RADIOACTIVE BEAM PROJECT AT HIMAC

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Abstract

Heavy-ion radiotherapy gives a good localized dose distribution just on a cancer tumor. In order to emphasize this advantage, the verification system of a particle range and an irradiated area in a human body has been developed for the Heavy Ion Medical Accelerator in Chiba (HIMAC) at National Institute of Radiological Sciences (NIRS). The idea comes from the fact that the stopping position of a short-lived positron emitting nuclei, such as ^{11}C, ^{15}O or ^{19}Ne, can be precisely detected by measuring annihilation gamma-rays.

1 MOTIVATION

Since 1994, the heavy ion cancer therapy has been carried out at HIMAC. The radiotherapy is able to preserve the organ and its function after the treatment, and does not give serious effects even on aged patients. In addition, the heavy-ion therapy has two advantages; the localized dose distribution just on a tumor in a human body and the short treatment period due to small numbers of irradiation fractionation[1]. The localized dose distribution comes from the physical characteristic of the charged particles in the material and the high biological effectiveness of the heavy ion. In order to emphasize this advantage, more accurate irradiation technique is necessary. Although many irradiation methods are applied in the world[2], a wobbler beam-delivery system is presently adopted to make a uniform lateral dose distribution at HIMAC for their reliability and adaptability to the respiration gated irradiation. To improve the dose distribution, NIRS has studied and developed 3D irradiation systems over 20 years[3]. In both methods, more accurate irradiation technique requires more accurate treatment planning and patient positioning in order to decrease their errors at the clinical treatment. Therefore the verification system of a particle range and an irradiated area in a human body is necessary. Our goal is to realize the highest Tumor Control Probability (TCP) with the least Normal Tissue Complication Probability (NTCP) by applying the radioactive nuclear beam (RNB).

2 TECHNICAL METHOD

The idea of the medical application with the radioactive nuclei has been realized as a commercial Positron Emission Tomography (PET) system, i.e. the stopping position of a short-lived positron emitting nuclei, such as ^{11}C, can be precisely detected by measuring annihilation gamma-rays. The positron emitting nuclei are introduced into patients by the injection in the case of the commercial PET. Alternatively, in the case of the charged particle therapy, these are produced by the beam itself.

Since a part of incident ^{12}C beam changes to ^{11}C by the projectile fragmentation, these ^{11}C, so-called 'autoactivation', are available for the measurement by using the PET[4-6]. The incident beam also produces various positron emitting nucleus, such as ^{15}O, ^{13}N, and ^{11}C, from human tissues by the target fragmentation[7,8]. However, these measurements have ambiguities due to the reaction and the production rate of radioactive nuclei is not enough.

Alternatively, the direct use of RNB gives a large advantage. Its signal-to-noise ratio is higher than the autoactivation's and the relation between the measured distribution and the actual stopping position of the beam is clear. The application of the RNB beam was originally studied at BEVALAC of the Lawrence Berkeley Laboratory[9]. Although their early results showed useful data on the error of the stopping power in the treatment planning causes from the difference between the X-ray CT numbers and the actual stopping power[10], unfortunately, BEVALAC was shut down before the full completion of the RNB application. HIMAC follows their pioneer work.

The RNB system consists of a secondary beam course, a beam irradiation system, a patient's positioning system, and annihilation gamma-rays detectors. The beam course is able to produce ^{11}C with an energy of 350MeV/u and a production rate of 8x10^{-3} by the projectile fragmentation. The maximum 3-D irradiation volume is 10x10x18 cm with a spot beam scanning. Details of the secondary beam course for the production of RNB and the beam irradiation system have been reported[11,12].

A commercial PET system detects the 3D image of the irradiation area. Fig. 1(a) shows the demonstration of the ^{11}C PET image. The irradiation volume and the physical dose were 3.5x3.5x4.3cm and 1Gy, respectively. The ^{11}C beam with two different passages stopped at the different positions shown in Fig. 1. The PET system is able to detect this difference of as low as 2mm. Fig. 1(b) shows the image of ^{12}C autoactivation with the same condition as Fig. 1(a). The improvement of the signal-to-noise ratio can be seen.

