美國費米國家加速器實驗室

考察暨招商報告

考察日期：93 年 2 月 25 日～29 日

報 告 人：許世明副院長、詹國禎教授

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內容摘要: The purpose of this trip includes the following three major points: 1. To establish collaboration between Fermilab and National Taiwan University in cancer treatment with advanced accelerator technologies. 2. To understand the current development of neutron therapy at Fermilab. 3. To introduce our plan of a future cancer hospital and proton center in Hsinchu Biomedical Science Park.

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Forward

Fermi National Accelerator Laboratory (Fermilab) is the first laboratory in the world to use neutron therapy on cancer patients. Since its first patient was treated in 1976, over 3,000 other cancer patients have benefited from this facility. We believe that Fermilab's experience and facilities in cancer research and treatment will be highly valuable to the new cancer hospital that is to be established in the Hsinchu Biomedical Science Park (HBSP). Hence our visit to Fermilab was particularly important in working towards a possible collaboration and/or partnership between Fermilab and the HBSP.

The visit took place at Fermilab, located in Batavia, Illinois, USA. Representatives from National Taiwan University included Vice Superintendent of National Taiwan University Hospital Dr. Su-Ming Hsu, Professor of Electrical Engineering Mr. Gwo-Jen Jan, Professor of Physics Dr. Shiung Yee and Associate Professor of Optoelectronic Biomedicine Tseng, Wen-Yih. Our hosts from Fermilab included Director of Fermilab Michael Mitherell, Ph.D., Assistant Director of Fermilab Roy Rubinstein, Ph.D., Director of Neutron Therapy Arlene Lennox, Ph.D., Senior Scientist Gong-Ping Yeh, Ph.D., Associate Director for Administration Mr. Bruce L. Chrisma and Head of the Business Services Section Mr. David A.Carlson

Purpose of the Trip

The purpose of this trip includes the following three major points:

1. To establish collaboration between Fermilab and National Taiwan University in cancer treatment with advanced accelerator technologies.
2. To understand the current development of neutron therapy at Fermilab.
3. To introduce our plan of a future cancer hospital and proton center in Hsinchu Biomedical Science Park.

Introduction to Fermilab

Fermi National Accelerator Laboratory (Fermilab), located in Batavia, Illinois, on the west suburb of Chicago, is one of the world's highest energy proton-antiproton accelerator. It was founded in 1967 by its first director Robert Wilson and later named in honor of 1938 Nobel Prize winner Erico Fermi, one of the preeminent physicists of the atomic age. The large accelerator complex of Fermilab was built to study fundamental phenomena of particle physics at the highest energy achieved today. It was built for high-energy physics research.

Neutron therapy

Neutron therapy in Fermilab started in 1976. Dr. Arlene Lennox, a scientist in high-energy physics, has directed neutron therapy facilities since 1985. In 1976, Fermilab using its Linear Accelerator (LINAC), part of the injection equipment, opened the world's first Neutron Therapy Facility (NTF) with fast neutrons to treat cancer patients. Since then, 3,000 patients have been treated at the NTF of Fermilab.

Neutron Therapy is a highly effective form of radiation therapy. Long-term experience with treating cancer has shown that certain tumor types (histologies) are very difficult to kill using conventional radiation therapy, such as X-rays and electron beam. These histologies are classified as being "radio-resistant." Neutron therapy specializes in treating inoperable, radio-resistant tumors occurring anywhere in the body. Initially the NTF treatment was experimental. The National Cancer Institute funded the operation until October, 1985. During that period the NTF conducted clinical trials to determine the appropriateness of using fast neutrons to treat various types of tumors.

One significant finding was that only neutron beams produced by protons with energy greater than about 60 MeV could produce tumor control with side effects no worse than low LET (linear-energy-transfer) radiation. For this reason the facilities which had performed clinical trials using relatively low energy beams either stopped treating patients or upgraded their accelerators to a higher energy. As of now, only 3 sites in the US offer this option. Therefore, neutron therapy is not yet a widely known option by cancer patients.

Currently, Dr. Arlene Lennox is helping Dupage Science Park design a hadron center that provides photon, proton and neutron beams for cancer treatment. She identified 60 MeV energy of neutrons optimum for cancer treatment because relative biological effectiveness (RBE) at this energy level is about 4, achieving the maximum effect of tumor-killing. The drawback of neutron irradiation is a relatively high dosage given to the intervening tissue between the tumor and skin. Therefore, the tumor must be treated with beams from multiple directions to increase the tumor dosage whilst minimizing the unnecessary dosage to the normal tissues.

Neutron therapy is indicated if tumors are resistant to photon irradiation such as hypoxic and bulky. In the treatment room of Fermilab, patients sit on a chair with appropriate immobilization and receive a horizontal neutron beam emerging from a linear accelerator. The entry point of the neutron beam can be changed by the rotation of the chair. They control the shape and area of the beam with thick cylindrical collimators made of hydrogen-rich materials. These collimators are custom-made for each individual patient. The planning of beam delivery is made based on conventional CT images. Recently, they designed a vertical CT scanner to ensure consistent positions of internal organs with the positions during treatment.

