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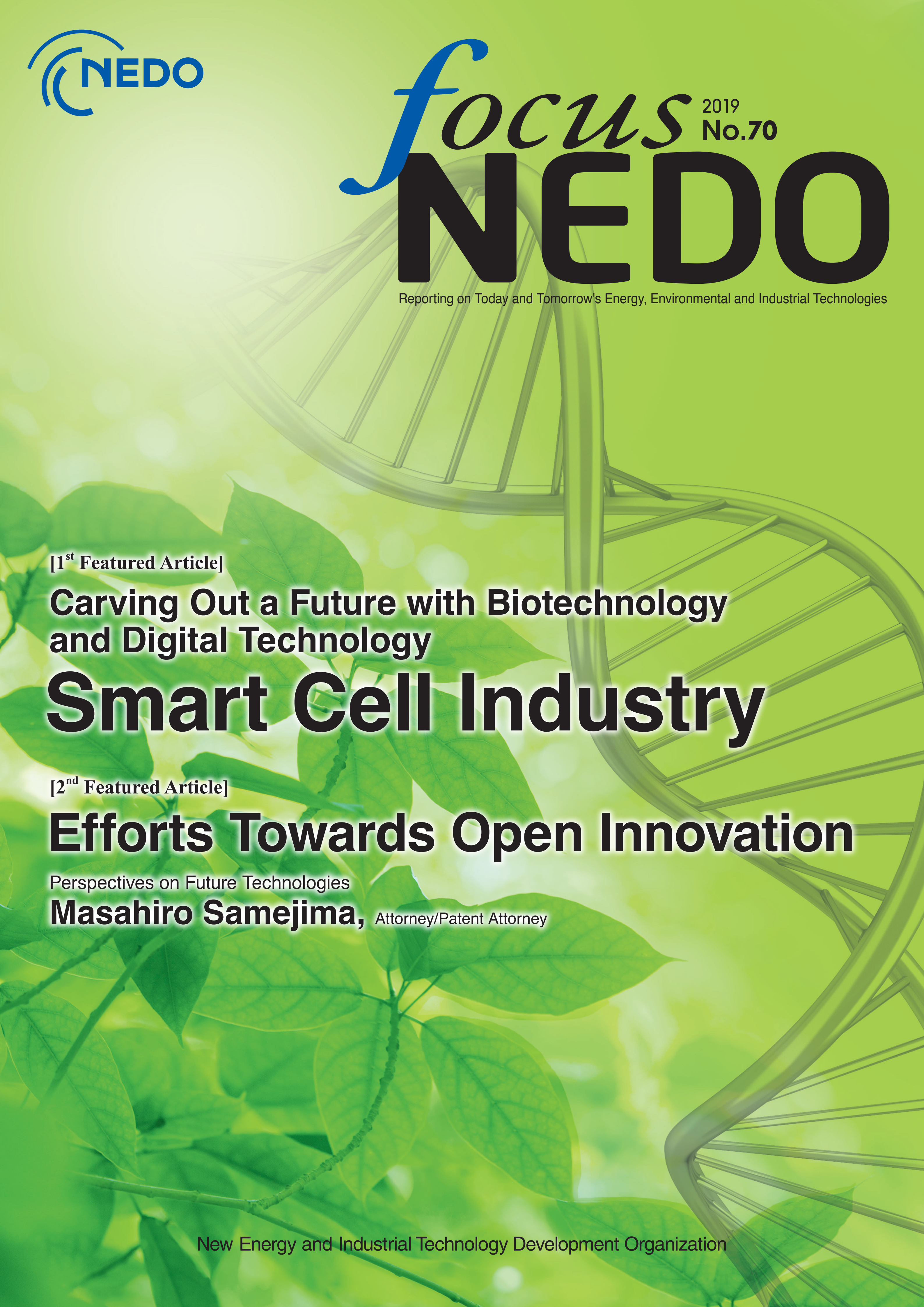
Reporting on Today and Tomorrow's Energy, Environmental and Industrial Technologies



[1st Featured Article]

Carving Out a Future with Biotechnology and Digital Technology

Smart Cell Industry

[2nd Featured Article]

Efforts Towards Open Innovation

Perspectives on Future Technologies

Masahiro Samejima, Attorney/Patent Attorney

New Energy and Industrial Technology Development Organization

"Open innovation that is linked by philosophies and technologies enhances competitiveness."

Masahiro Samejima

Attorney/Patent Attorney

After graduating from the Department of Metallurgical Engineering of the Tokyo Institute of Technology in 1985, Masahiro Samejima joined Fujikura Electric Wire Corporation (currently Fujikura Ltd.) in the same year. In 1992, he joined IBM Japan Ltd. and worked in the intellectual property department. While working for IBM, he became a registered patent attorney. He also became a registered attorney in 1999. In 2004, he opened Uchida & Samejima Law Firm. He became the chairperson of the local SME intellectual property strategy promotion project of the Japan Patent Office. In 2012, he won the Intellectual Property Achievement Award (from the Minister of Economy, Trade and Industry). In 2014, he became one of NEDO's catalyzers. Three years later, he became a lecturer of the NEDO Technology Startup Supporters Academy (SSA). In 2018, he served as an official supporter and recommendation committee member of J-Startup. He has also carried out many other venture-related activities. The character of Kamiya, who is an attorney, in Jun Ikeido's Naoki Prize winning novel *Downtown Rocket* is based on him.

Open innovation broadly means "departure from closed innovation." In recent years, this term has had a more specific meaning: the introduction of technologies from small and medium-sized venture-capital companies in large enterprises. Similar to electric cars and renewable energy technology, which come from a combination of technology and knowledge in various fields, you cannot win if you specialize in only one technological field. Since it is inefficient from a management viewpoint to develop all necessary technologies independently, it is natural that more and more large enterprises are introducing technologies from small and medium-sized high-tech venture companies.

On the other hand, such small and medium-sized venture companies, which have served as the prime contractors or subcontractors of large enterprises, can now establish an equal relationship with them if they have the technical strength. It has finally been socially recognized that the overall competitiveness of Japanese companies will decline unless large enterprises evaluate and introduce the technologies of small and medium-sized venture companies properly.

I believe that one of Japan's strengths is that it has all kinds of technologies. When we plot various technological fields on the horizontal axis and academia, mass production, and workmanship on the vertical axis, we can see that Japan has a larger technology portfolio than other countries. In other words, Japan may lose to other countries in a 100-meter sprint or shot putting, but Japan can overwhelm the rest of the world in a decathlon. This means that if we collaborate through open innovation, we may be able to overcome all social challenges with our technology alone.

The final key that is needed to use this potential to enhance national competitiveness is our ability to create new businesses. The key to the success of high-tech venture companies is marketing rather than cutting-edge technology. The most important thing for a venture company to do is to clarify the social challenges that it intends to overcome and have a corresponding philosophy.

Silicon Valley is often mentioned as an example of successful ventures. A crucial difference in venture culture between Japan and Silicon Valley is the mindset of company founders. While venture founders in Silicon Valley assume that they will make money from an exit strategy based on M&A, many owners of Japanese high-tech venture companies seem to have an emotional attachment to their technology or business.

Start-up companies with a current valuation of US$ 1 billion or more called unicorns have recently attracted public attention, but not all venture companies should try to become one. High-tech venture companies cannot become unicorns easily because they need capital investment. If they operate on a small scale, they should instead help and work with other venture companies that share the same philosophy of overcoming social challenges.

Since non-marketable technology does not attract investment, venture companies should always put social challenges ahead of technology. There are still many social challenges to overcome. Open innovation is the path to revitalizing large enterprises by changing their corporate cultures. I believe that Japan will become more competitive if Japanese companies with philosophies and technologies, including small and medium-sized venture companies, build a win-win relationship with one another through open innovation.

(Interview conducted by the Public Relations Department, NEDO)

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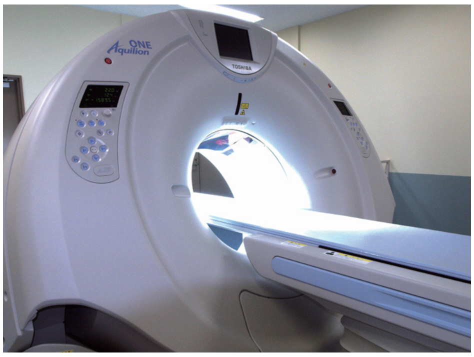


A Few Words from the Editor

Have you heard of "smart cells"? Plastic and other types of waste are social problems. Featured Article 1 introduces NEDO's efforts to biotechnologically reduce the environmental load of manufacturing processes as well as products by maximizing the substance production capabilities of plant and microorganism cells. Featured Article 2 highlights the efforts of venture companies towards open innovation. At the start of this magazine, we interviewed Masahiro Samejima, on which a lawyer from the novel *Downtown Rocket* is based, and asked him about the future of Japan's open innovation. Like the lawyer in the novel, he is a passionate supporter of small and medium-sized venture companies that own excellent technologies.

focus NEDO 2019 No.70
Reporting on Today and Tomorrow's Energy, Environmental and Industrial Technologies

"Focus NEDO" is the public relations magazine of the New Energy and Industrial Technology Development Organization (NEDO), introducing the public to NEDO's various projects and technology development activities related to energy, environmental and industrial technologies.

