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NEWSLETTER

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English translation of Japanese newsletter

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Greetings from the New Chairman

I am honored to be appointed as the third chairman of the American Medical Devices and Diagnostics Manufacturers' Association (AMDD), as of April 1. I have been serving as president of Medtronic Japan Co., Ltd. since 2008.

Established in 2009, AMDD represents the Japanese operations of 67 companies (as of March 2012), mainly headquartered in the United States, that provide advanced medical technologies such as medical devices and in-vitro diagnostics (IVD). AMDD member companies create employment opportunities for more than 21,000 people in Japan and have carried out a wide range of activities to contribute to the improvement of Japanese healthcare via advanced medical technologies.

With our mission to "improve the welfare of patients in Japan using the latest medical technology," AMDD is committed to delivering advanced medical technology in a safe manner, as soon as it becomes available. Through dialogue, we are collaborating with the relevant authorities about the measures required to resolve problems such as "device lag" and "device gap," which delay the introduction into Japan of advanced medical devices and IVDs that are already accessible and highly regarded in other countries. With regard to "device lag," thanks to the efforts made by all the concerned parties, actions have been taken to shorten the total review period for approval of medical devices and IVDs. However, we believe that it is critical to continue addressing this issue. In terms of "device gap," there is still a long way to go to resolve the issue, and this can only be achieved with

the understanding and cooperation of everyone involved, along with greater efforts on our part.

In the past year, we have enhanced our activities to establish a regulatory framework that recognizes the characteristics of medical devices. AMDD has been working closely with other medical device associations to generate policy proposals that recommend a regulatory structure that classifies "medical drugs, quasi-drugs and cosmetics" and "medical devices" separately. In order to establish this framework, we will continue our dialogue with all the parties concerned, including the Japanese government.

In addition, to carry out AMDD's other mission to "realize a healthcare system that fully appreciates the value of innovation in medicine," we will raise awareness of the value of innovative medical technology and promote a broader understanding of its contribution to healthcare.

By liaising closely with the United States government and the US-based Advanced Medical Technology Association (AdvaMed), AMDD will aim to further contribute to the development of Japanese healthcare through its activities. This will be carried out in collaboration with the Japanese government, medical societies and related industry associations, while also maintaining our close relationships with patient communities and healthcare professionals.

We deeply appreciate your continued guidance and encouragement.

Takashi Shimada
Chairman, American Medical Devices and Diagnostics Manufacturers' Association (AMDD)
President, Medtronic Japan Co., Ltd.

The Need for Automatic Contrast Medium Injectors for CT & the Requirements for their Safe Use

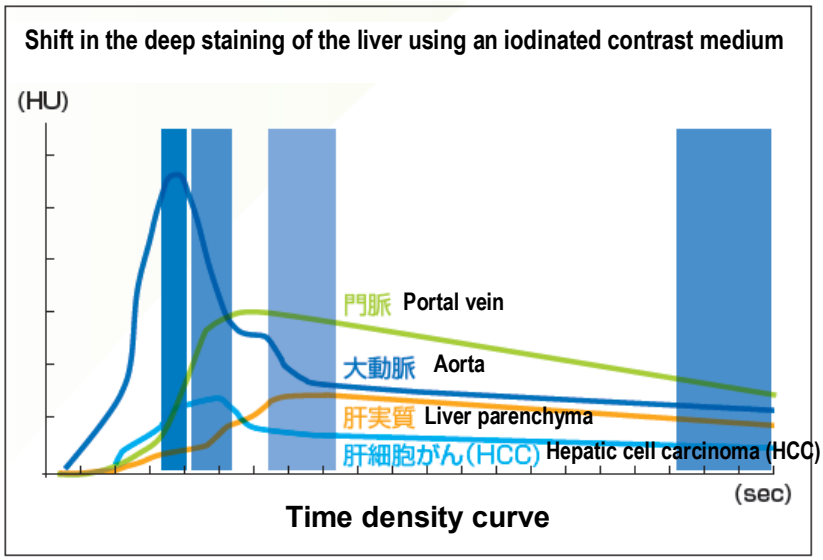
Automatic contrast medium injectors are used frequently in X-ray CT. High-contrast cross-sectional images facilitate detection of lesions such as cancer. However, as the contrast medium does leak out of the blood vessels in under 1 percent of cases, it is necessary to have the correct safety measures in place.

