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STATUS OF THE PROTON THERAPY COMPLEX PROMETHEUS

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Abstract

The report overviews present status of the proton therapy complex Prometheus. The PTC Prometheus was developed and successfully implemented in the PhTC LPI RAS in conjunction with Protom Ltd. The complex is a Russian development and is fully produced within the territory of the Russian Federation.

At the moment, there are two such complexes are using for treatment in Russia - in the city hospital of Protvino and in the A. Tsyb Medical Radiological Research Centre (MRRC). PTC LPI RAS and Protom ltd. along with MRRC have accumulated almost three years of experience in the usage of the complex under clinical conditions. PTC Prometheus has proved to be efficient and reliable in two years of clinical use in the treatment of head and neck cancer. If there is a developed infrastructure, the capacity of the facility will able go up to 1000 people a year.

The low weight, low power consumption and compact dimensions of the complex allow it to be placed in ordinary hospitals, without constructing separate buildings.

In addition to that, PTC Prometheus was licensed to irradiate the entire human body in March 2017. The phase of preparation of a modified immobilization system for irradiating a recumbent patient was completed by summer 2018.

INTRODUCTION

Proton therapy (PT) is one of the most accurate and modern methods of radiotherapy and radiosurgery [1]. Protons can reduce the radiation load on surrounding tissues up to 30-50% in comparison with gamma rays. Therefore, in cases of tumors located near critical organs (for example head and neck cancer), proton therapy is the most advantageous of the available types of treatment for many patients. Given the advantages of this type of treatment over radiation therapy, using gamma radiation and electron beams, proton therapy is increasingly being used in the treatment of cancer. There is an increase of PT centres around the world [2].

In the world, active work is being carried out aimed at increasing the accuracy of dose delivery to the tumor, reducing the time that patients stay under the influence of radiation and increasing the availability of this method for a larger range of patients. New proton accelerators, as well as more cost-effective and accurate immobilization systems for patients are being developed for these purposes.

According to statistics, PT can be assigned to 50 thousand patients per year in Russia [3]. Unfortunately, in recent years, insufficient attention has been paid to this problem. Only four PT centres are working with patients in Russia now (except those mentioned above, there is Medico-Technical Complex JINR, which started its work in 1968 and annually irradiates several dozen people and MIBS in Saint-Petersburg that started treatment only this year). In addition to two proton therapy complexes Prometheus operating in the Russia, PhTC LPI RAS and Protom Ltd. successfully developed and produced two synchrotrons for the proton therapy complex “Radiance 330”. Two of these complexes have already been introduced in the Massachusetts General Hospital (Boston, MA, US) and McLaren Health Care Hospital (Flint, MI, US) and are preparing for irradiation of the first patients. Also one PTC Prometheus was delivered to Slovakia for radiobiological studies and possible applications in the future for therapeutic purposes.

THE PROTON THERAPY COMPLEX «PROMETHEUS»

The proton therapy complex “Prometheus” (PTC) (see Table 1) consists of an injection channel providing primary acceleration of protons, a synchrotron cyclically accelerating protons to the required energies, an extraction channel for slow extraction of the proton beam and a patient immobilization system.

Table 1: Main Characteristics of the Accelerator Complex

Characteristics	Values
The range of accelerated proton energies, MeV	30 - 330
Magnetic field at injection, mT	80.66
Maximum magnetic field, T	1.9
Outer diameter of the ring, m	5
Accelerator weight, tons	15

Injection Channel and Ion Source

The injection channel and the ion source were designed for the initial production of protons and their acceleration to the energy of approximately 1 MeV.

These modules consist of a pulsed arc source of ions with a pulsed hydrogen inlet, electrostatic lenses, a tandem high-voltage accelerator and a 630 kV voltage source. With the help of a pulse valve, hydrogen enters the ion source, an electric arc is ignited, which leads to the formation of plasma. The electrostatic lens draws negatively charged hydrogen ions and electrons from the plasma. Electrons are discarded by a separator. Hydride

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ions enter a tandem accelerator, where they are recharged on a carbon film. Then, protons accelerated to 1 MeV are injected into the synchrotron. The voltage for the tandem accelerator is produced by a cascade generator. It is now being developed to increase the injected energy of protons up to 1.5 MeV.

Synchrotron

The synchrotron (Fig. 1) serves to accelerate the proton beam from the injection energy to the required energy in a given range. The synchrotron provides a high rate of particle acceleration equal to 330 MeV per 1.2 s.

The magnetic system of the synchrotron is formed by four identical quadrants, separated by large gaps. Each quadrant is formed by four iron blocks with parallel poles. Four magnets with a homogeneous field of each quadrant are arranged in a pairwise common winding. Warm magnets are used in the design of the synchrotron and all transport channels. This solution in a compartment with compactness of the setting allowed to achieve low power consumption, the data on the synchrotron energy consumption in the mode of working with patients are shown in Fig. 2.

