1000 MeV Proton beam therapy facility at Petersburg Nuclear Physics Institute Synchrocyclotron

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Abstract Since 1975 proton beam of PNPI synchrocyclotron with fixed energy of 1000 MeV is used for the stereotaxic proton therapy of different head brain diseases. 1300 patients have been treated during this time. The advantage of high energy beam (1000 MeV) is low scattering of protons in the irradiated tissue. This factor allows to form the dose field with high edge gradients (20%/mm) that is especially important for the irradiation of the intra-cranium targets placed in immediate proximity to the life critical parts of the brain. Fixation of the 6 mm diameter proton beam at the isodose centre with accuracy of ± 1.0 mm, two-dimensional rotation technique of the irradiation provide a very high ratio of the dose in the irradiation zone to the dose at the object's surface equal to 200:1. The absorbed doses are: 120-150 Gy for normal hypophysis, 100-120 Gy for pituitary adenomas and 40-70 Gy for arterio-venous malformation at the rate of absorbed dose up to 50 Gy/min. In the paper the dynamics and the efficiency of 1000 MeV proton therapy treatment of the brain deceases are given. At present time the feasibility study is in progress with the goal to create a proton therapy on Bragg peak by means of the moderation of 1000 MeV proton beam in the absorber down to 200 MeV, energy required for radiotherapy of deep seated tumors.

1. Introduction

The Proton Therapy Facility is a joint Project of Petersburg Nuclear Physics Institute (PNPI) and Central Research Institute of Roentgenology and Radiology (CRIRR) St.Petersburg starting proton therapy of patients in 1975. The Gatchina synchrocyclotron has a fixed energy of extracted proton beam-1000 MeV. The advantage of the high energy proton beam is a low scattering of protons in the tissue. Protons of such energy easily penetrate through irradiated
object producing a uniform ionization along their track. Due to low scattering of protons in the tissue, a narrow beam with sharp edges formed at the entrance of irradiated zone inside the object. Such irradiation method combined with two direction rotation technique allows to provide a very high ratio of the dose in irradiated zone to the dose at the object’s surface. Obtained by such method the dose fields with high edge gradients are especially important in the cases when the irradiation is used for selective damage of the volumes placed in immediate proximity to the life-critical organs. Our method gives the most effective results at proton treatment of the hormone-dependent forms of cancers such as a cancer of mammary glands, prostate and uterine cervix as well as different types of hypophysis adenomas, diabetic angioretinopathy, malignant tumors of eyes, arterio-venous malformations, etc.

Usually protons used for the irradiation have the energy of (70-200) MeV. Their range in the biological tissues appropriate to the location of the irradiated neoplasm. The effect of enhancement of proton ionization losses in the end of the range (Bragg peak) helps to shape the proper dose fields. To strengthen this effect a technique of multiple irradiation of the selected zone from various directions in combination with conformal collimator system for forming of necessary dose field distributions is used in proton therapy on Bragg peak-see, for example, (1,2). In this paper we present results of 1000 MeV proton stereotaxic therapy of different head brain diseases performed during 1975-2005 and the description of medical beam-line upgrade has been done in 2003-2004. Data of our early experience in proton therapy are given in (3-5).

2. Technical features of proton therapy facility

The PNPI proton therapy facility is based on synchrocyclotron with fixed proton energy E=1000 MeV, built with the aim to use it for the investigation on nuclear and particle physics at moderate energies. Schematic view of synchrocyclotron and layout of beams are shown in Fig.1 and Fig.2.

![Figure 1. Schematic view of PNPI synchrocyclotron](image)

Accelerator has three extracted in experimental hall proton beams with fixed energy E=1000 MeV and regulated intensities in the range 10^7-10^11 proton/sec (P1, P2, P3). The current inside vacuum chamber of accelerator is 3 μA. There are also two pion ("+" and ") beams with maximum momentum of 250 and 450 MeV/c and intensity 10^4-5·10^5 (pion/sec (π1 and π2 A, B) used only for physical experiments. The structure of proton medical beam P2 is shown in Fig.2. The extracted from the accelerator proton beam is collimated by the beam shaping collimator placed just at the entrance of beam channel and it regulates the size of beam spot and consequently the intensity of the beam. In point (1) meson forming target and the degrader to obtain variable proton energy.
Figure 2. Scheme of synchrocyclotron beams. P1, P2, P3 -proton beams, π1, π2A, π2B -pion beams, μA, μB-muon beams. P2-medicine beam-line. 1-degrader used only to obtain 200 MeV proton beam, 2-bending magnet, 3-intermediate focus, Q1-Q4-quadrupoles.

