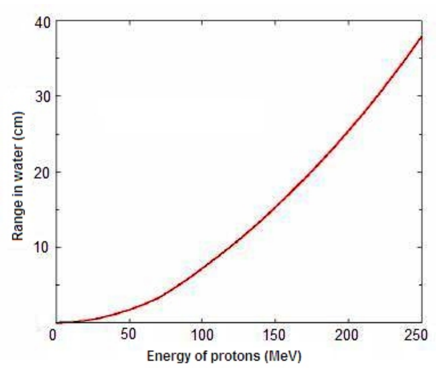

Fig. 5. Range-energy distribution of protons in water.

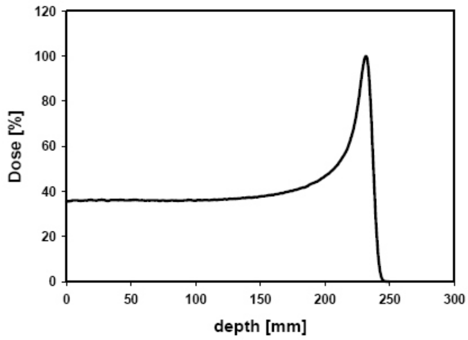

Fig. 6. Bragg's peak for protons with energy of 180 MeV in water.

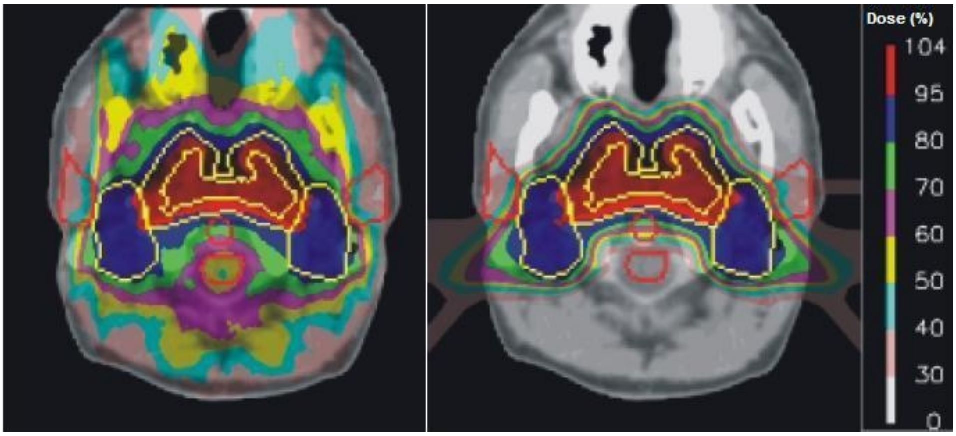

Fig. 7. Comparison of IMRT and proton therapy. The tumour is located near the skull base. Target volume (tumour + lymph nodes) is delineated yellow, critical organs (salivary glands, brain stem) red. In the left – IMRT plan with 9 fields. In the right – proton therapy plan with 4 fields.

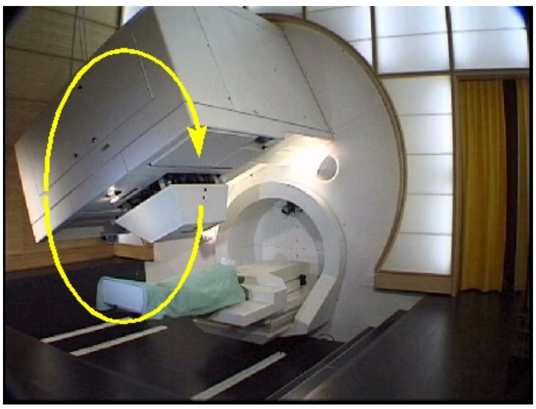

Fig. 8. Proton gantry in Paul Scherrer Institut, Switzerland.