Featured Article 1

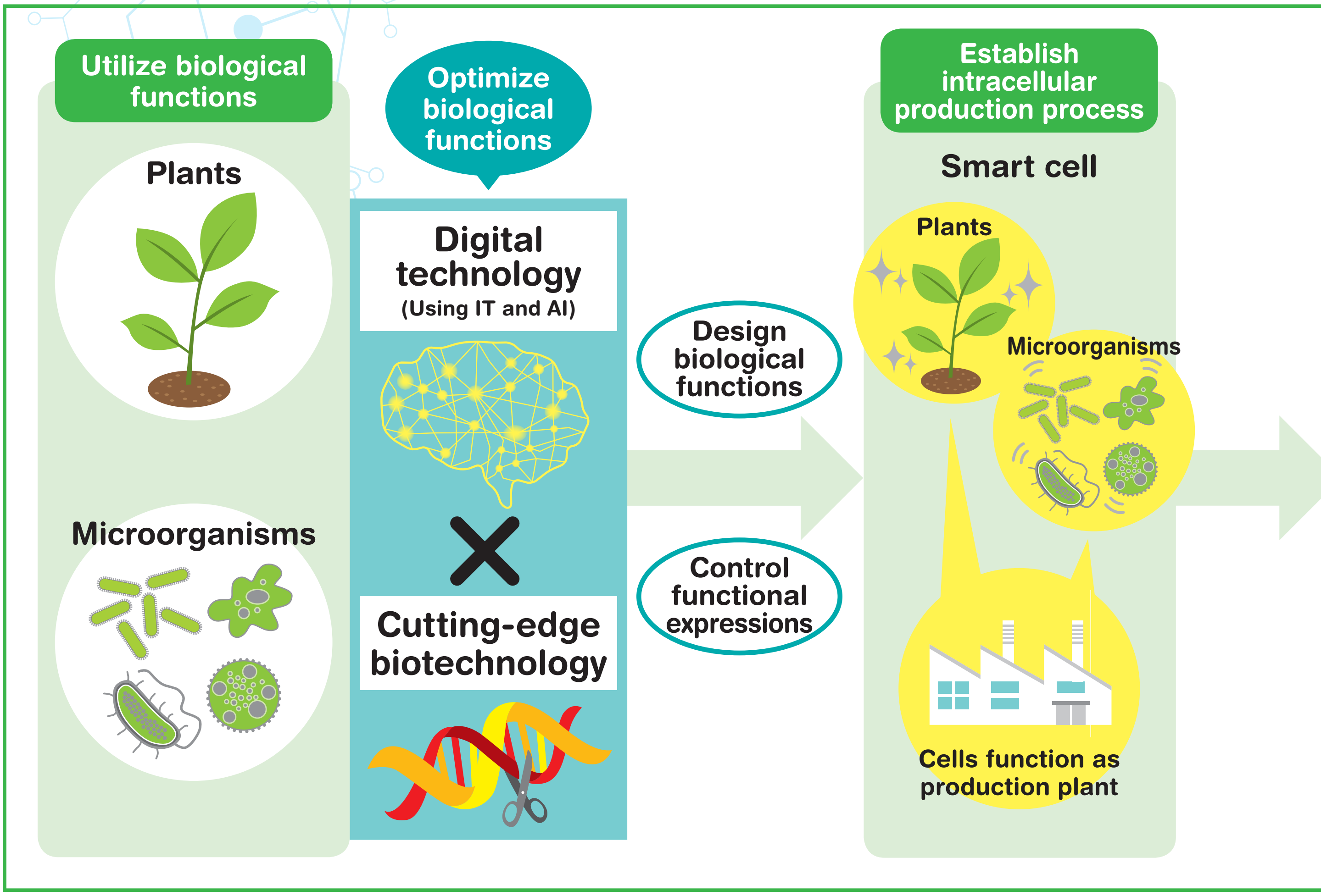
Unlocking the Future by Convergence Research: Biotech × Digitech

Smart Cell Industry

The "Smart Cell Industry", which owes its emergence to recent advances in biotechnology and digital technology, is drawing much attention.

NEDO aims to make an impact on sustainable society by commiting to develop and establish production technologies which utilize biological functions through the "Project for Development of Producion Techniques for Highly Functional Biomaterials Using Smart Cells of Plants and Other Organisms."

Conceptual Diagram of the NEDO Project



What are smart cells?

Smart cells are artificially modified biological cells whose intracellular production process are optimized.

Advanced technologies in biology and digital, such as information analytics, are used to design smart cells with optimum production capability. Smart cells function as biomaterial production plant. The term "smart cell" originates from the intrinsic smartness of cells and their intracellular production process.

Industrialize

What is the smart cell industry?

It is a new industry platform whereby smart cells are used to produce high performance biomaterials applicable to various industrial sectors.

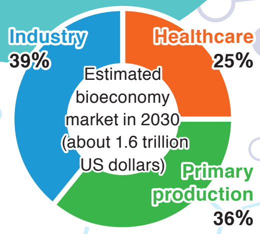
Smart cell enabled high performance biomaterials production will lead to advanced usage of biological resources and functions in various industries such as manufacturing, energy, agriculture, forestry, fisheries and heathcare. In particular, applying smart cells in manufacturing process may enable sustainable production in industrial sectors which rely heavily on oil and other natural resources. *In vivo* application of smart cells may revolutionalize healthcare technologies as well.

Market

What is bioeconomy?

It is a set of economic activities relating to the use of biomass and biotechnology

The Organization for Economic Cooperation and Development (OECD) defines the bioeconomy as a set of economic activities relating to the invention, development, production and use of biological products (enzymes, microorganisms, cells, plants and animals) and processes. It is estimated that within the OECD region, biotechnology could contribute to 2.7% of GDP (about 1.6 trillion US dollars or 190 trillion yen) in 2030, with the largest economic contribution of biotechnology in industry and in primary production acounting for 39% of overall value. As a result, many western countries invest heavily on the policies for the bioeconomy.



Source: OECD report on "The Bioeconomy to 2030" (2009) adapted by NEDO

The usage of smart cells in anticipated in the emerging industrial sector of bioeconomy market

The landmark accomplishements of biotechnology owes much to its convergence with cutting-edge digital technology such as IT and AI. We can now accumulate, analyze and modify large amount of genome data (genetic informations) in short period of time and at a low cost, allowing us to bring out and control the "potential of biological function" in full. These are now utilized in various industries such as agriculture, forestry, fisheries, heathcare or energy but in the future, the use in manufacruring industrial sector is expected to expand significantly accounting for about 40% of the bioeconomy market. Potential applications of smart cells in manufacturing sector are drawing attention globally.

In 2016, NEDO launched the Smart Cell Project "Project for Development of Producion Techniques for Highly Functional Biomaterials Using Smart Cells of Plants and Other Organisms" to create smart cells that are highly optimized for the use in manufacturing process from plants and microorganisms.

Being able to "shift biomaterial production from chemical process to biological process" or being able to "synthesize biomaterials which is difficult to do so by chemical process" will enhance Japan's competitiveness globally as well as decrease the carbon emission thereby offering a solution for the global environmental issues.

Smart cells have the potential to solve various needs of several industrial sectors. The following pages describe NEDO's Smart Cell Project in detail.

Expectations for the Smart Cell Industry

Food company We depend on plant extracts for raw materials of chemicals with complex structure that are difficult to synthesize artificially but there are many challenges associated with it such as plant cultivation and waste disposal post extraction. Smart cells from plants could be the solution for stable and sustainable production of these raw materials.

Chemical company By biologically manufacturing the raw materials used at large scale, we can reduce the stress on environment. Smart cells may be applied to the production of commodity chemicals once the smart cell model using data from microorganisms is established. This may then allow us to achieve economic rationale and reduce environmental stress concurrently.

Use smart cells for industrial scale production

Smart cell industry

- PET bottles
- Synthetic rubber
- Dietary supplements
- Tires
- Cosmetics

and others

Sustainable biomaterial production

NEDO Project's Grand Challenges

Sustainable Future innovated by Smart Cells

We asked the three key leaders of the NEDO's Smart Cell Project: How can the Project address opportunities in building sustainable society? What are the grand challenges and key features of the Project?

History of biotechnology leading to Smart Cells

Hayashi: The research in smart cells in Japan was inspired by the concept of bioeconomy proposed by the OECD in 2009. The most obvious industrial use of biotechnology maybe in solving environmental issues such as replacing plastics but the NEDO Project aims to create a whole new "Smart Cell Industry" using Smart Cells as the core in various manufacturing processs.

Kuhara: We saw major advances in molecular biological techniques this century and this led to the development of smart cells. We can now sequence the genetic information of organisms at a low cost and manupulate genes easily. The founding of the field of "Synthetic Biology" was based on the idea that if we can manipulate genes artificially, then we can artificially create optimum cells. Concurrently, NEDO was promoting a research on "minimal genome"concept. The concept assumes that genomes can be reduced to bare minimum for substance production. These studies led to the the concept of smart cells.