Then the beam is deflected by bending magnet and focused by quadrupoles (Q1-Q4) onto the irradiation hall (see Fig.3). The total length of the beam line is 70 m. Before the quadrupole doublet Q3 anti-halo collimator is installed. Such simple beam optic scheme allows to obtain in the irradiation zone a narrow beam of 6 mm in diameter with sharp edges. From the entrance of beam-line in accelerator hall up to irradiation hall the beam is transported in a vacuum pipe to prevent the multiple scattering and inelastic interactions of protons in the air. Profiles of proton beam in horizontal (X) and vertical (Y) directions at the entrance of the beam-line in accelerator hall, at the exit of Q4 and at the isodose centre of the irradiated target are shown in Fig 4.a-Fig 4.c. The irradiation hall is separated from the experimental hall by two shielding walls from iron and concrete provided the radiation background in the hall at quite low level. The beam position in accelerator and experimental halls as well as in the irradiation hall and beam intensity are under permanent control from accelerator and medicine control rooms. Any deviation of the beam parameters beyond the preset limits stops immediately the acceleration process in the synchrocyclotron thus excluding completely any danger of over irradiation of patients. The main technical parameters of medical proton beam are given in Table 1. The most important parameters are: edge gradient of the dose field-20%/mm and ratio of the dose in the isodose centre to that at the head surface-maximum 200:1.

In 2003-2004 the full upgrade of all proton beam-line has been performed. It was included:

1. The exchange of beam forming collimator in accelerator hall and anti-halo collimators in experimental hall. To obtain high quality beam the collimation is being done in vacuum and collimator’s plates must be oriented strictly on the direction of the beam. Beam forming collimator is the system of 8 degrees of the freedom, consisting of two pairs moving plates by length of 250 mm along beam, collimated it in horizontal and vertical planes from 0 up to 180×180 mm. For set of necessary dimensions in the collimator 4 remote control electro-systems are used. Anti-halo collimator placed in experimental hall between Q2 and Q3 has minimum diameter of 20 mm and it is changed up to 150 mm at the length along the beam 700 mm.

2. For control of beam position in the accelerator and experimental halls are used semiconductor plates moving in two perpendicular directions and measuring beam current. Profiles obtained by means of such profile-meters are shown in Fig4.a. Profiles in the
irradiation hall are measured by two wire proportional chambers (X0Z plane) with anode gold-tungsten wire of 20μm diameter and cathode wires from stainless wire of diameter 50 μm. The distance between wires is 1 mm, the surface of entrance window is 128×128 mm. Profile’s shapes from MWPC in horizontal and vertical directions at the exit of Q4 are shown in Fig.4.b.

3. The final proton distribution at the position of patient head on the rotation table is measured by the silicon detector (scanner) precisely moving on X axis by step of 153 μm and on Z one by 9 μm. The range of such scanning is 25×25 mm. Profiles of proton intensity at the isodose centre of irradiated target is shown in Fig.4.c. The intensity of proton beam in the irradiation hall is measured by MWPC in current regime and then transformed in dose distributions which periodically calibrated by diamond detectors. The constancy of planning for each patient irradiation dose is controlled from accelerator and medicine control rooms. All elements of proton medicine beam-line were upgraded by the installation of new mechanical systems and the exchange of electronics components of all detectors on the contemporary base ones.

![Figure 2. Irradiation hall](image)

**Table 1.** Main technical parameters of the proton beam for the irradiation of patients

| Parameter                      | Value          |
|-------------------------------|----------------|
| Proton energy                 | 1000 ± 10 MeV  |
| Proton beam intensity         | 10³ s⁻¹        |
| Beam divergence               | 0.5 degree     |
| Fixation of isodose centre    | ± 1 mm         |
| Rate of the absorbed dose     | 0.50 Gy min⁻¹  |
| Edge gradient of the dose field| 20 % mm⁻¹      |
Figure 4. Profiles of exacted 1000 MeV proton medicine beam in horizontal (X) and vertical (Z) directions. a) at the exit of accelerator; b) at the entrance in the irradiation hall. FWHM (X)=20.7 mm, FWHM(Z)=7.0 mm; c) at the isodose centre of irradiated target, FWHM(X)=5.8 mm, FWHM(Z)=5.9 mm.