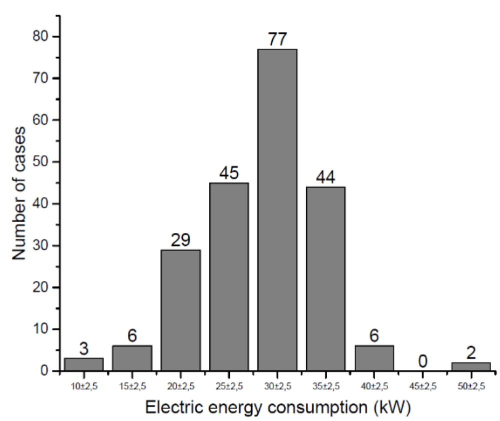

Figure 2: The diagram of the average electric energy consumption for each patient (total number is 211).

Extraction Channel

The slow multi-turn extraction is used for homogeneous irradiation. Observation of the beam is carried out from the phosphor-coated screens using the system of visual control. The area of active beam scanning on the target is 90 mm × 700 mm. Formula (1) is used to describe the spatial distribution of proton beam. Parameters of extracted beam (the beam intensity was 10^9 protons per cycle) Gaussian function are shown in Table 2.

$$f(x) = A \cdot e^{-\frac{x^2}{2 \cdot \sigma^2}} \qquad (1)$$

Table 2: Parameters of Extracted Beam Gaussian Function for Different Energies

E, MeV	A_x	σ_x, mm	A_y	σ_y, mm
70	96	3.8	98	6.4
100	173	3.4	167	4.9
150	242	3.0	247	4.7
200	245	2.8	244	3.9
250	271	2.2	247	3.5

Patient Immobilization System

The system includes an armchair designed to fix the patient and move him to the irradiation zone, an x-ray unit represented by a small-dose X-ray tube and a digital X-ray panel (detector). With their help, the X-ray photographs are taken with a subsequent process of reconstructing them into a three-dimensional image for subsequent irradiation planning. The individual radiograph mode has been put into place in order to verify the patient's position before the start of the treatment. Now for treatment only sitting position (Fig. 3) is used [4]. However, the modification of the immobilization system allowing the recumbency has successfully undergone laboratory tests and after finishing new software, it will be available for clinical trials (Fig. 4).

Figure 3: Patient immobilization system for head and neck cancer cases.

Figure 4: Patient immobilization system in lying position.

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Figure 1: The synchrotron and injection channel for the proton therapy complex “Prometheus”.

Measurement of the Parameters of Proton Beams Using the Radiochromic EBT3 Film

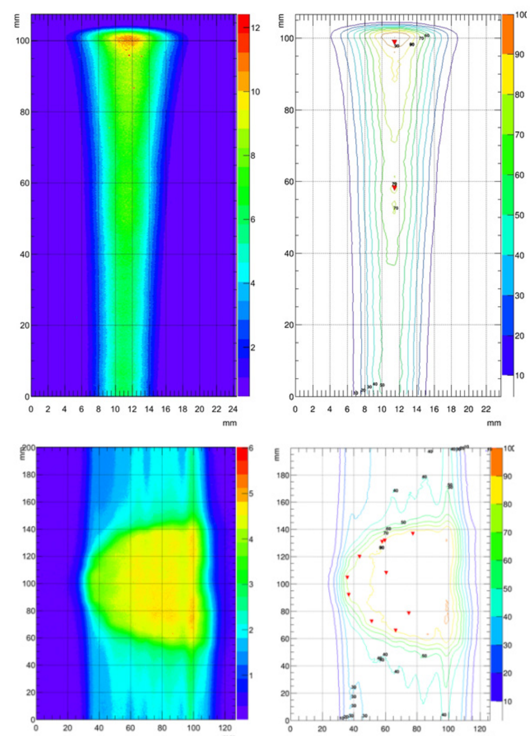

Figure 5: EBT3 film showing a proton beam with an energy of 120 MeV in water (up). Dose distribution for EBT3 film is irradiated in a solid-state phantom IBA in two intermittent directions in preparation for prostate irradiation. Preparation for patient irradiation in lying position (down).

Proton beam parameters were determined using the X-ray sensitive radiochromic EBT3Gafchromic film, which is designed for a wide range of measurements, and has a dynamic dosage range of 0.1 to 20 Gy. (Optimum dosage range is from 0.2 to 10 Gy). The energy independence of the EBT3 film is in the energy range of 100 keV. In addition, the EBT3 film has a high spatial resolution (<25 μm). It provides for the presence of a yellow marker dye for the possibility of three-channel dosimetry.