As the research progressed, we were accumulating various biological information and at the same time, there were significant advances in information technology and artificial intelligence. The convergence of information science and biotechnology led to a whole new level of control over biological functions. It is now possible to use microorganisms to manufacture raw materials for industrial products. The landmark accomplishments represents a new opportunity for biotechnology, not only in agriculture or healthcare industries but in petrochemical industry as well.

Matsumura: The term "smart cell" was first used in 2008 mainly by Finnish research institutions in an EU's project but we now use the term in more advanced way. The NEDO Project has two research themes; plants and microorganisms. I am leading the plant research. In the context of smart cells, what is possible in microorganisms is not always the case for plants. While microorganisms have simple structure, plants have a complex metabolic system which may be affected by growth enviroment, process, etc. Thus, gene modification in plants takes time.

Chikako Hayashi
Manager of the NEDO Project for Development of Production Techniques for Highly Functional Biomaterials Using Smart Cells of Plants and Other Organisms (Smart Cell Project)
Ph,D (Science)
Project Coordinator, Materials Technology and Nanotechnology Department, NEDO

Dr. Satoru Kuhara
Leader of the NEDO Smart Cell Project
Ph,D (Agricultural Science)
Professor emeritus, Kyushu University

Dr. Takeshi Matsumura
Sub-leader of the NEDO Smart Cell Project
Ph,D (Agricultural Science)
Plant Molecular Technology Research Group Leader, Bioproduction Research Institute, Department of Life Science and Biotechnology, National Institute of Advanced Industrial Science and Technology (AIST)
Visiting Professor, Graduate School of Agriculture, Hokkaido University

> We will create a new industry of smart cells and stimulate the market.
>
> —— Chikako Hayashi

On the other hand, plants require only light H_2O and CO_2 for photosysnthesis to grow and this means energy requirement for production is small. The choice of plants or microorganisms is case-by-case.

The Project's mission is to create an infrastructure based on "smart cells".

Converging Biotech and Digitech

Hayashi: The key feature of this Project is the convergence research led by leaders from different scientific discipline.. Dr. Kuhara's expertise is in bioinformatics and microbiology. Dr. Matsumura's expertise is in plant biology.

> It was not easy to mix researcher who have diverse perspectives and foster the robust collaboration culture.
>
> ——— Dr. Satoru Kuhara

Kuhara: Although plants and microorganisms are distinctly different, I majored in agriculture at university and Dr. Matsumura is familiar not only with plants but also with microorganisms so we share mutual understanding needed to pursue common research challenges.

Experts from different discipline are participating in the Project; we refer to information analysis experts as "dry experts" and biological material experts as "wet experts". And they have their own languages. Those who find something through data and those who obtains data from findings have totally different perspectives. It was not easy to mix researcher who have diverse perspectives and foster the robust collaboration culture.

Matsumura: Indeed, the key success factor for the Project will be the collaboration between dry and wet experts more than that of plants and microorganisms experts. At this stage, plant theme has few dry experts involved but we can see from microorganisms theme that as the project progress the collaboration becomes more and more intense.

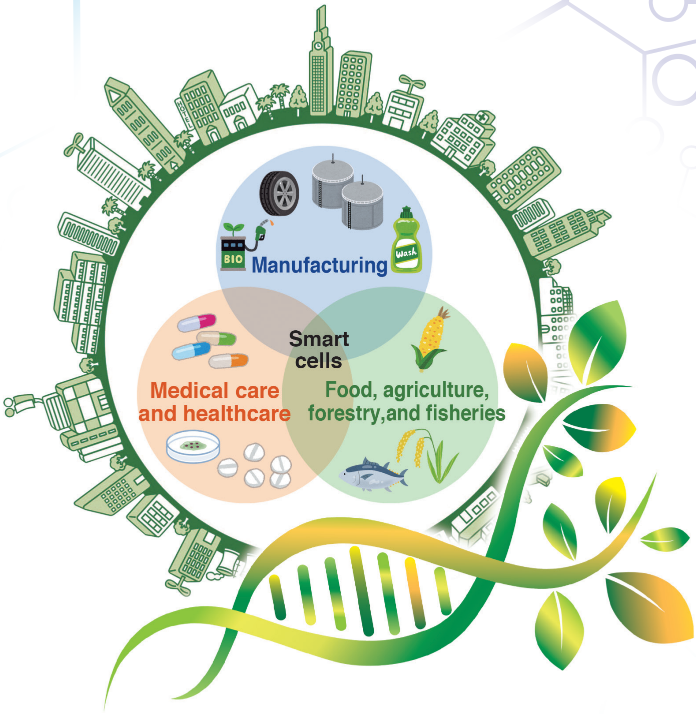
Systematization of individual technologies

Hayashi: We are half way through the Project this year. During the first half of the Proejct we focused on developing underying technologies necessary for building "smart cells" and for the established technolgies, upgrade them to common fundamental technologies. In the latter half, we will focus on systematizing these technologies so that many companies can make practical use of them.

Kuhara: I agree. Instead of using our technologies individually, they need to be systematized as common fundamental technologies and made available for industrial use. Otherwise, the field of application will not expand.

Matsumura: If we think of "smart cell" as a production plant, it is essential to show that it is an automated system which works flawlessly and not just a collection of individual functional technologies. Then we can compete with the world. Scientists tend to focus just on advancing their research but in order to systematize various technologies, we must address the challenges together with the industrial players and only by doing so, we can overcome tough technological problems associated with practical use cycle.

Kuhara: The concept of using biological functions in plants and microorganisms is simple, just like fruit thinning process. In order to grow large fruits, the tree must be thinned out. Information analytics should be used to figure out what to cut off and what to add in order to increase the size of fruits. I would like to put out many practical use case of "smart cell" as possible.



Sustainable future innovated by Smart Cells

Hayashi: Our goal is to make an impact on 7 trillion yen industrial bioeconomy market by 2030. In 2030, the bioeconomy market is projected to reach 1.6 trillion US dollars or 190 trillion yen (see page 3). Industrial field is expected to be about 70 trillion so 7 trillion yen is 10% of that market.

Futhermore, by pursuing the challenge, we will also be tackling the environmental issues such as reducing carbon emmission so we hope to get various industries involved and contribute to the sustanable future.

> I want to show the world that our technologies work as a system and not just as single technologies.
>
> ——— Dr. Takeshi Matsumura

Engineering Plant Secondary Metabolisms

by Combination of Genetic Engineering and Growth Environment Control

The chemical compounds currently used in various industries are chemically synthesized or originates from plants. There are still issues to be solved in stable cultivation method and for efficiently producing secondary metabolites. There are as many as one million varieties of metabolites in plants. In order to ensure that chemical compounds that are biosynthesized by plants are used in many industries in an efficient and stable manner, we must conduct research on metabolic pathways of plants and promoting the development of growth condition for target substance production. Through these activities, NEDO aims to shift from chemical to biological process and reduce the energy that is necessary for chemical process to make the smart cell industry more eco-friendly.

Technology for Controlling Metabolic Gene Expressions

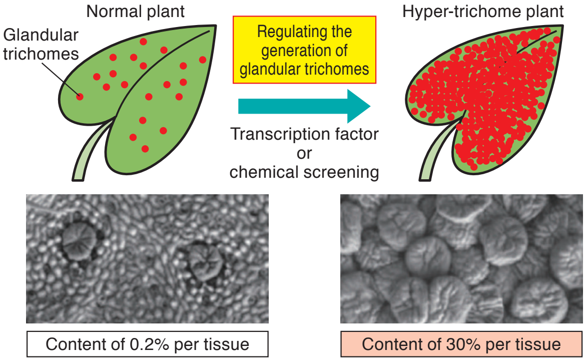
Development of a technology controlling “transport and accumulation” of plant metabolites taking hops as an example.

Development of a technology to control transport and accumulation of plant metabolites

Hops are an essential raw material for beer brewing. The hop corns (female flower) have many dot-like “glandular trichomes”, where valuable hydrophobic metabolites, such as bitter substances and flavors necessary for beer, are accumulated. Hops play also an important role in keeping fine foam of beer. In a NEDO project, Professor Kazufumi Yazaki of Kyoto University focuses on transport and accumulation mechanisms of metabolites in plants. By a combination of controlling technique of “accumulation process” and increment of “accumulation sites, e.g. glandular trichomes”, he is trying to develop a technology toward efficient production of valuable metabolites in plant cells. Future application of this technology include the production of high value metabolites such as medicinal compounds.