The movable patient’s table seen in Fig.3 provides pendulum-like oscillations in the horizontal plane around the Z-axis within +/- 40 deg. The anterior part of the table represents a head fixation device which can perform independent pendulum-like oscillation around the X-axis within +/-36 deg. The crossover of the X and Z axes is the centre of rotation (isocentre). The adjustment system allows to position the isocentre precisely in the beam axis. Then the patient’s position on the table is regulated in such a way that the zone selected for irradiation would be exactly in the centre. This zone is determined in the hospital by NR tomography and its coordinates are fixed in the protocol. The installation procedure in the irradiation hall is performed by means of a special head mask under the control of a high sensitive X-ray setup which has two fixed positions –along the Z-axis and along the beam axis-Y. The final precision in such installation is better 1 mm. Fig.5. shows the scheme of simultaneous rotation of the patients table and head fixation device and also beam trajectories on the patient’s head. Fig.5(b,c) show the dose distributions in XOZ and XOY planes which characterized very sharp decreasing in both directions.
Figure 5. Scheme of the patient's head rotation around Z and X axis. The proton beam is
directed along the Y axis. a) The beam trajectory at the patient's head surface at
simultaneous rotation of patient's head fixation device; b) spatial distributions of the
radiation doses for beam size x=z=6mm. Isodoses: 1-90%, 2-50%, 3-20%, 4-5%; c):Profiles
of dose distribution in plane XOZ (1)and XOY (2).

3. Patient's treatment procedure and results of therapy

The regular treatment of patients at PNPI began in 1975. The diagnosis of the decease and the
recommendation for the proton therapy treatment was done by the specialists in the
St.Petersburg’s hospitals (mostly Neurosurgery Institute). All the preparation work with the
patients was performed at the Central Research Institute of Roentgenology and Radiology. This
work included the localization of the zone for irradiation relative to the reference points on the
head surface and preparation of the special head mask used to fix firmly the patient's head on the
table for irradiation. In this way a group of 20-30 patients was prepared, and they were
transported to the PNPI clinics a day before the medical run was scheduled at the
synchrocyclotron. The time necessary for positioning of the patient on the table for irradiation is
15-20 min, and the irradiation time ranges from 8 to 20 min. The oscillation movement of the
patient’s head proceeds quite slowly, so the patients practically do not notice it. The proton
therapy is painless, and it is carried out without anesthesia. During the irradiation process the
doctors perform continuous control of the patient's state (pulse, breath rate, ECG). There is also a
television control and audio communication with the patient from the control room. After the
irradiation the patients are transported back to the hospitals at St. Petersburg for further survey.
Statistic of proton therapy at PNPI synchrocyclotron is presented in Table 2.

Table 2. Status of proton stereotaxic therapy at
PNPI synchrocyclotron 1975-2005

| Disease            | Number of patients |
|--------------------|--------------------|
| Pituitary irradiation | 333                |
Below we present results of the treatment of some diseases shown in Table 2.

4. Proton therapy of pituitary adenomas (PA)

In treatment of the somatotropinomas (201 patients) clinical remission during the period from 1 to 10 years was achieved in 83% of the macroadenomas cases. The remission was manifested by regress of the acromegalic syndrome, by normalization of the carbohydrate exchange, and by restoration of the working capability. The concentration of the growth hormones in blood was reduced, and in 5 years it was within the limits of physiological fluctuations (2.8±0.3 µg /l). Stabilization of the symptoms was observed in 4%, while there was no effect in 13% of the cases (mainly, in the cases with pituitary adenomas) when the initial symptoms of the tumor spread out of the borders of the turkish saddle.

In treatment of the prolactinomas (114 patients) the clinical remission was stated in 80% of the case (the patients with microprolactinomas). It was accompanied by disappearance of the galactorhea, by restoration of the ovarian menstrual cycle, and by decrease or normalization of the prolactine concentration. Thirty women had a pregnancy ended in a live birth. The stabilization was observed in 17% and no effect was found in 3% of the cases.