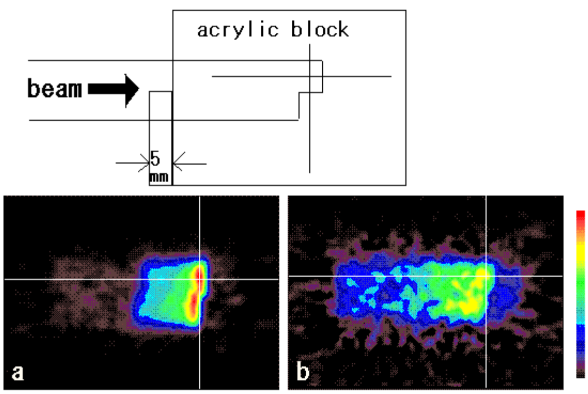

Fig. 1 Observed PET images. (a) and (b) are irradiated by ^{11}C and ^{12}C beams, respectively.

The PET image gives the 3D distribution, but its resolution is limited by the performance of the PET detector. A more simple system was developed in order to obtain the 1D range information[13]. For the detection of the precise depth location with the least dose given to a patient, we developed the Positron Camera detector[14]. In order to realize the high efficiency, this detector uses two large NaI crystals with a diameter of 60cm and a thickness of 3cm. The centroid of the stopping point is statistically determined by numbers of the detected gamma-ray pairs. The noise is mainly caused the activated scintillation crystal itself. Therefore the detector is set off beam axis during the irradiation. Fig. 2 shows the typical observed range distribution of ^{11}C irradiated into the uniform plastic block under the typical irradiation condition. The range spread of the beam was 2mm. The ideal resolution of 0.4mm is obtained with the physical dose of 0.05Gy; only the real resolution in the human body depends on the other effects described in Sec. 4. In addition, ^{10}C beam is also useful for the range measurement. Although the production rate is lower and the end-point spread is larger, the short measurement time and the good signal-to-noise ratio are expected.

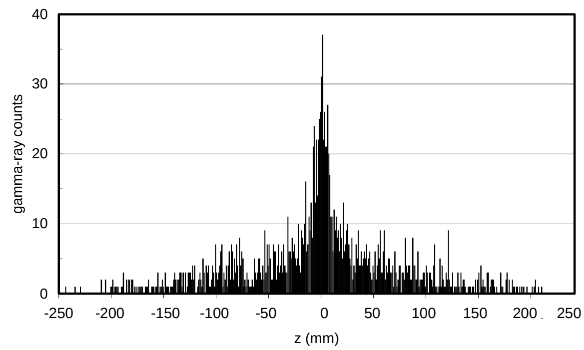

Fig. 2 Range distribution measurement by the positron camera.

3 SCENARIO TO THE TREATMENT

To utilize the RNB for the cancer therapy, it is expected that the following tumor's treatments will be improved. The first case is for the brain tumor or head and neck tumor near the critical organ. For example, several head and neck tumors are surrounded by the eye balls, optics nerves and brain stem. The RNB verify the actual irradiation volume, so that a margin for error in such difficult treatment planning can be reduced. The highest TCP with the least NTCP will be realized for less serious after effects of critical organs. The second case is like a lung cancer. The range calculation is difficult in the case of such cancer which has a complicate trajectory included bones or air. The calculation can be verified to measure the actual stopping position by the RNB.

In each case, a treatment planning is necessary to make a uniform dose distribution on the target volume of tumor. The treatment planning system also has to give a distribution of the RNB stopping position to compare an observed value with an original plan. The system is under development. The physical dose distribution has to be checked by comparison between the planned value and the experimental measurement. The biological effectiveness in the planning calculation has to be treated carefully. We will insure this problem to measure the survival rate of the cell at the irradiation area. These measurements are now in progress.