Development of a technology to create hyper-trichome plants

This is to develop a technology regulating the generation of glandular trichomes that are the storage sites of metabolites toward dramatic improvement of productivity of high value substances, which are solely stored in glandular trichomes



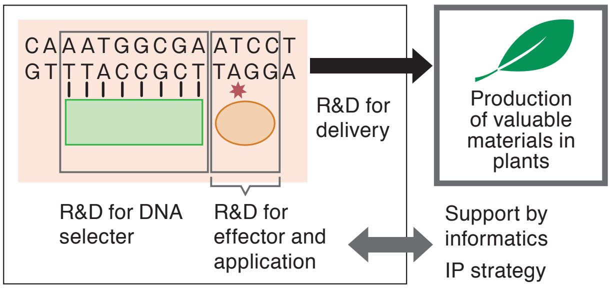
Genome Editing Technology

Establishment of independent technological platform for genome editing by joint R&D program in Japan.

Development of an new genome editing technology

Genome editing technology enables rational gene modification in living organism by using designer DNA cleavage enzyme. This technology significantly improves the production (or breeding) period of useful genetically engineered organisms, and the precise gene modification has been started to apply in therapeutic purpose. Although techniques including ZF, TALE and CRISPR are used over the world, original and non-interfered genome editing technology should be established to facilitate the smart cell industry in Japan and the commercial use. In this NEDO project, R&D program to establish new genome editing technologies has been promoted by Japanese researchers with various expertise.

Development of an new genome editing technology



Control Techniques of Metabolism-related Gene Expressions by Changing Cultivation and Growth Environments

Improvement of the efficiency of useful substance production by controlling cultivation environments

Development of an efficient useful substance production technology utilizing the analysis of metabolism-related gene expression profiles on cultivation technology under a controlled environment

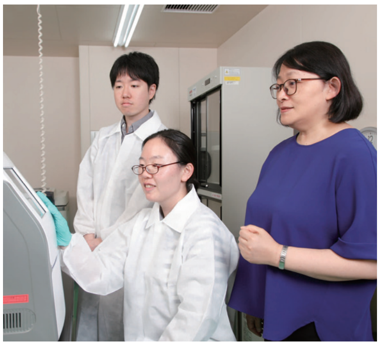
Perevious studies on substance production using plants have focused on improving the previous target substance production efficiency of specific plant species. In these cases, if the target plant species or substances are changed, it is difficult to apply the same technologies to other plant species or substances without modification.

In a NEDO project, the Green Chemical Research Center (GCC) of the Northern Advancement Center for Science & Technology, Hokkaido is collecting data of stimulants and environmental factors that affect the metabolism-related gene expression of plants. And then, they are creating an index that lists the relations between such factors and the metabolism-related gene expression profiles of plants, which can be applied to various plant species.

The study is being conducted in one of the world's few top-class plant factories that are fully contained. This facility can control the air-temperature, humidity, light intensity, carbon dioxide concentration, air flow, and other environment conditions unlike ordinary plant factories. Dr. Kae Sueda, a GCC researcher in charge of gene expression analysis, explains the study as follows: "We are studying whether the metabolism-related gene expressions are affected when the specific growth condition is changed. The target gene cluster is located in the upstream process of a metabolic pathway that begins with photosynthesis. These upstream process are probably common in various plant species. If we can find out how the target gene cluster responds to changes of environmental factors or chemicals, we can apply the findings to various purposes. There is no extensive analysis conducted like this study that targets many genes and substances for industrial application."

Even if the cultivation conditions are strictly controlled, the timing for sampling and analysis is very important because the enviroment is constantly changing as plants continue to grow. Therefore, this work needs to be performed in a timely manner. "Our aim is to clarify how the upstream gene expression changes, caused by environmental factors or chemicals, can affect substance production in its downstream process," says Dr. Kenji Nanya, a GCC researcher. "The goal of this study is to improve the production efficiency of useful substances by about five folds. We have already discovered that some plants are more response than expected. We will also work on medicinal plants that are difficult to cultivate under an artificial environment in the future."

Naoko Onoe, a Chief Officer of NEDO's Materials Technology and Nanotechnology Department, is satisfied with the progress of the project. She says, "The NEDO project is focused on accumulating the data on the change of the metabolic gene expressions profiles of plants as a platform benefitting company. If we can demonstrate that this technology can improve the production efficiency of useful substances as a common infrastructure technology, we can promote the industrial use of plants."



(From left)

Dr. Kenji Nanya
Researcher of the Green Chemical Research Center (GCC), Northern Advancement Center for Science & Technology
Ph.D (Agricultural Science)

Dr. Kae Sueda
Researcher of the Green Chemical Research Center (GCC), Northern Advancement Center for Science & Technology
Ph.D (Agricultural Science)

Naoko Onoe
Project Coordinator, Materials Technology and Nanotechnology Department, NEDO

Cultivation of perilla subsidized by NEDO. Dr. Nanya is in charge of cultivation.

Dr. Sueda is in charge of gene expression analysis. After extracting RNAs from plants, she measures the expression levels of target genes with a real-time PCR and analyzes the metabolic gene expression profiles.

Designing Optimum Cells with Information Analysis Systems to

Create Useful Microorganisms

Compared with plants, microorganisms have simpler structures and faster growth. To improve the production efficiency of substances derived from microorganisms that are necessary for the industry, NEDO is working to establish a common infrastructure that is based on the Design-Build-Test-Learn cycle using with information analysis. This project analyzes the informartion obtained from biological experiments and integrates various infrastructure technologies to achieve the fast optimization of useful functions of microorganisms. NEDO aims to create highly efficient smart cells that can be applied to industries in this project.

D L Construction of Informatics Analyzing System

Dr. Sachiyo Aburatani
Ph,D (Agricultural Science)
Vice-Director of the Computational Bio Big-Data Open Innovation Laboratory, National Institute of Advanced Industrial Science and Technology (AIST)
Senior Researcher of the Biotechnology Research Institute for Drug Discovery, AIST

Application of theoritical models for implementation of SMART microbial biosynthesis

Dr. Sachiyo Aburatani, a senior researcher of the National Institute of Advanced Industrial Science and Technology (AIST), is developing a comprehensive informatics system in this project. This system compiles Database part and Mathmatical Modeling Tools part. Various types of biolgical data has been accumulated into the database part, and several types of theoritical/mathmatical approaches can be applied to those biological data. She says, "In our former analyses, we simply constructed some mathmatical models from biological measured data. But in this project, we carry out theoritical modeling at first, and we have to calcurate back to maximize outcome results based on our inferred theoritical models."

The remaining problem for industrial use of smart cell is arbitrary control of microbial bioprocess system. In this project, the developed theoritical approaches and mathmatical models are evaluated of their effectiveness by several types of bioproducts in micorbials.

"Generally, only the high productive strains have been thought to be vauable in bioprocess field. But in informatics viewpoints, the information from both high and low productive strains have same values. By using both positive and negative data, we can improve our theoritical approch to fit the real bioproduction themes. Theoritical approcah gave us reasonable suggestion of modification candidate genes and how to modify the candidate genes' sequences. The system will become a fundamental technology that will help Japan's smart cell industry to win global competition." (Dr. Aburatani)

D B T L Validaion of Informatics Analyzing System

Dr. Hiroaki Takaku
Ph,D (Agricultural Science)
Professor, Laboratory of Applied Microbiology, Faculty of Applied Life Sciences, Niigata University of Pharmacy and Applied Life Sciences

High efficency of oil production for oil supply expasion and marine resources conservation

Dr. Hiroaki Takaku, a professor of Niigata University of Pharmacy and Applied Life Sciences, is developing the health functional oils containing omega-3 polyunsaturated fatty acids (omega-3 oil) in this project. The supply of fish oil, a primary dietary source of omega-3 oil, can not keep up with increasing demand. He says, "If We can design microorganism which produces a large amount of omega-3 oil in a fermentor unaffected by climate and weather, we can make industry grow much bigger."

Working with the informatics analyzing team, our research, of designing new metabolic pathways and selecting adequate target genes improvement based on the analysis of omics data[*1] is largely accelerated. "While the global demand for omega-3 polyunsaturated fatty acids, such as EPA and DHA, is increasing due to the health benefits, the cost is rising as a result of indiscriminate fishing. The mass production of EPA and DHA by oleaginous yeast could lead to marine resources conservation and market expansion. Increase in development speed by the use of the DBTL cycle enbles us to construct efficient production system of omega-3 oil at a low cost." (Dr. Takaku)

[*1] Omics data: Data obtained as a result of the comprehensive analysis of genomes, transcription products, proteins, metabolic products, etc., within organisms.