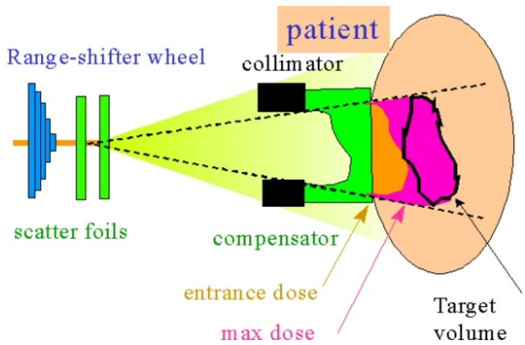

Fig. 9. The principle of scattering technique. The beam propagates from the left to the right in the scheme passing through a range-shifter, scatter foils, collimator and compensator and finally reaching the target volume in the patient's body.

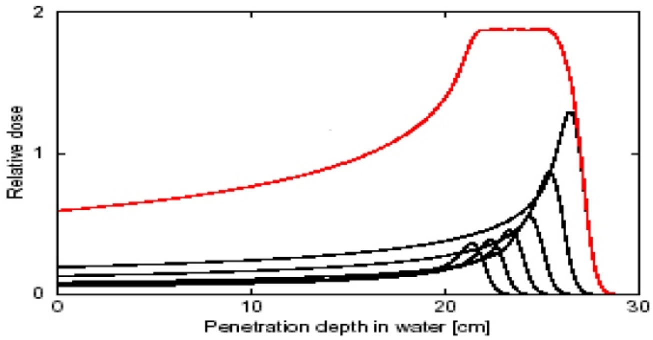

Fig. 10. Spread-Out Bragg's peak as a result of superposition of proton impulses of various range and relative weight. The parameters of impulses were chosen to achieve a homogeneous dose distribution in the tumour.

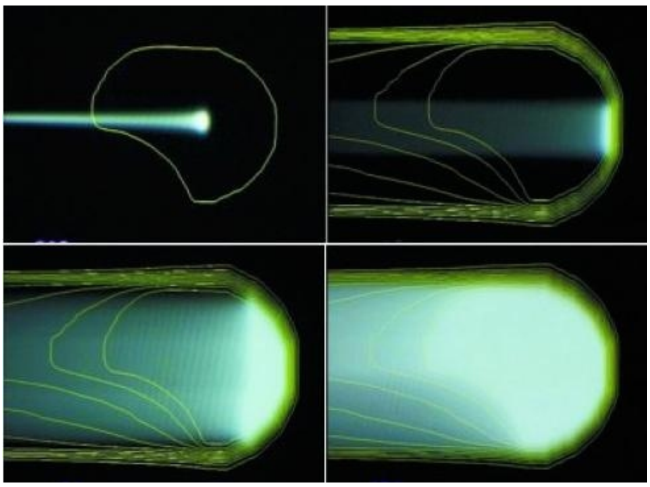

Fig. 11. The principle of scattering technique. A narrow beam scans the individual layers of the tumour starting at the deepest layer. After each layer the energy of protons is decreased.

Fig. 12. Cyclotron DC-72 with a maximal energy of protons of 72 MeV constructed in Dubna for the Cyclotron Centre of the Slovak Republic. One of the intended applications of the cyclotron is proton therapy of eye tumours.

Fig. 13. Medical proton synchrotron for Slovakia at the construction site in Protvino, Russia.