Automatic injectors are essential for contrast-enhanced CT

I belong to the Division of Radiology in the Department of Medical Technology at Kyushu University Hospital, and handle X-ray and MRI equipment regularly. Last year, 63 radiology technicians performed about 140,000 X-ray scans and about 31,000 X-ray CT scans. About 18,000 scans, which account for 57 percent of these CT scans, were contrast-enhanced CT scans using contrast media. Automatic contrast medium injectors were used in all cases.

Contrast-enhanced CT produces cross-sectional images (slice images) by rapidly injecting iodinated contrast media at an average of 3 ml per second via an elbow or forearm vein. After a period of time, an X-ray can be taken, collecting data and processing it as cross-

sectioned images on a computer. Because the intensity of color in each organ changes depending on the time after the injection of contrast media, it is necessary to take images at the right time to obtain the desired information.



The horizontal axis shows time (seconds) and the vertical axis shows the intensity of staining. Vertical stripes show the aorta, portal vein, liver parenchyma and equilibrium layer from the left.

As a concrete example, we will examine a case where the focus was on the liver. The above figure shows a shift in the deep staining of the liver after rapid injection of an iodinated contrast medium. The aorta reached a peak at 3 to 4 seconds after the start of injection, followed by the stronger intensity of staining in the portal vein and the liver. In this way, lesions such as hepatic cell carcinoma can be detected by integrating information about the shift in deep staining by an iodinated contrast medium on images.

The right timing for photographing is determined by the density curve

As explained, automatic contrast medium injectors are essential for taking CT images right when the contrast medium reaches the vessels. Traditionally, photographing begins after about 100 cc of the contrast medium is injected over several minutes. However, it has now become possible to obtain 64 to 320 images at once in under a second, thanks to the emergence of an apparatus called a multi-detector CT. Because the staining of each organ changes rapidly, the density curve of the organ is monitored in order for images to be taken at the correct timing.

With the current contrast-enhanced CT, 50 to 150 ml of contrast medium is injected at a constant speed. The total injection time is less than one minute. Images of abnormal lesions in the normal tissue can be taken using high contrast, unless the timing of the photographing is wrong. The anatomical morphology can also be understood by creating a three-dimensional image.

However, in some rare cases, contrast media can leak out of the blood vessels as a result of rapid injection. Due to the fragility of blood vessels, especially in elderly patients, there is a 0.3 to 0.4 percent probability of extravasation of contrast media, no matter how much care is taken. The incidence of extravasation is estimated to be 18,000 to 24,000 a year.

When the contrast medium leaks out of the blood vessels, the injection site in the arm swells and can cause pain. Therefore, scans must be discontinued immediately and the appropriate measures must be taken. If compartment syndrome develops, it is necessary to make a surgical incision to remove the contrast medium. As it is difficult to prevent extravasation of contrast media, early detection of leakage and immediate response are vital.

The emergence of detection systems for extravasation

In response to this situation, contrast medium injection pressure monitors that allow early detection of extravasation have been developed. These monitors can measure the pressure in real time with the injector sensor in the operation room or examination room. A medical radiology technician starts the injection and simultaneously asks the patient, "Do you feel hot?" through a microphone. If any abnormal waves appear on the monitor, the injection should be discontinued at the technician's discretion. Then the injection site must be inspected for swelling.

There are currently no established evaluation criteria for variation in the injection pressure. This has put radiology technicians in a difficult position as they must make a quick judgment call on whether or not to discontinue the injection. Since it requires a great deal of work to start over, they must have the courage to make a prompt decision.

Some recent leakage detectors utilize reflected or high-frequency waves of infrared light rather than variation in the injection pressure. Many hospitals, however, refrain from introducing extravasation detectors due to concerns over increased hospital costs, even though this safe technology is useful for patients. This is because the number of points for CT scans is irrespective of the use of extravasation detectors under the current medical reimbursement system. The additional point system for medical safety management is still unsatisfactory, and I look forward to further progress on this in the future.

(This is a summary of the interview with Mr. Nakamura, edited by the editorial desk.)

Mr. Yasuhiko Nakamura
Head Medical Radiology Technician, Division of Radiology, Department of Medical Technology, Kyushu University Hospital

Mr. Nakamura graduated from the School of Health Science, Kyushu University in 1979, and joined the Department of Radiology at Kyushu University Hospital. He served as Clinical Associate Professor, Department of Health Sciences, School of Medicine, in 2006. He assumed the positions of Head Medical Radiology Technician and Clinical Professor, Department of Health Sciences, in 2010.