Developing Technology for Creating and Evaluating Microorganisms

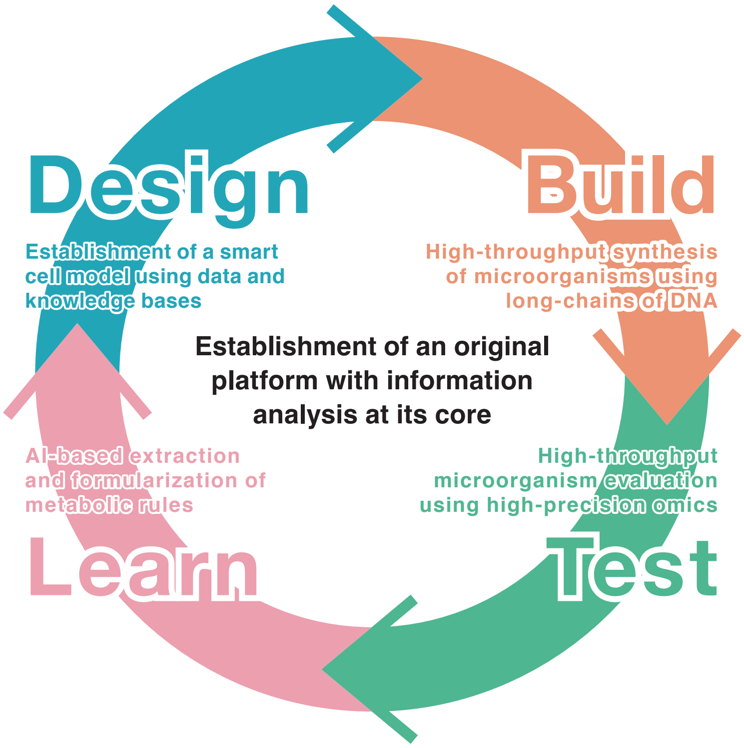
Development of an ultra-high-speed smart cell creation platform with information technology as the core technology

Kobe University Professor Tomohisa Hasunuma, a metabolic engineering expert, is developing a technical platform to create smart cells with significantly enhanced production efficiency of useful substances (smart cell creation platform). "Using long-chain DNAs that can control expression of great variety of genes with one genetic operation enabled to create a variety of microorganisms in a short time. By analyzing the relationship between transcriptome, proteome, metabolome and target production in recombinant strains, we can design smart cells. Our future challenges include creating smart cells more quickly and efficiently by narrowing down the data set necessary for smart cell design."

He has successfully developed a robot that semi-automatically modifies geneome of model organism such as Escherichia coli and yeast. It is now possible to conduct a high-throughput evaluation[2] of the performance of genetically modified microorganisms. These technologies enable companies to significantly improve the productivity of their target substances. These technologies will also enable to produce substances that they have not been able to biologically produce. "There is a series of smart cell creation processes and once we can automate, speed up, and reduce the cost for the processes, we will be able to biologically manufacture various commodity chemical products and highly functional substances to contribute to the development of a sustainable society." (Dr. Hasunuma)

Dr. Tomohisa Hasunuma
Ph.D. (Engineering)
Professor of Graduate School of Science, Technology and Innovation, Kobe University
Director of Engineering Biology Research Center, Kobe University

[2] High-throughput evaluation: Conduction of biological and chemical tests quickly in large quantities at once.



"At the beginning, the information analysis team and the microbial research team faced some communication difficulties caused by different definitions of terms used and so on. However, the cooperation between the teams had a positive impact on this project because it drastically increased the analysis volume and speed and generated new ideas." (Saito)

Hoping for the participation of companies that are strongly motivated to commercialize their products

"It is important to systematize the optimum combinations of underlying technologies used for the Design-Build-Test-Learn (DBTL) cycle of this project because the methods and data used depend on the actual targets of companies," says Takahiro Saito, a Project Coordinator of NEDO's Materials Technology and Nanotechnology Department who is in charge of this project.

"In the first half of the project, it was important for us to test the effectiveness of common infrastructure technologies first. In the second half, we hope this DBTL cycle-based technology will help companies improve the production efficiency of their targets until they can visualize the commercialization of their products."

Takahiro Saito
Project Coordinator, Materials Technology and Nanotechnology Department, NEDO

Efforts Towards Open Innovation

Japan is finally making real efforts towards open innovation, which aims to create innovation by collaborating and cooperating with other companies and different industries and fields. Here are the real voices of startups at the forefront of open innovation and the activities of the Japan Open Innovation Council (JOIC), whose secretariat is operated by NEDO.

Report on "JOIC Presents NEDO Dream Pitch & Seminar"

Necessary Preparations for a Global Business Operation

Innovation Japan 2018

University fair and business matching

August 30 and 31, 2018

This large event co-hosted by NEDO and the Japan Science and Technology Agency (JST) attracted more than 500 universities, startups, small and medium-sized companies, and other organizations from across Japan, which exhibited and presented their research and development achievements. On August 31, NEDO held a pitch contest and seminar titled "Necessary Preparations for a Global Business Operation."

[Moderator] **Mr. Yasuhiro Yamakawa**
Associate professor of entrepreneurship at Babson College

[Commentator] **Mr. Hiroyuki Nara**
Director of the Innovation Promotion Division, Intellectual Property and Innovation Department, JETRO

[Commentator] **Daisuke Baba**
Chief Officer of the Startup Group, Innovation Promotion Department, NEDO

NEDO serves as the secretariat of JOIC as one of its activities to promote open innovation.

In Innovation Japan co-hosted by NEDO and JST in August 2018, JOIC held a panel discussion with six promising start-ups selected from among the exhibitors for J-Startup, a start-up support project promoted by the Ministry of Economy, Trade and Industry.

In the discussion about "Necessary Preparations for a Global Business Operation," the moderator, Mr. Yasuhiro Yamakawa from Babson College, talked about the current situations and challenges of businesses and how to work with business partners as the key to achieving global business success among other issues.

The six startups explained their current situations and mentioned important things for overseas business operations. Some startups said that they often get the first business chance at exhibits like Innovation Japan or through networking. Mr. Yamakawa agreed with them, saying, "Opportunities for exchanging information like this are very important. Candid exchanges of opinions will bring the next opportunity."

Mr. Hiroyuki Nara, a commentator from JETRO, said, "Everyone here is very well aware of the market. To enjoy business success outside Japan, it is crucial for you to be tough and prepared. On the other hand, it is also important to go to the target country and get a sense of the field with your own eyes." Another commentator, Daisuke Baba, a chief officer of NEDO, showed NEDO's eagerness about its future startup support. "I found that the six startups have similar goals, but are different in how they show their passion and approach people. NEDO promises to provide detailed support to them, while valuing their passion and uniqueness."

The following page introduces the real voices of the six promising startups.

The video of the panel discussion is now available on NEDO Channel (YouTube).

Voices of J-Startup Companies That Joined the Panel Discussion

【Holoeyes, Inc.】 Development of a medical VR system capable of virtually finding internal organs and diseased parts

Mr. Naoji Taniguchi
CEO, Holoeyes, Inc.

We exchange information beforehand with social media and other tools.

■Current situations and challenges

Since virtual reality (VR), augmented reality (AR), and mixed reality (MR) technologies are new to the medical field, it takes time for people to recognize the technologies. I think that medical appliance dealers and manufacturers need to take the initiative in establishing a new business model.

■Key to global business success

We are creating a network of people with social media and other tools. It is efficient to exchange information through videos or other means before meeting in person.

【Triple W Japan Inc.】 Distribution of devices that predict and communicate when elderly people need to go to the bathroom

Mr. Atsushi Nakanishi
CEO, Triple W Japan Inc.

Whenever we find a business partner, we will immediately start establishing our business base there.

■Current situations and challenges

Incontinence is a serious problem for us, but we feel embarrassed about telling others that we need to go to the bathroom. This psychological barrier needs to be broken. I want everyone to see incontinence positively and have an interest in finding solutions because incontinence is common for elderly people.

■Key to global business success

We always put out feelers for information. Whenever we find a reliable business partner, we will immediately start establishing our business base there.

【euglena Co., Ltd.】 Distribution of food products and cosmetics using Euglena and biofuel research

Mr. Kengo Suzuki
Director and CTO, euglena Co., Ltd.

We share technology-focused visions.

■Current situations and challenges

Thirteen years after the company was founded, we now find it necessary to develop a new market before consumers become bored with Euglena as raw materials of food products and cosmetics. We are working on technological development to become the first Japanese company to operate a large commercial plant of bio-jet fuel by 2025.

■Key to global business success

We believe that the closest way to a new market is to share technology-focused visions and establish a network of reliable business partners.

【Challenergy Inc.】 Development of next-generation wind turbines capable of generating power even from typhoons

Mr. Atsushi Shimizu
President and CEO, Challenergy Inc.

First-hand information locally obtained is the most important.

■Current situations and challenges

In our efforts to reduce the cost of our wind turbines and conduct demonstration experiments to achieve mass production by 2020, we are currently working on how to comply with strict domestic regulations. Since the current law in Japan does not allow us to connect our wind turbines to domestic power generation networks, we are considering operating them in the Philippines or other countries.

■Key to global business success

I believe that we cannot obtain real local information unless we actually visit the country, see things with our own eyes, talk with local people, and use our five senses.

【Spacelink Co., Ltd.】 Development of carbon nanotube capacitors and products that use them

Mr. Akikuni Abe
Senior Managing Director, Spacelink Co., Ltd.

We need to compete with industrial leaders with vested rights.

■Current situations and challenges

To expand our business, we sought reliable domestic partners because it was difficult for us to work with overseas business partners due to language differences and distances. It took two years to find reliable domestic business partners. Though the idea of open innovation has spread, we still have difficulty in finding investors.

■Key to global business success

We are considering forming a team of venture companies to compete evenly with overseas industrial leaders with vested rights.