In treatment of the corticotropinomas (104 patients) clinical remission was observed in 90% of the cases. In these cases the progression of the Icenko-Cushing’s syndrome was stopped already in 3 months after the irradiation, its regression was observed in 6 months. There was decrease of ACTG and of the cortisone secretion, as well as restoration of the daily secretion rhythm. Stabilization was observed in 4% and there was no effect in 6% of the cases. In the treatment of the hormone-non-active pituitary adenomas (31 patients) the clinical remission was observed in 97% of the cases.

5. Proton therapy of cerebral arterio-venous malformation (AVM)

490 patients with the AVM were divided into two groups according to the AVM volume: the first group – AVM volume less than 8 cm$^3$, the second group – AVM volume larger than 8 cm$^3$. The absorbed doses ranged from 40 to 80 Gy.

The angiographic control performed after the irradiation showed that the positive effect had been achieved in 74% of the patients with the AVM volume less than 8 cm$^3$. The complete elimination of the AVM from the blood circulation was obtained in 65% of the cases. This process continued for a year after the proton therapy. Only 27% of the patients from the second irradiation group showed a positive effect. After the proton therapy the majority of the patients revealed a complete or partial regress of the neurological symptoms, discontinuation or decrease of the rate and degree
of the epileptic attacks. None of the patients revealed and complications in the nearest or in the distant (up to 10 years) terms. The accumulated experience allowed to establish the indications for possible application of this method: the proton therapy is recommended to the patients with a deeply located cerebral AVM with the volume less than 8 cm³, including the patients with inoperable AVM.

6. Proton therapy of endocrine ophthalmopathy (EO)

The method of precision single-run irradiation of the adenohypophysis with the proton beam (the doses of 100-120 Gy) allowed to obtain the positive effect - regress of ophthalmopathy for 29 patients. Prior to the proton therapy, the applied medicinal therapy in these cases was non-effective or the positive effect was transitory. Those patients had a severe progressive EO of the stage II or III, with the pronounced infiltration at the background of the diffuse toxic goitre, as a rule without symptoms of thyreotoxicosis.

In severe forms of the infiltrative EO, before the proton therapy an intensive medical treatment had been given before PST by corticosteroids in maximum doses up to 80 mg/day, thereafter the hypophysis was irradiated. There was observed not only subjective (elimination of the photophobia, of the colic and pain in the eyes, of the fatigability of the eyes at visual loads), but also an objective improvement of the state according to the data of ophthalmometric and ophthalmoscopic examinations.

The proton therapy prognosis in DR cases depends on many factors, firstly, on the state of diabetes mellitus compensation, its severity and duration.

7. Proposal for 200 MeV proton therapy at PNPI

At PNPI synchrocyclotron for the study of nuclear fission in the proton energy range 200-900 MeV a new proton beam with variable energy has been developed. The energy variation is provided by the degrader placed in point 1 (see Fig.2). The 200 MeV beam intensity was 6.4·10⁷ which was insufficient for medical application, required the dose rate in irradiation hall not less than 4Gy/min. Now a new special medicine beam line was calculated by GEANT 3 code which provided of 200 MEV proton beam intensity at the intermediate focus in experimental hall (point 3, Fig.2) at the level of 10⁹ proton/sec for momentum distribution with σ=22 MeV/c. See Fig.6 and 7. Calculations of the final beam parameters in the irradiation hall are being done to show the possibility of 200 MeV proton Bragg peak therapy at PNPI synchrocyclotron.

Figure 6. Horizontal (X) and vertical (Z) profiles of 200 m\MeV proton beam at the intermediate focus
8. Conclusion

The use of the 1000 MeV proton beam for stereotaxic therapy at the PNPI Medical Centre has demonstrated the high efficiency of this method. In combination with the rotation irradiation technique this allows to deliver large radiation doses to small targets selected for the irradiation without damaging of neighbor areas. This advantage is especially valuable in the radioneurosurgery.

The 30 years experience accumulated at PNPI medical facility about 1300 patients showed also a high reliability and safety of the method. None of the patients treated in PNPI Medical Centre had any complications related with the quality of the irradiation process. Nowadays this method can be applied for the treatment of wider spectrum of head brain diseases. With possible therapy of deep suited cancer tumor, using Bragg peak method ,PNPI Medical Facility can satisfy the need of North-West Region of Russia in bloodless radio surgery.

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