Patient's Voice

Our Gratitude for the Advances in Medical Technology and the Need for Further Development

By Ms. Yukie Saito
Chairperson, Japan Network for Children with Heart Disease

The Japan Network for Children with Heart Disease was established in 1963. Fifty years have passed since then. There is an enormous difference between the medical technology that was available back then and that of today. It used to be very expensive to undergo

surgery. According to an old bulletin from our network, most of the parents of children with heart disease could not do anything but just stand by and watch.

Even so, parents of children with heart disease gathered together out of a desire to save their children, bringing attention to the situation and carrying out various activities to increase people's understanding. Their wishes moved the government, and consequently surgical and outpatient costs for congenital heart disease came to be covered by public funds.

This system and the persistent efforts of pediatric cardiologists and healthcare professionals have saved the lives of many children with heart disease. As a result, issues that arise during adulthood, such as employment and childbearing, have now become important themes for our network.

The development of medical equipment and devices such as heart-lung machines are essential for advancing medical technology. Among these devices, the development of catheter-based therapy was very good news for children with heart disease. I hope that there will be further development and improvement of surgical procedures and less burden on patients.

There are no surgical methods available for some children with severe congenital heart defects, such as a single ventricle defect or hypoplastic left heart syndrome. Those children and their parents place their hope in heart transplantation, regenerative medicine, and the development of artificial hearts.

Seventeen years have passed since our network held a heart transplant symposium and started calling for the approval of transplantation in Japan. At last, children under 15 years of age can now undergo organ transplants. However, there has not been a single case of transplants in small children. They have no choice but to rely on risky transplant operations abroad. Efforts to seek understanding are necessary.

Internally implantable auxiliary artificial hearts have been so large that only adult male patients were able to receive implants. However, downsized auxiliary artificial hearts have now been developed, authorized, and put into practical use. There have been reports of success in the recovery of myocardial function by regenerative medicine.

Our network has high hopes for advances in medical technology, and our goal is to support affected children to find the courage to face their disease. Therefore, we would like to deepen our ties with children with heart disease and their parents, as well as with healthcare professionals.

This year, our network celebrates its 50th anniversary. There will be a convention in Yokohama in November to celebrate our anniversary with the many people who have walked this path with us, and we promise to move forward toward new goals. We are looking forward to many people attending this convention.

Japan Network for Children with Heart Disease http://www.heart-mamoru.jp/

Medical Journalist Viewpoint

Issues Facing the Medical Device Industry: My Observations from Covering the Chuikyo

Mr. Junji Maki
Medical journalist

I write a regular column, "Actions Taken by the Chuikyo and the Government Regarding Medical Supplies," in a professional medical supply journal. In it, I always cover the Central Social Insurance Medical Council's (Chuikyo, headed by Akira Morita, Chairman) Special Meeting on Insurance-covered Medical Supplies. I would like to summarize the key issues facing the medical device industry observed from the 2012 medical reimbursement revisions.

One of the reasons that reporters for Chuikyo have difficulty in understanding medical devices is that the "medical devices" handled by the Chuikyo's Special Meeting on Insurance-covered Medical Supplies under the Pharmaceutical Affairs Law are called "Medical Supplies." These two terms are being confused. Furthermore, less-experienced reporters are not familiar with the fact that insurance-covered medical supplies have about 700 functional classifications, with items under each classification having the same pricing. With such a pricing system, incentives for innovation do not work well. This is a significant difference from pharmaceutical products that are priced by brand. Meanwhile, many reporters cannot answer the question of why clinical trials of medical supplies and devices are seldom conducted. It will probably be necessary to provide lectures on these fundamental issues.

A medical device industry hearing was conducted at the Chuikyo's Special Meeting on Insurance-covered Medical Supplies on September 28, 2011. On the pricing issue mentioned above, the industry side suggested not only a listing system by product, but also proposed transitional measures prior to implementing this system. However, these proposals were not approved. Rather than the proposals being rejected by the attendees, it seemed more that the points being discussed by each side were out of step. It will be necessary to make renewed efforts to have a more streamlined discussion in the future.