【FLOSFIA Inc.】 Development of power devices using semiconductor materials with low power loss

Mr. Takuto Igawa
Marketing Manager, FLOSFIA Inc.

It is important to secure our intellectual property rights.

■Current situations and challenges

We are a B-to-B venture manufacturer. When we are in the stage of supplying parts to our customers, they tend to strongly demand the reduction of costs. One of our major challenges is to find out at which stage we should invest in order to reduce cost and establish overseas operating bases.

■Key to global business success

It is important to secure our intellectual property rights. We gather the necessary information by sending emails to manufacturers in Asia and visiting them.

Efforts to Promote Open Innovation

JOIC, whose secretariat is operated by NEDO, was established in March 2017. To enhance Japan's competitiveness by promoting open innovation, JOIC is carrying out various activities including NEDO Pitch, which is a pitch contest for business matching.

What is JOIC?

Contribution to creating innovation and boosting competitiveness

JOIC was established in March 2017 as a result of a merger between the Open Innovation Council and the Venture Business Creation Council. JOIC aims to promote the innovation of Japanese industries and boost their competitiveness. For this purpose, JOIC promotes open innovation efforts in the private sector as well as realizes a favorable cycle of venture creation in order to form groups of enterprises that can be future industrial leaders and revitalize Japanese economy with their new energy. JOIC is operated by the Startup Group of NEDO's Innovation Promotion Department with NEDO's President serving as the director of its secretariat.

JOIC holds many seminars and events.

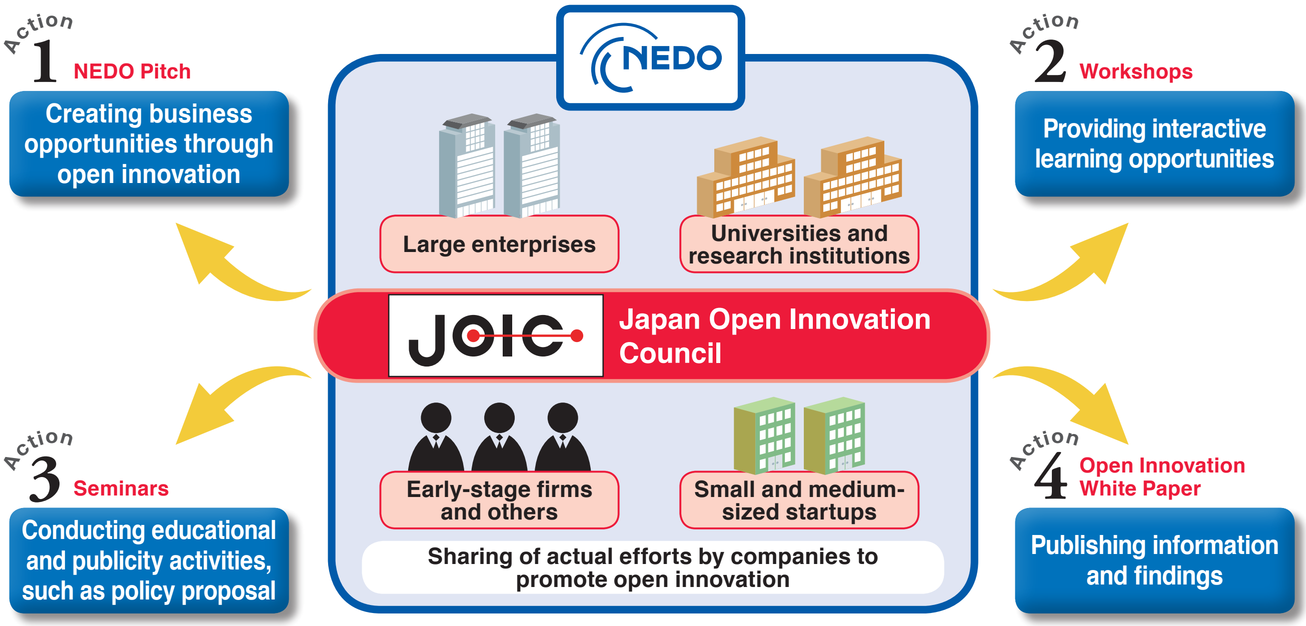
As a membership-based organization, JOIC has about 1,200 members, including about 800 corporate members. With these members, the organization is conducting various activities to promote open innovation with R&D venture companies and large enterprises. For example, NEDO Pitch is a unique activity of JOIC that aims to create business opportunities that couple startups with large enterprises and venture capital firms.

"JOIC provides various opportunities, such as workshops and seminars. We hope many people and organizations will use these opportunities," Nobuyuki Taniguchi, a Chief Officer of NEDO's Innovation Promotion Department, which serves as JOIC's secretariat, says enthusiastically.

Nobuyuki Taniguchi

Chief Officer of the Startup Group, Innovation Promotion Department, NEDO

Conceptual Scheme of JOIC's Activities



Action 1

NEDO Pitch

Matching event aimed at commercialization

NEDO Pitch is the core activity of JOIC that takes place about ten times a year. In this business matching event, four to six R&D startups and other companies make a short, focused presentation of their projects to managers who are responsible for new business development in large enterprises, venture capital firms, and others in a bid to commercialize their projects. Since the start of NEDO Pitch in 2015, more than 120 venture companies have taken the platform, many of which have achieved business success as a result of business ties established through this event.

NEDO Pitch

Action 2

Workshops

Interactive learning opportunities for discussions among members

JOIC annually holds about six small members-only workshops (for up to about 50 participants) as interactive learning opportunities. Every workshop has specific themes, which are actively discussed by participants. Past themes include effective business-academia collaborations; the need to promote open innovation; the potential of corporate venture capital (CVC); key points to search for and work with overseas startups; open innovation coordinators; and the promotion of open innovation through M&A.

Workshop

Action 3

Seminars

Educational and publicity activities to change mindsets

To lead the global market through innovation, Japan needs to change the mindsets of businesses and universities towards open innovation using external technologies, ideas, and resources. For this purpose, JOIC organizes open innovation seminars (about three times a year), Japan Venture Awards, and other related events as part of its educational and publicity activities to deepen and promote open innovation further.

Seminar

Action 4

Open Innovation White Paper

White paper showing successful cases of domestic and overseas open innovation

JOIC researches successful cases of domestic and overseas open innovation and publishes policy proposals based on the findings of such researches and events in the Open Innovation White Paper. Following the first edition published in 2016, JOIC has published the second edition in June 2018, which has updates on the statistical data of current open innovation, international comparison of ecosystems, and domestic open innovation efforts. Please feel free to read it.

JOIC

NEDO

オープン
イノベーション白書

第二版

Open Innovation

オープンイノベーション・ベンチャー創造協議会（JOIC）
事務局　国立研究開発法人 新エネルギー・産業技術総合開発機構（NEDO）

The PDF version of the white paper can be downloaded from NEDO's website.

Membership application

If you support the aims of JOIC's activities, please consider joining JOIC (no membership fees required). Members are provided with event information and other news earlier than non-members through email newsletters.

JOIC's website: https://www.joic.jp

Videos available on NEDO Channel (YouTube)

Videos about researches and events related to NEDO are available on YouTube. Videos about previous NEDO Pitch events are also available. Search "NEDO Pitch" on https://www.youtube.com.

Easy to Understand!