In the past 20 years, Dr. Lennox has gained profound experience in neutron therapy. However, it has been difficult to establish therapeutic effects through rigorous study because the patients were arrived from referral hospitals, most of whose diseases were in advanced stages and had already received various treatments. To date, neutron therapy in oncology patients has not been fully explored due to lack of multi-center trials.

Proton therapy

There are presently three active proton therapy centers in the United States, 22 worldwide. At least 14 centers in the U.S. and a comparable amount abroad are under construction and being proposed. The first proton therapy machine in the US was commissioned at Fermilab for use in cancer treatment at the Loma Linda University Medical Center in 1990. Currently Fermilab is developing a new generation proton therapy machine, changing the beam delivery system from continuous to pulsed mode, and is capable of vertical and horizontal scanning. The most significant difference between proton and photon therapy is in the dosage distribution. Photons deposit most of their dosage at shallow depths of a few centimeters with a gradual decay of depth in the patient. By the Laws of Physics, protons deliver most of their dosage in the Bragg peak, which can be delivered at most clinically required depths followed by a sharp fall-off. This unique property can be designed to yield a uniform dosage across the target and then virtually zero deep to the target and lower dosage proximal to the target.

By improving the beam delivery techniques, proton beams can be employed in comparable numbers, direction, weight, angulation, intensity modulation as is feasible for photon beams. The result is a smaller treatment volume, and hence a lower incidence and frequency of treatment-related morbidity. Most importantly, the reduction in treatment volume permits a higher dosage to the tumor. This means an improved tumor control probability and a lower normal tissue complication probability. Clinical gains appear to have been realized in the treatment of patients with uveal melanoma, skull-base sarcoma, para-nasal sinus carcinomas, selected stages of lung carcinoma and hepatocellular carcinoma, comprising approximately 10% of radiotherapy patients.

Prospective clinical evaluations are in progress for tumors at many anatomical sites. Although proton therapy shows promising benefits to some cancer patients, other novel technologies have also shown their clinical potential. For instance, intensity modulated radiotherapy (IMRT) or radioactive plaques implanted in the back of the eye to treat uveal melanoma. So far, it is difficult for proton therapy alone to demonstrate its uncontestable advantage over competing therapies.

Proton Therapy in Loma Linda

In late the 1980s with the technical help of Fermilab, Loma Linda University and Medical Center built the world's first Proton Therapy Facility for patient treatment and research in a hospital setting. Proton treatment began at Loma Linda in October 1990, since then they have treated more than 8900 patients. Clinically proton therapy is more effective to treat the early stages or localized cancers of the brain, eye, head and neck, spinal cord, lung, abdomen, pelvis, etc. However, the design of the Loma Linda facility has been more than 10 years old. Better design and more precise beam control have been called for in the recent joint-venture cancer treatment center of Fermilab/Dupage County Science Park.

Hadron therapy project in Dupage County Science Park

With 30 years of experience in accelerator technologies in cancer treatment, Fermilab is helping Dupage County Science Park, located right next to Fermilab, to build a hadron center. Dr. Lennox designed the center as one providing comprehensive modalities of radiation therapy including photon, proton and neutron beams. There is one linear accelerator for photon therapy, one linear accelerator for neutron therapy, and one cyclotron for proton therapy. The cyclotron can also be used to produce isotopes for positron emission tomography (PET) imaging tracers.

Collaborating and Partnership with Fermilab

After 30 years of experience in clinical hadron (neutron and proton) therapy, it is clear that a cancer treatment center should provide both hadron and conventional therapy facilities in a hospital setting to provide the best options for the patients, and perform studies on clinical treatment and medical research. Such a facility will be the first one in the world that will be able to provide the best treatment for patients. With the expertise of Fermilab in designing and building accelerator equipment and clinical research in hadron therapy, and its experience in the newly developed cancer treatment center in Dupage County Science Park, it is an excellent opportunity and benefit for Hsinchu Biomedical Science Park to collaborate and establish a partnership with Fermilab, as well as with the Dupage County Science Park to develop a new cancer treatment facility in Hsinchu with state-of-art design and technology within the next 4 years. In the future, this new center will be able to provide the best regional cancer therapy center in Asia and around the world. Technical design and support of the accelerator facilities should come from Fermilab as well as the local National Synchrotron Radiation Laboratory.

The strength of Fermilab is her accelerator technologies. Fermilab is able to transform these technologies to state-of-the-art hadron therapy machines. Experience of hadron cancer treatment will not begin until the full operation of the Dupage County Science Park in 2008. It will be important to have another hadron center in Asia, working simultaneously with Fermilab and the Dupage County Science Park, to acquire first-hand experience of hadron cancer treatment in both a western and an Asian country. NTUH has excelled in health care and can become a competent partner to apply these novel technologies to various cancer treatments. Through collaboration with Fermilab, standardization of treatment protocols and equipment settings will also be established. This knowledge is crucial to economize the construction and operation, facilitating wider use of hadron therapy.

If the cyclotron in the hadron center is optimized to produce medical isotopes, it will be helpful to researchers to develop target/pathway specific tracers. In addition, new imaging techniques such as proton-induced PET or proton CT will be developed to monitor the proton/neutron dosage during treatment. Therefore, molecular and therapy-related novel imaging technologies can be developed with the hadron project.

The hadron center will also provide an opportunity for Fermilab and accelerator experts in Taiwan to work together to build better therapeutic accelerators in the future.