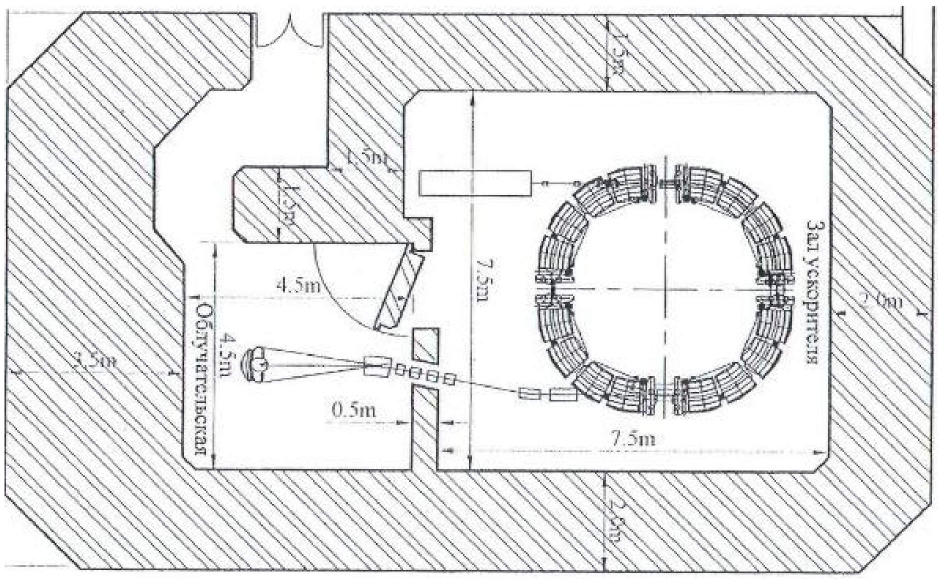

Fig. 14. Plan showing the position of the synchrotron in the treatment room and the radiation protection requirements.

Abbreviations used in the text

BEV – beam's eye view
CT – computer tomography
CTV – clinical target volume
IMRT – intensity modulated radiotherapy
MLC – multi-leaf collimator
MRI – magnetic resonance imaging
PET – positron emission tomography
RIMPT – range-intensity modulated proton therapy
SOBP – spread out Bragg's peak
TCP – tumour control probability

Reference

[1] H. Paganetti, T. Bortfeld: Proton Beam Radiotherapy – The State of the Art *http://www.aapm.org/meetings/05AM/pdf/18-4016-65735-22.pdf.*
[2] M. R. Bussiere: Northeast Proton Therapy Center *http://neurosurgery.mgh.harvard.edu/ProtonBeam/NPTCbrochure.pdf.*
[3] S. Peggs, 2002: Proton Accelerators for Therapy & Imaging *http://scipp.ucsc.edu/~hartmut/Radiobiology/IEEE_2002/nss_021113_Peggs.pdf.*
[4] J. Flanz, 2006: Beam Requirements for Particle Therapy *http://www.c-ad.bnl.gov/ffag-2006/presentations/Thursday/JFlanz.pdf.*
[5] M. Schippers, D. Anicic et al.: Commissioning of the New Proton Therapy Facility – PROSCAN, PSI Scientific Report 2005, Vol. 1 *http://atk.web.psi.ch/8800/2005/2005_1page98.pdf.*

[6] U. Amaldi: Future Trends in Cancer Therapy with Particle Accelerators. Zeitschrift für Medizinische Physik **14** (2004) 7 16 *http://www.tera.it/ise/attach/DFILE/569/HUG_ZMP_Amaldi.pdf.*
[7] T. Parisi: Proton Proponents *http://www3.niu.edu/devrel/northernnow/Images1/proton.pdf.*
[8] S. Ternier: Proton Therapy *http://www.protontherapyillinoisnews.com/Background/ProtonTherapyWhitePaper.pdf.*
[9] R. W. Schulte: Strategies for Image-guided Proton Therapy of Cancer *http://www.touchbriefings.com/pdf/2812/Schulte.pdf.*
[10] E. Pedroni: Latest Developments in Proton Therapy *http://epaper.kek.jp/e00/PAPERS/WEXF102.pdf.*
[11] P. Watson: Use of Proton Therapy Expands. Oncology Times, Vol. 28, No. 24 *http://www.oncology-times.com/pt/pt-core/template-journal/oncotimes/media/ /Watson-ProtonTherapy-OT-Dec252006.pdf.*
[12] S. Wampler: First Compact Proton Therapy Machine for Cancer Treatment Centres Development. Published on the web site of Lawrence Livermore National Laboratory: *https://publicaffairs.llnl.gov/news/news_releases/2007/NR-07-06-06.html.*

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