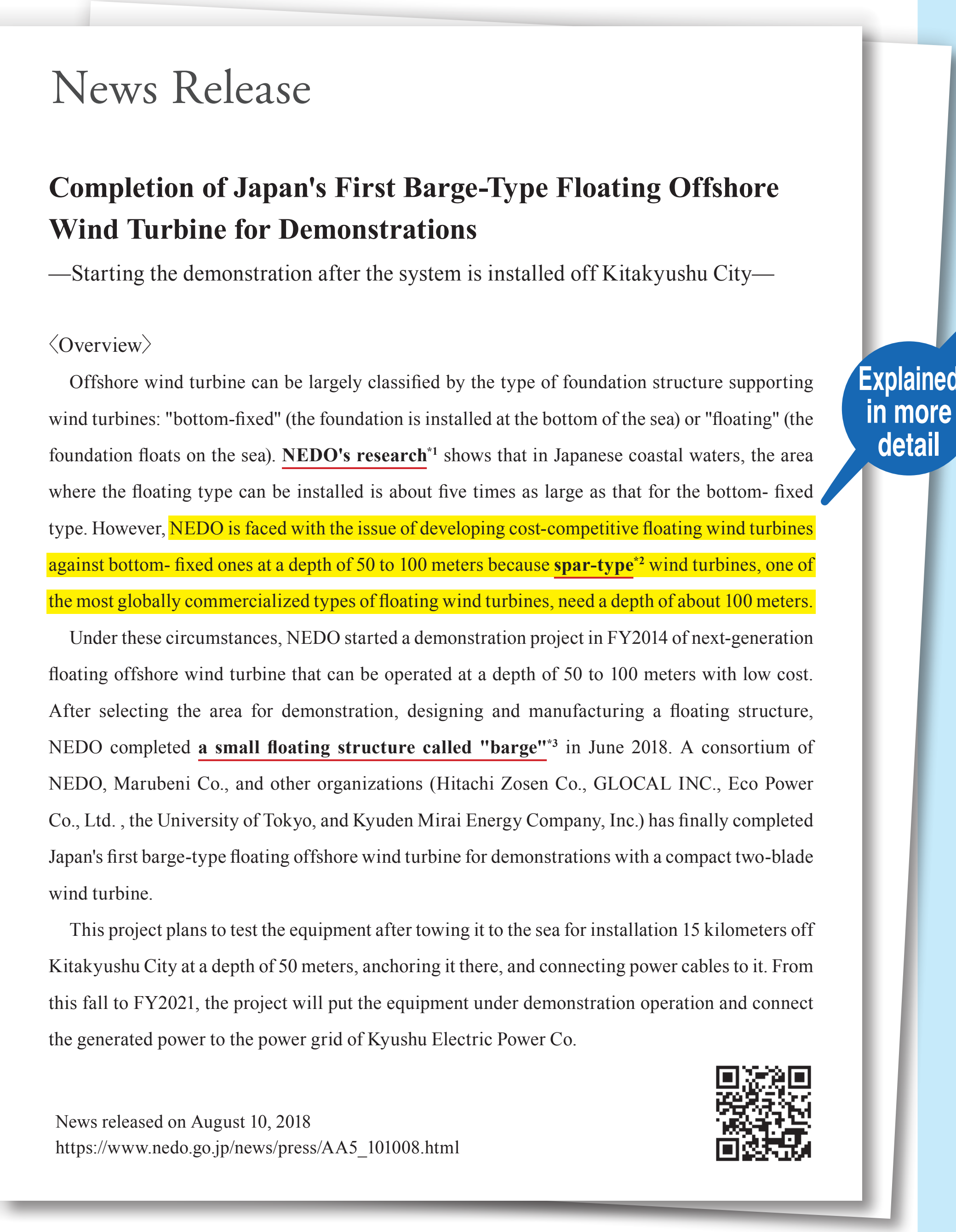
News Release Commentary

A special feature that aims to make news releases full of jargon, technical terms, and difficult technologies easier to understand by focusing on the important points. This section states NEDO's state-of-the-art technological achievements and activities with explanations that are easy to understand.

Featured news release

News release on the demonstration project of next-generation floating offshore wind turbine (barge type) (FY2014–2021)

by the New Energy Technology Department



News Release

Completion of Japan's First Barge-Type Floating Offshore Wind Turbine for Demonstrations

—Starting the demonstration after the system is installed off Kitakyushu City—

〈Overview〉

Offshore wind turbine can be largely classified by the type of foundation structure supporting wind turbines: "bottom-fixed" (the foundation is installed at the bottom of the sea) or "floating" (the foundation floats on the sea). **NEDO's research**[*1] shows that in Japanese coastal waters, the area where the floating type can be installed is about five times as large as that for the bottom- fixed type. However, NEDO is faced with the issue of developing cost-competitive floating wind turbines against bottom- fixed ones at a depth of 50 to 100 meters because **spar-type**[*2] wind turbines, one of the most globally commercialized types of floating wind turbines, need a depth of about 100 meters.

Under these circumstances, NEDO started a demonstration project in FY2014 of next-generation floating offshore wind turbine that can be operated at a depth of 50 to 100 meters with low cost. After selecting the area for demonstration, designing and manufacturing a floating structure, NEDO completed **a small floating structure called "barge"**[*3] in June 2018. A consortium of NEDO, Marubeni Co., and other organizations (Hitachi Zosen Co., GLOCAL INC., Eco Power Co., Ltd. , the University of Tokyo, and Kyuden Mirai Energy Company, Inc.) has finally completed Japan's first barge-type floating offshore wind turbine for demonstrations with a compact two-blade wind turbine.

This project plans to test the equipment after towing it to the sea for installation 15 kilometers off Kitakyushu City at a depth of 50 meters, anchoring it there, and connecting power cables to it. From this fall to FY2021, the project will put the equipment under demonstration operation and connect the generated power to the power grid of Kyushu Electric Power Co.

News released on August 10, 2018
https://www.nedo.go.jp/news/press/AA5_101008.html

Explained in more detail

Terminology

1. NEDO's research
This refers to the basic research on floating offshore wind turbine conducted in FY2011. NEDO researched the potential of floating offshore turbine within an offshore distance of up to 30 kilometers and at a depth of up to 200 meters in Japanese coastal waters. It concluded that the bottom- fixed type (at a depth of up to 50 meters) can be installed in an area of about 14,000 km^2, while the floating type (at a depth of 50 meters or more) can be installed in an area of 77,000 km^2, about five times as large as the area for the bottom-fixed type (social constraints were not taken into consideration).

2. Spar-type
A vertically-extended floating structure with most of it going under the water due to its reduced water plane area.

3. Barge-type floating structure
A floating structure that can be installed in shallow waters because it is mostly above the water.

Key Technology

Suitable for wind and marine Conditions in Japanese Coastal Waters

Barge-Type Floating Offshore Wind Turbine

NEDO aims to reduce the cost of the system by loading a light two-blade turbine on a barge-type floating structure body that can be installed in shallow water about 50 meters deep.

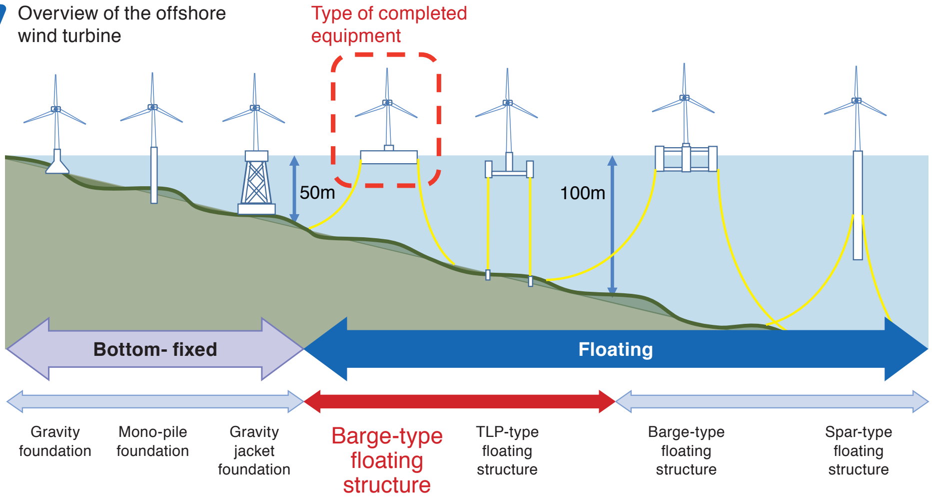
Key Points!

- ☑ Low-cost floating offshore wind turbine suitable for Japan's wind and marine conditions.
- ☑ Can be installed at sea at a depth of 50 to 100 meters, which are relatively shallow for floating systems.
- ☑ Combination of a light two-blade wind turbine that can be easily installed and a barge-type floating structure of shallow draft.
- ☑ Equipped with a chain and drag anchor system that can safely anchor the floating structure under severe wind and marine conditions.

Commentary

Low-Cost Next-Generation Floating Offshore Wind Turbine

Overview of the offshore wind turbine



Completed barge-type floating offshore wind turbine for demonstrations

NEDO has focused on the technological development of offshore wind turbine to further promote the introduction of wind power generation. Its research has found that Japan has vast areas of coastal water where floating offshore wind turbine equipment can be installed. However, NEDO had to establish a technology to install floating offshore wind turbines at sea at a depth of 50 to 100 meters because preceding demonstration project (Fukushima FORWARD and GOTO-FOWT) were conducted at sea at a depth of 100 meters and more.

Since the barge-type floating structure adopted in this project has a shallow draft and is smaller and lighter than ordinary semi-submersible floating structures, it can be installed in shallow waters about 50 meters deep. The completed equipment has a compact two-blade wind turbine on a steel barge-type floating structure and can be installed at a low cost. It is anchored by nine anchoring systems with a combination of stud-less chains and ultra-high holding power anchors so that its safety can be secured even under severe wind and marine conditions.

After installing the equipment, NEDO will inspect its design with measurement data and develop an efficient maintenance technology for the floating structure and anchoring systems that uses a remote-control unmanned underwater vehicle in order to establish the technology for a low-cost floating offshore wind turbine.

Also Check Here!

Website with information on the project

This website provides the project outline, research news, photos of the wind turbine, floating structure, and anchoring systems, and other information on the demonstration project of next-generation floating offshore wind turbine.

https://floating.nedo.go.jp

[YouTube] NEDO Channel

This channel shows the computer graphic images of the processes from manufacturing to installation of the floating offshore wind turbine at sea. In or after this fall, it plans to upload video footage of the processes, which are currently being shot.

Post-Project Follow-Up!