The industry side did achieve a few things that should be mentioned. At the meeting, two expert advisors representing the industry side used financial data as evidence to state their case and make suggestions. Thanks to these efforts, it was decided that measures to relieve sudden pricing changes will be taken into consideration for the recalculation of insurance-covered medical supplies from fiscal year 2012, in response to the sudden changes in the exchange rate and sharp appreciation of the yen during the past two years. Further details regarding the 2012 revisions for the insurance-covered medical supplies system were decided on at another Special Meeting on Insurance-covered Medical Supplies on January 25, 2012. Some consideration was also given to incentives for the development of medical supplies.

Having reported on the fiscal year 2012 revisions, the things that struck me once again were the significance of the Chuikyo's industry hearings, and the important role played by expert advisors.

The Great East Japan Earthquake Main Topic at the 3rd AMDD New Year's Party

The American Medical Devices and Diagnostics Manufacturers' Association (AMDD) held a New Year's party on January 11, 2012 at the Imperial Hotel. In the opening address, Mr. David W. Powell, Chairman of the AMDD (Executive Advisor of Johnson & Johnson KK), expressed his hope for the coming year, saying, "Last year was very challenging for our industry, due to the confluence of the prolonged economic recession and the Great East Japan Earthquake on March 11. Nevertheless, AMDD was able to achieve the resolution of a variety of issues thanks to the warm support of the Japanese and US governments and industrial organizations. I hope that we will be able to face the coming year with a sense of renewal and continue our cooperation for the benefit of Japanese patients."

The next speaker was Ms. Yoko Komiyama, Minister of Health, Labour and Welfare. She delivered a congratulatory speech for the second year in a row since becoming Senior Vice-Minister, saying, "The excellent advanced medical devices that have been developed through your research have been widely adopted in Japan, contributing to an improvement in the standard of our health services. The pharmaceutical and medical device industries make up a major pillar of the new strategy for Japan. We are working to eliminate device lag and device gap by improving the structure of the Pharmaceuticals and Medical Devices Agency (PMDA) in order to provide safe and effective pharmaceutical products and medical devices to medical practices more quickly. For this purpose, I would like to establish core clinical research hospitals that conduct clinical research using international standards, as well as global clinical trials. We will also make efforts to restore and reconstruct medical institutions and secure healthcare professionals in the areas affected by last year's earthquake, as well as to develop new medical devices in those regions. We deeply appreciate your continued support."

Mr. John E. Peters, Minister-Counselor for Commercial Affairs at the U.S. Embassy, said, "Japanese people showed their strength in last year's earthquake. I would like to continue to reinforce the cooperative relationship between Japan and the United States." Mr. Takashi Wachi, Vice-Chairman of the Japan Federation of Medical Devices Associations (JFMDA) (Director and Honorary Chairman of Terumo Corporation), then said, "We will face a variety of challenges this year, but we should not hesitate to face reality. Let's not act like ostriches, who bury their heads in the sand when they encounter enemies. Under the current economic recession, it is especially important that we have the following three perspectives: a bird's eye view that grasps the whole situation, the view of an insect that watches its step, and a fish eye view that reads the current of the water."

The Value of Medical Technology

(Ophthalmic Materials)

SHCLs Have Become the Mainstream of Contact Lenses

Silicone hydrogel contact lenses (SHCLs) are one type of soft contact lens (SCL). In SHCLs, hydroxyl methacrylate is polymerized with silicone. Now SHCLs occupy the mainstream of contact lenses (CLs).

Oxygen is essential to maintain a healthy cornea. A certain level of oxygen transmission is necessary to avoid edema in the cornea when CLs are worn all day. All SHCLs largely exceed this level. While oxygen is transmitted through water contained in the material in traditional SCLs, SHCLs' material can transmit oxygen directly. The incidence of hyperemia in the corneal limbus due to oxygen deficiency has therefore become rare.

The longer that traditional SCLs are worn, the drier the eye feels. The sense of dryness is caused by rapid evaporation of tears due to the wearing of SCLs. In contrast, the sense of dryness is alleviated in SHCLs because of the limited extent of evaporation. There are also reports that SHCLs remain comfortable even when worn for an extended period of time.

SHCLs thus have a significant benefit in that not only is sufficient oxygen supplied to the cornea, but the sense of dryness is also alleviated. However, the incidence of corneal infections due to inappropriate lens care is not decreasing. Therefore, appropriate prescriptions and instructions for use by ophthalmologists are still important for SHCLs.