TREATMENT PROCESS.

The Irradiation Time of a Patient

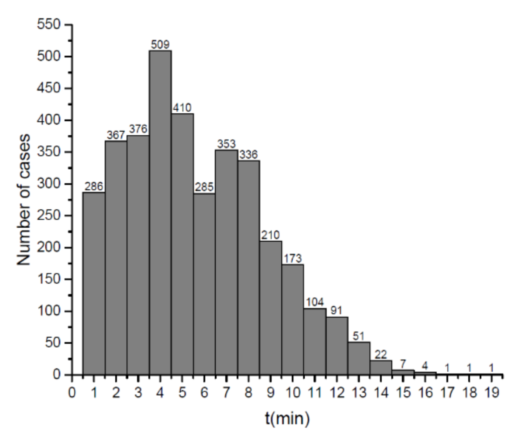

Figure 6: The execution of the treatment plant time diagram (including irradiation process and changing position of the immobilization system).

An important characteristic of PTC is the presence of the patient in the immobilizing device. It is believed that the duration of a single therapy session should not exceed

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several minutes in order to minimize accidental patient movements. In real conditions, the irradiation time has not exceeded 15 minutes, and the average time was 5 minutes 52 seconds for 3587 cases (Fig. 6), which easily meets the accepted standards. Average time of the patient stay in the treatment room was 10 minutes 12 seconds for first 82 patients [5].

Tumor Volumes in Case of Head and Neck Cancer

It is believed that proton therapy is mainly used on neoplasms of small volumes (several dozens of cubic centimeters). Experience gained on PTC allows us to state the efficiency of the complex for the treatment of tumors of a much larger size. The average size of tumors was 145 cm^3 for 212 cases (Fig. 7).

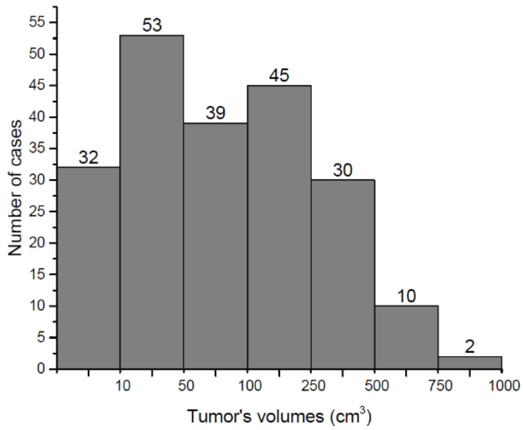

Figure 7: Diagram of the volumes of tumors that underwent the therapy.

ANALYSIS OF THE RESULTS OF TREATMENT

Table 3: Treatment Results for 86 Patients

Change in tumor volume after a course of PT			Number of cases
CR	Complete response	Decrease >70%	8%
PR	Partial response	Decrease 20-70%	32.5%
SD	Stable disease	Decrease <20%	39.5%
PD	Progression disease	Increase	20%

108 patients have a follow-up of sufficient duration (from 1 to 24 months) necessary for making preliminary conclusions about the results of the therapy. 19 of them have died during this period. There were three cases of development of radionecrosis. 7 patients have 24 months follow-up period. Acute radiation toxicity has not exceeded degree II (radiodermatitis III, mucositis I-II).

CONCLUSION

Thus, PTC "Prometheus" has proved to be efficient and reliable in three years of clinical use in the treatment of head and neck cancer. If there is a developed infrastructure, the capacity of the facility can go up to 1000 people a year. The low weight, low power consumption and compact dimensions of the complex allow it to be placed in ordinary hospitals, without constructing separate buildings. In addition to that, PTC “Prometheus” was licensed to irradiate the entire human body in March 2017. Therefore, this complex is by far the only Russian development capable of solving the problem of proton therapy at the country level.

Table 4: Types of Tumors Affected by PT (for 105 patients)

Types of tumors	Patient status after PT				
	CR	PR	SD	PD	D
Meningioma	1	1	13	2	1
Metastases		4	4	7	3
Glyoblastoma		2		2	7
Neurostezioblastoma	1				
Astrocytoma	1	6	5	4	4
Adenocarcinoma	1	1		1	3
Estesioneuroblastoma	1				
Hemangiopericytoma		2			
Skull Base Chordoma			3		
Pituitary adenoma		2	2		
Cancer of the salivary gland	1	1			
Flat cell carcinoma head and neck	1	5	1		
Ganglioglioma			1		
Schwannoma		1	3	1	
Melanoma			1		
Nasopharyngeal cancer		2			
Sarcoma		1			
Chondrosarcoma			1		
Mucosal cancer					1
Total:	7	28	34	17	19

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