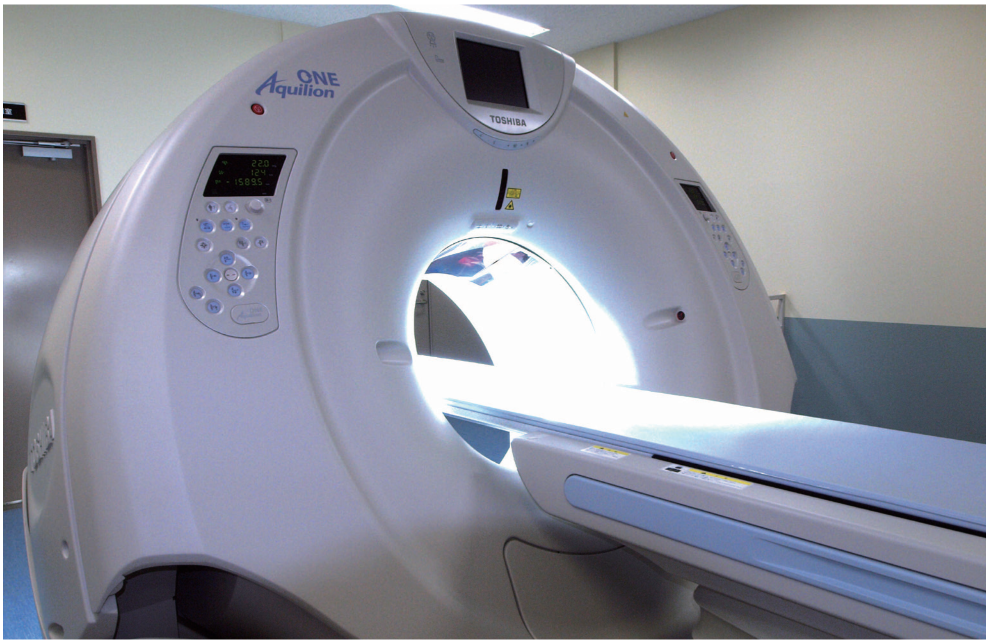
NEDO Project Success Stories
Looking Back at History

**The results of NEDO projects are utilized in manufacturing processes used by companies and final products available for consumers.
In this series, we look at untold stories of how technology development projects scaled the high, difficult wall to successful commercialization and what came after, summarizing past articles in "NEDO Project Success Stories."**

Vol.10 Development of Real-Time 4D Imaging System

4D X-ray CT system capable of taking images of an entire heart in only 0.35 seconds

Toshiba Medical Systems Corporation (currently Canon Medical Systems Corporation)



4D X-ray CT system "Aquilion ONE™"
The angle of the gantry (rotating part) can be adjusted for head scanning.

The 320 detector rows have considerable width as a CT system.

NEDO Project

Development of a real-time 4D imaging system

(from FY2001 to FY2003)

X-ray CT systems in the 1990s could take cross-sectional images of organs, but it was difficult to take high-definition 3D images of an entire organ, such as hearts and brains. With the help of clinical professionals as well as enterprises and universities, NEDO conducted a medical-engineering collaboration project to develop a technology of 3D diagnostic imaging called "high-speed cone beam 3D X-ray CT system" from FY1998 to FY2001.

As part of its efforts to make the system smaller and faster to improve image quality and reduce radiation exposure, NEDO went on to develop a real-time 4D imaging system. Toshiba Medical Systems Co. (currently Canon Medical Systems Co.) successfully developed the world's first 4D X-ray CT system, which can obtain clear 4D images by adding a time axis to 3D images.

BEGINNING —— Road to development

Taking images of an entire heart in one rotation (one rotation for one organ)

A CT system is a diagnostic imaging system essential to modern medicine that takes black-and-white cross-sectional images of organs by rotating around a human body while radiating X-rays. The colors are differences in X-ray absorption rates. It took about 10 minutes to obtain 20 images with early CT systems called "helical CT systems," which moved the patient's bed after taking each image with one detector row. These systems required patients to hold their breath as many as 20 times for each rotation.

In 1990, Toshiba Medical Systems Co. released the world's first CT system equipped with helical scanning functions, which could scan an entire organ in tens of seconds while rotating helically around the human body, so patients only had to hold their breath once. However, this new system still needed some time to complete scanning, provided poor images of repeatedly scanned parts, and exposed patients to a significant amount of radiation. For this reason, the company joined NEDO's project to develop a high-speed cone beam 3D X-ray CT system, which started in FY1998, in order to create a CT system that can take images of an entire organ in a single rotation. In the joint research and development project with Sony and the National Institute of Radiological Sciences, Toshiba Medical Systems succeeded in arranging 256 detector rows for X-ray tubes that radiate cone beam X-rays at the target. Since CT systems for medical use only had 16 detector rows at the time, the new CT system provided a field of vision that was 16 times larger than previous ones.

BREAKTHROUGH —— Project breakthrough

Drastically increasing detector rows from 256 to 320 to achieve a coverage of 160 millimeters

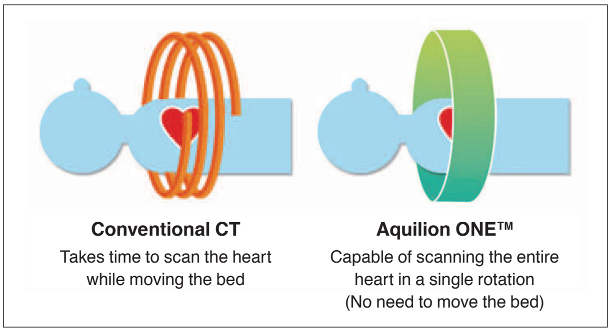
As the number of detector rows increases, detector elements also increase drastically (one detector row has about 900 elements, so 256 rows have about 230,000 elements) and it becomes necessary to significantly increase the packing density of data collection circuits that process the signals. As the data volume increases, it also takes more time to collect and transmit signals from elements and reconstruct images. This is why it became important to make CT systems smaller and faster to achieve better image quality and lower radiation exposure.

In FY2001, Toshiba Medical Systems started developing a real-time 4D imaging system as a project subsidized by NEDO. This project increased the density of data collection circuits, developed original circuit systems capable of high-speed data transmission, and adopted a system for reconstructing all scanned images at once, instead of the conventional system of reconstructing scanned images one by one. As a result, the initial rotation speed of one second per rotation was reduced to 0.5 seconds before being further reduced to 0.35 seconds for the CT system that was eventually put on the market.

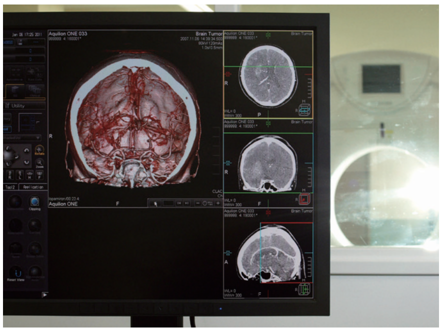
On the other hand, the coverage needed to be improved further. Although the real-time 4D imaging system development project increased the coverage to 128 millimeters with 256 detector rows, it was still insufficient for clinical purposes. For example, the system could not cover an entire heart if the heart moves up and down in conjunction with respiration and body movements or is enlarged. The system also could not cover an entire brain, depending on its size or shape. Compared with the conventional CT systems, the 128-mm coverage seemed more than satisfactory, but the company does not want to sell products that are less than perfect, so it decided to arrange 320 detector rows that can provide 160-mm coverage and cover entire brains and hearts.

FOR THE FUTURE —— Current and future development

Revolutionary CT system for revolutionary diagnosis



The helical CT system that scans the body while moving the bed (left) takes some time to complete scanning, provides poor images of repeatedly scanned parts, and exposes patients to a significant amount of radiation.



4D X-ray CT images and a monitor display during head scanning.

In November 2007, Toshiba Medical Systems finally released Aquilion ONE^{TM}, the world's first X-ray CT system capable of taking images of an entire organ, such as hearts and brains, in single-rotation scanning. This CT system drew global attention as an innovative CT system that can take high-resolution 4D images with 320 detector rows, more than the 64 detector rows provided in top-end models at the time. For heart scanning, for example, the new system can reduce scanning time to about one-twentieth, radiation exposure to about one-fourth, and the usage of contrast agent to about half, compared with the previous top-end models. Since the new system can scan seamlessly, it can produce images of extremely high quality that is free from misregistration (image degradation caused by image processing errors).

Aquilion ONE^{TM} has suddenly expanded the potential of diagnostic imaging. It enables us to observe the fast blood flows of brains and easily observe arteries separately from veins. It has relieved patients of the burden of vessel catheterization and made it easier to scan children and dementia patients who have difficulty holding their breath.

By June 2018, 1,453 units of Aquilion ONE^{TM} have been sold in the world. The introduction of this new CT system will also reduce the burdens of doctors and medical technologists, making further contributions to medical fields.

This article provides an updated summary of an article published in a past edition of "NEDO Project Success Stories." The original article describes more incidents related to the development process. For further details, please visit the website.

Project Success Stories **Search**

In "NEDO Project Success Stories," we interview representatives of the companies who have participated in NEDO projects and other related parties for publication on the website. To date, we have published 100 articles in this series.

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