(By Yoshihiro Igarashi, Johnson & Johnson Vision Care Company)

Overview of 23rd Media Lecture

The American Medical Devices and Diagnostics Manufacturers' Association (AMDD) held the 23rd Media Lecture on March 6, 2012 at the Imperial Hotel. The theme of the lecture was "Advanced Medical Technologies to Improve Therapeutic Techniques Safely – The Latest Technologies that Protect Patients from Pain and Readmission Risk."

The first lecture, "The Clinical Benefits and Future Prospects of Hip Surgery Navigation," was given by Dr. Nobuhiko Sugano, Endowed Chair in the Department of Orthopedic Medical Engineering, Graduate School of Medicine, Osaka University. He explained that navigation could be used to project a three-dimensional image of the tip of the chisel used for hip surgery in real time on a monitor, allowing less-experienced surgeons to perform the accurate replacement of artificial joints. The range of motion in the hip joint can also be checked, and a restriction of movement can be set for each patient, leading to an improvement in the quality of life (QOL) of patients. This advanced medical technology originated in Japan and has been covered by medical insurance since April this year, and is expected to become more popular in the future.

The second speaker, Mr. Yasuhiko Nakamura of the Division of Radiology, Department of Medical Technology, Kyushu University Hospital, gave a lecture on the theme, "The Need for Automatic Contrast Medium Injectors for CT & the Requirements for their Safe Use." Mr. Nakamura explained the necessity of safety measures to protect against the extravasation of contrast media, which has less than a 1 percent chance of occurring in contrast-enhanced CT, and the importance of medical insurance coverage to the implementation of such measures.

(The lecture provided by Mr. Nakamura is summarized on page 2).

Healthcare Reform Starts from a Good Working Environment for Healthcare Providers

Japan is blessed with excellent human resources in healthcare, as well as outstanding research and development capabilities and technological strength. So why has this country been overtaken by Western nations in the competition between healthcare products? Mr. Ryozo Hayashi, Professor at the University of Tokyo Graduate School of Public Policy, spoke about how Japan can recover its position.

Countries around the world are focusing on the healthcare industry

Since the late 20th century, the technological innovations in the fields of information technology (IT), biotechnology and nanotechnology, and the expansion in the application of such innovations to medical settings have been astonishing. New minimally-invasive technologies have drastically changed therapeutic methods, prognoses, and the quality of life (QOL) of patients. These changes, along with the aging population, have resulted in the rapid expansion of the healthcare industry in major advanced nations. Consequently, each country is now focusing on the healthcare industry, not only from the aspect of social security but also as an industry that drives economic growth.

With this recognition, governments have started to seek various new approaches to advancing the healthcare field as an industry and not just an extension of traditional methodologies, to realize the social security policy challenge of putting new technologies into practical use at an early stage, and providing sustainable, fair and easy access to healthcare.

Japan, the model student, has been left behind

Japanese healthcare has been left behind in these changes, probably due to its long-term success compared to other advanced nations in achieving a long average lifespan with low public burden under its universal health insurance system. In spite of Japan's excellent human resources in the healthcare and manufacturing industries, with world-leading research and development capabilities and technological strength, it has been left far behind the U.S. and Germany in terms of product competitiveness in rapidly advancing therapeutic areas.

Furthermore, the effect of the delay in policy change has not only eroded the competitiveness of the healthcare industry, but it has also created situations like drug lag and device gap (where modern healthcare is not accessible), produced the distortion of medical resource allocation (e.g. a shortage of doctors in emergency medical care), and begun to have a visible influence on the devastation of medical facilities.

Trial and error by a variety of entities is the driving force

Behind this situation, there is a delay in the recognition and understanding of changes in the medical environment. The wave of technological innovation in the late 20th century and concurrent globalization changed all paradigms of economic and industrial activity. As typified by the Internet, the information transmission speed for technologies and systems has become instantaneous. This has linked the seeds of technology with the needs of a variety of areas, and also attracted a flow of funds, resulting in further acceleration of technological innovation. Moreover, various entities such as companies and individuals now move freely to a comfortable systemic environment and select areas of activity in response to the policy choices of the government.

Even with the current provision of healthcare within a single country, various entities such as physicians, hospitals, companies and patients are similarly dynamic, react to incentives created by various systems, exercise ingenuity from their respective positions and take a process of trial and error, resulting in the formation of the whole.

From the policy side, this means that it is necessary to consider the premise that various healthcare entities think, act, and move on their own. Rather than a central command that designs and controls details, it is vital that we design a system that can activate these activities as a whole and lead us to the desired destination.