At first, a clinical trial to treat a brain tumor by the ^{11}C beam is planned. Because of this treatment requires the simplest thinking to apply the RNB; i.e. the brain tumor is not moved with the respiration, and the head is easily fixed for the positioning. In addition, the 360 degree rotating chair easily realizes the quick mult-port irradiation, thus the improvement of the dose distribution will be expected. The 3D distribution observed by an off-line PET system will verify the result of the treatment. This method requires high RNB intensity. In our system, an irradiation time of 3 or 4 minutes was needed for a physical dose of 1Gy with a target volume of

3.5x3.5x5cm. The improvement of the primary beam intensity is necessary for larger tumor. Another disadvantage of this treatment is that the patient positioning has to be required two times at the beam irradiation and at the measurement. The patient positioning system of the PET room will be constructed as same as the treatment room by the summer of 2002.

On the second stage of the clinical trial, the positron camera will be also utilized for the lung tumor. The pilot pencil-beam of ^{11}C or ^{10}C will check the end point of the range, and then the intense ^{12}C beam will be irradiated into the target volume. In order to extend the verification method to tumors located in the trunk, a patient couch, an on-line PET system, and the respiration or pulsation gated irradiation will be utilized.

4 PLANS OF BASIC EXPERIMENTS

The heavy-ion cancer therapy is based on many fundamental researches in the fields of physics, biology, and medical science. For the verification system with the RNB, the basic experiments in these fields are also necessary. And furthermore, the RNB gives a new technique for study of the radiotherapy. The following plans of basic experiments are in progress.

The study of the biological and chemical process of the metabolism is one of the most important themes for the RNB application. The detected image of the positron emitting nuclei is distorted due to the metabolism in the tissues. We measured the lifetime of the ^{11}C injected into the alive and dead rabbit's muscles. The lifetime in the alive rabbit has at least three components[15]. These components are due to the very fast blood-stream in the blood vessel, the regional blood flow in the muscle tissue, or unknown products which had the slow diffusion speed. For the investigation of the metabolism, the experiments with various alive and dead tissues are planned. The comparison between C isotopes with different lifetimes or other beta emitting nucleus, ^{13}N, ^{15}O, ^{18}F, ^{19}Ne and so on, is useful for these experiments. The amount of radioactive nucleus carried away from a tissue by regional blood flow depends on its chemical form. However, it is unknown what chemical form of products produced by the incident ^{11}C nuclei. In order to determine the chemical form, we also have a plan to analyze products of ^{11}C and ^{14}C irradiated into the tissue-equivalent material by the liquid chromatography.

The microscopic process around the cell is also interested to study the biological effectiveness. For example, the experiment of ^{8}B or ^{8}Li beam is scheduled for the research of the multi-hit cell. Because of the incident ^{8}B produces ^{8}Be, and then it emits two alpha particles. The range of these alpha particles in the water is about 10μm and it is equivalent as the size of normal cell. It means the cell is hit by three charged particles at the same time. The result will show the difference between the single-hit and multi-hit processes. In addition, the measurement of the emitted beta or gamma rays is expected to know its location and amount in the cell.

The study of the cross section of the projectile fragmentation has a long history, but its measurement is still important for our project[16]. In particular, we are interested in the lower side of the momentum distribution and the precise structure of the angular distribution of the reaction between the ^{12}C target nuclei and the incident nucleus, O, C, N, Ca, and so on, which are elements inside of the human body. Because of the projectile fragments of these nucleus shows the behavior of the target fragments at the treatment by ^{12}C.

5 HISTORY AND TIME SCHEDULE

The RNB project at HIMAC was funded since 1995. The first RNB was obtained in 1997. The construction of the beam irradiation system and the annihilation gamma-ray detector system had been finished in 2000. The patient positioning system has been constructed just in the summer of 2001. The connection between the RNB system and the accelerator facility, such as the beam interlock system, the computer control data acquisition system, the data transfer system of the treatment planning, and so on, will be completed by the spring of 2002. Although many precise system verifications described in Sec. 3 are still required, we expect to start the first clinical treatment by the autumn of 2002. Moreover, the knowledge given by the research with the RNB has been already improved the ordinary treatment day by day.

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