Development of a Next-Generation 4D Radiation Therapy System That Enables Irradiation of a Moving Cancer

**Irradiation Precision Error: ± 0.1 mm**

**Realization of High-Precision and Safe Cancer Therapy**

Today, the most common cause of death in Japan is cancer; which accounts for one out of every three deaths. Against this backdrop, NEDO has contributed to a reduction in the number of cancer patients through early social reintegration of cancer patients and improved quality of life (QOL) as a result of the development of cutting-edge medical equipment that enables early cancer diagnosis and therapy. There are three types of cancer therapy: surgery, chemotherapy, and radiation therapy. Among them, greater expectations are placed on technological advancement of radiation therapy because it puts the least strain on the body and is highly effective as a cure. The greatest challenge in radiation therapy is to avoid damaging normal cells when irradiating cancer cells.

Mitsubishi Heavy Industries, Ltd. carried out NEDO’s Fundamental Technology Research Facilitation Program/Development and Research on a High-Precision 4D Radiation Therapy System project for four years from 2003 in collaboration with Kyoto University Hospital’s Department of Radiation Oncology and Image-applied Therapy and its Clinical Research Center for Medical Equipment Development to establish fundamental technology. It subsequently carried out the Subsidized Project for Practical Development of Next-Generation Strategic Technology (Analysis of the Behavior of Affected Parts and Development and Research of Feedback Technology Toward Adaptive 4D Radiation Therapy project for two years to resolve technical issues for practical application. This then led to the Veren4DRT, a next-generation 4D radiation therapy system that made it possible to irradiate a moving cancer for the first time in the world.

As a newcomer in the medical equipment business, Mitsubishi Heavy Industries initially carried out medical-related activities through intrapreneurship. In this situation, it was able to realize an innovative and safe high-precision radiation therapy system in which the irradiation precision error of therapeutic X-rays (referred to as “therapeutic beams”) is within ±0.1 mm. This was accomplished by combining a medical company and technology for medical equipment development with interdisciplinary expertise.

In order to cure a cancer that moves because of respiration or some other movement, the Veren4DRT was designed as a 4D high-precision radiation therapy system by adding temporal axis to the concept of 3D therapy that enables irradiation from various angles. As a result, the system has numerous new advanced functions not seen in previous radiation therapy systems.

As of February 28, 2015, 24 units of the system were installed in hospitals not only in Japan but also in Europe, the US, and Asian countries. These hospitals have successfully performed irradiation of lung, liver, and pancreatic cancers. The Veren4DRT is attracting attention as an innovative therapy system that enables a radical cure without putting much strain on the body.

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**Measurement of a Hepatic Fibrosis Glycosylation Marker in Blood Within 17 Minutes Development of Fast and High-Precision Measurement Technology Which Received Approval for Health Insurance Coverage in January 2015**

The most common cause of chronic hepatitis in Japan is infection with the hepatitis B virus and hepatitis C virus. The number of infected people is said to be approximately three million nationwide, of which nearly two-thirds are asymptomatic carriers. Chronic hepatitis that develops from infection with the hepatitis virus causes chronic cell destruction in the liver, and can advance to hepatic cirrhosis in 20 to 25 years due to fibrosis of the liver (hepatic fibrosis), and can eventually lead to liver cancer or serious disease. The progression of chronic hepatitis and the likelihood that treatment can be determined by checking the level of hepatic fibrosis.

Today, the mainstay test for hepatic fibrosis is a biopsy in which the state of hepatic fibrosis is ascertained by collecting liver tissue with an inserted needle. However, the test imposes a heavy burden on patients, such as the necessity of hospitalization. Therefore, there is a public need for the development of a simple and high-precision liver fibrosis test such as blood testing. A technology that meets this need is Sysmex Corporation’s HICL M2BP or reagent which uses a hepatic fibrosis glycosylation marker: a biomarker using sugar chains.

NEDO has implemented the world’s most advanced research and development projects related to sugar chains since the Technology for the Production and Utilization of Glycoconjugates project started in 1991. The National Institute of Advanced Industrial Science and Technology (AIST), which has led these projects, found a new glycosylation marker involved in the progression of hepatic fibrosis. In order to utilize this achievement, AIST started to work with Sysmex Corporation, a manufacturer of clinical examination devices and test reagents, for the practical application of the hepatic fibrosis glycosylation marker, and then developed the HSICL M2BP or reagent. This reagent received manufacturing and marketing approval in December 2013, was released in March 2014, and received approval for health insurance coverage in January 2015. It is expected to be widely used in the future.

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**Mitsubishi Heavy Industries, Ltd**

**Kyoto University Foundation for Biomedical Research and Innovation**

**Fundamental Technology Research Facilitation Program/Development and Research on a High-Precision 4D Radiation Therapy System**

**The World’s First Reagent to Determine the Progression of Hepatic Fibrosis by Measuring Changes in the Sugar Chain**

**Sysmex Corporation**

**National Institute of Advanced Industrial Science and Technology (AIST)**

**Technology Development Utilizing Sugar Chain Functions**

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**Automatic immunoassay system used in testing HSICL-5000**

**Reagents placed in HSICL-5000**

**Twenty-four R1 to R1 reagent sample sets can be tested at the same time.**
Q. Why did this project start?
To improve the fundamental technologies of private companies and disseminate their research results, NEDO has been carrying out the Fundamental Technology Research Facilitation Program since 2001. This program aims to support the development of technology that is beneficial to the nation’s economy but which involves a high level of risk for individual companies and requires considerable investment and a long time period to realize results. The 4D radiation therapy system project was selected from applications submitted following a public solicitation for new projects in the life science field.

Q. What was the aim of the project?
When this project started, there were no domestic manufacturers developing radiation therapy systems. However, the project was expected to develop a radiation therapy system with a unique feature (i.e., irradiation of a moving cancer) that was the first of its kind in the world. This would enhance therapeutic efficacy and thereby contribute to the spread of diagnostic and therapeutic equipment that serves as a common base for radiation therapy systems, industrial development in related fields, and the creation of new markets.

Q. What is the role of NEDO?
Since this project involved new technology that required a large amount of investment, a long period of time to achieve results, and also posed a high level of risk to individual companies, NEDO recommended collaboration between industry, academia, and government. This facilitated the early realization of advanced fundamental technology. In addition, the fundamental technology that was developed in this project was subsequently incorporated into technology development for practical application in NEDO’s Subsidized Project for Practical Development of Next-Generation Strategic Technology/Analysis of the Behavior of Affected Parts and Development and Research of Feedback Technology Toward Adaptive 4D Radiation Therapy (FY2006–FY2007). This support system from fundamental technology to practical application led to the early practical application of high-precision radiation therapy.