The most important factor is that the various systems and policies eliminate discretion, and instead are rational and based on data. Doing so would create a good working environment for healthcare providers that would improve over time. Ultimately, patients will be drawn to such an environment. This virtuous cycle will make the medical field active and extensive.

From a discretionary system to a scientific system

Up to now, the provision of healthcare has had a strong public aspect and has been carried out through a variety of institutional frameworks to provide effective and safe healthcare at low cost. These frameworks include the review and approval process for safety and efficacy of new technologies prior to their availability, a public health insurance system providing a range of benefits to citizens at a fixed rate, a national system guaranteeing citizens in each region sufficient access to physicians and hospitals, and a legal framework determining compensation for medical malpractice and for failure to provide healthcare.

These institutional frameworks include various interests that must be reconciled. Before information disclosure principles were established, these frameworks had gradually become opaque and discretionary so that people could not voice complaints. From now on, we must reaffirm the objectives of these institutional frameworks at all points, and transform discretionary systems into transparent and scientifically-based ones.

A well-balanced allocation of hospitals and physicians

For example, it has gradually become obvious that the objective of the review and approval system is not to designate safety solely under the criteria "Safe" or "Dangerous." Rather, it is to determine how preliminary safety assessments and practical application in the early stages can maximize benefits to society. Meanwhile, the medical reimbursement system is simultaneously pursuing three objectives—accelerated technological development; ease of access; suppression of rising medical costs—as the population is rapidly aging. Thus, as a country with a public health insurance system, it is vital that we design a system that sets prices that are not arbitrary but instead appropriately reflect value.

The allocation of hospitals and physicians must ensure that specialists in various fields can satisfy the overall medical needs of a region. Therefore, we must aim for an arrangement that considers the optimal balance between medical specialists and deployment costs. Moreover, the medical malpractice system should be designed not with the aim of punishing those who commit malpractice but rather to compensate victims and to prevent recurrence of accidents. The system must be structured so that it counterbalances risks and rewards for healthcare providers.

Attempts at reform have finally started

Due to increased public interest over the last several years, various attempts at reform have begun in Japan. For example, in terms of the review process, there have been increases in both the quality and number of personnel at the Pharmaceuticals and Medical Devices Agency (PMDA). In terms of the payment system for medical services, too, there has been less of a focus on the balancing of vested interests and more on the applicability to Japan of the Health Technology Assessment (HTA) system, which has quickly been gaining ground in Europe.

As more and more medical institutions adopt the Diagnosis Procedure Combination (DPC) system, issues in areas such as the sharing of basic data on diseases in specific medical fields and the relationships between medical institutions have come to light. In addition, it is hoped that needless medical errors will be prevented now that standardized, basic data on the management of medical activities and institutions has started being collected from a quality control perspective.

An overall, shared roadmap is essential

Various components have come together in the way described above, but they have yet to show their overall effect. With regard to the review and approval system, there are still noticeable delays in implementing and devising specific reform measures. Japan can hardly call itself a rival to top-class clusters in other countries.

We have not yet reached the point where the decision-making process is scientific, rational and transparent. A number of issues still exist, including a shortage of doctors with an excess of hospitals, a lack of specialization, the difficulty of clinical trials, and increased distribution costs. The criminal liability system has also atrophied, leaving behind the possibility of unnecessary legal risk. It is therefore essential to create a roadmap with a common overall stance on these issues, and to establish a system that ensures its implementation. This will accelerate the finding of solutions, thereby allowing Japan to provide high-quality healthcare that can compete with the rest of the world.

Currently, the Cabinet's Medical Innovation Promotion Office has been making various attempts to eliminate the negative effects from a top-down hierarchy and micromanagement from government bodies. This will hopefully create an environment in which Japan can demonstrate its potential. Japan has affluent consumers of advanced medicine, excellent physicians, and strong manufacturing industries. There will be a huge opportunity for growth by reforming the structure of these institutional systems.

Ryozo Hayashi
Professor, Graduate School of Public Policy, the University of Tokyo

Mr. Hayashi graduated from the Kyoto University Faculty of Law in 1970. He entered the Ministry of International Trade and Industry (MITI). He studied at Harvard Law School (US) and worked as a research fellow at JETRO New York. He returned to the MITI in 1988 and also worked for the Agency for Natural Resources and Energy. He became Director-General of the Consumer Goods Industries Bureau in 2000. He served as Deputy Vice-Minister of Economy, Trade and Industry before assuming his current position in 2005.