

Embarking on a Journey towards the Medical Care of the Future

Kobe Vision for the Healthcare of Tomorrow



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About the Kobe Vision for the Healthcare of Tomorrow

This vision is a new initiative, which aims to create an ecosystem that will continuously generate innovation in the field of medical device development. Under this initiative, representatives from industry, government, and academia will collaborate to establish a research hospital that will act as a demonstration base for medical devices at the Kobe Biomedical Innovation Cluster. In addition, they will also engage in research and development of medical devices using cutting-edge medical technology.

Through collaboration with Kobe University, this vision aims to foster personnel that will be able to bring together medical science and engineering to develop new devices based on the needs of the medical industry. Furthermore, the initiative also strives to promote the development of medical industry in order to keep young people in the region and provide them with more employment opportunities, thereby stimulating the economy of our city.

Greetings

Message from the Mayor of Kobe

Supported by the government grant for the establishment of regional universities and industries, and based at the Kobe University Hospital's International Clinical Cancer Research Center, Kobe Vision for the Healthcare of Tomorrow is a new initiative that aims to bring together numerous companies, startups, healthcare professionals and researchers working in the field of engineering, and enable them to work as a team to bring about innovations in the field of medical devices.

We expect that the establishment of such a research hospital, where medical device manufacturers and technical researchers will be able to easily demonstrate and improve their devices based on the needs of healthcare professionals, will attract new companies to the city and help us retain those of them that are already here.

Using the framework provided by the Kobe Biomedical Innovation Cluster, we aim to create an ecosystem that would keep producing innovations in the field of medical devices at this research hospital. We anticipate that this facility will be used by many researchers, businesses and startup companies supported by the city government, strengthening the mutual cooperation between them. This, in turn, will support the continued development of the Kobe Biomedical Innovation Cluster and further stimulate the city economy.

It is my sincere hope that you will keep a close eye on the development of this project!



Hisamoto Kizo
Mayor of Kobe

Message from the President of Kobe University

Under the Kobe Vision for the Healthcare of Tomorrow, Kobe University aims to be involved in the development of devices that meet the requirements of medical settings and to foster integrated medical-engineering professionals capable of implementing these devices into society. Through this, Kobe University seeks to attract and retain students who want to study at the university and contribute to regional revitalization.

To this end, we will develop Kobe University Hospital's International Clinical Cancer Research Center (ICCRC) as a research hospital by inviting top-level personnel from Japan and abroad to advance cutting-edge research and development in the field of medical devices, with particular emphasis on surgical robots.

Although a number of integrated majors and departments exist in Japan and abroad that foster skilled medical-engineering personnel, we are proud to say that there is no other place in all of Japan that truly integrates medical and engineering fields by training personnel capable of developing medical devices based on medical needs associated with an actual medical setting.

By further enhancing the brand value of Kobe University through these activities, we will strive, together with Kobe City, to make Kobe the city of choice for young people.



Takeda Hiroshi
President
Kobe University

Message from the Project Manager

The Kobe Biomedical Innovation Cluster (KBIC), which will serve as the base of operations for the Kobe Vision for the Healthcare of Tomorrow, is already home to a large number of research institutes, highly specialized hospitals, companies, and universities, providing a unique environment that is unprecedented in Japan for emerging companies.

As the project manager of this Vision, I would like to take the collaboration among industry, government, and academia, which has currently acts as individual collaborations, and push it to a new level where KBIC as a whole will be capable of generating new industries, including the development of practical applications by emerging companies based on the seeds originated in academia, as well as on-the-spot evaluations by hospitals.

In this Vision, the first step is the creation of innovation by combining cutting-edge technologies such as remote communication and liquid biopsy, with surgical robots as a platform. First, however, it is important for all parties involved to share a common vision and discuss the future of the healthcare industry in Kobe to achieve this common goal.

Since I myself was born and raised in Kobe, I will do my utmost to make KBIC even more successful, and a leader in the medical industry throughout Japan.



Asano Kaoru
Member of the Managing Board
and Senior Executive Officer
Senior Managing Director
COO LS Business Unit and CTO
Sysmex Corporation

Development of a Next-Generation Surgical Robot Platform

Japan's First-Ever Development
of Surgical Robots: Past and Future

Core of the Kobe Vision for the Healthcare of Tomorrow— Japan's first-ever domestic Surgical Robot. Q&A from its birth to the future evolution.



Fujisawa Masato

Dean

Kobe University
Graduate School of Medicine

Tanaka Hirofumi

Executive Vice President
Medicaroid Corporation

What is the background to the development of the surgical robot, which is the core of the Kobe Vision for the Healthcare of Tomorrow?

Dr. Fujisawa : It all started in 2010, when Kobe University Hospital introduced the foreign-made surgical robot for the first time in the Kansai region. The high cost of foreign-made equipment has long been a challenge in the medical field, and surgical robots were no exception. At the same time of the introduction of the robot, our University was discussing what should be the core industry-academic collaboration, and we wondered if it would be possible to produce a surgical robot at low cost in Japan. We therefore consulted with Kawasaki Heavy Industries.



Mr. Tanaka : Around that time, Kawasaki Heavy Industries and Sysmex formed a research group to collaborate in the advancement into the medical robotics business. At first, we were unsure what kind of robot we were going to develop, but as long as Kawasaki Heavy Industries and Sysmex were working together, we wanted to undertake a major business that could be a signature business for

medical robots. Based on that idea, we decided to start developing surgical robots. From there, we established Medicaroid, did further marketing research, and then officially started to develop surgical robots in 2015.

The surgical robot was approved for production and marketing. What special features does it have?

Mr. Tanaka : First of all, we are confident in its reliability and durability since we have more than 50 years' experience with industrial robots. In addition, we would like to incorporate the needs of the doctors on the frontline into our products as much as we can, seeing that we releasing the robot in the Japanese market.

Dr. Fujisawa : For example, the special features would include the fact that the robot's body is very compact. In robotic surgery, the maneuverability of the robot is important, not only for the operator but for the assistant around the robot. The compactness of the robot body is directly related to the high maneuverability. I have asked for it, and I feel that it was successfully achieved.

Mr. Tanaka : Our concept is "evolutionary robots". To avoid changing the complete specifications due to a model change, we are going to incorporate additional options to evolve the robot. During this evolution, we will capture the needs of the doctors in the field and make more user-friendly products.

What is the significance of the adoption of the Kobe Vision for the Healthcare of Tomorrow?

Dr. Fujisawa : Prior to this Vision, surgical robots have been developed by utilizing research laboratories such as the Medical Device Innovation Platform (MeDIP). Going forward, I believe that new innovations will be created in rapid succession by using the research hospital of ICCRC as a base, inviting top overseas talent and having many researchers gathered in one location.

Mr. Tanaka : From the corporate perspective, without such a project, we would have to manage everything, not only the development, but also communication with healthcare professionals and the companies who have imaging and communication technologies. In that sense, I believe that development will speed up going forward.

Dr. Fujisawa : We also expect the participation of start-up companies with related technologies. In terms of education, I think we can accelerate the cultivation of human resources who are capable of identifying the needs in the actual work environments and developing medical devices and equipment accordingly.

Development of
an individualized navigation system
for supporting precision surgery

Addressing the uneven regional distribution of surgeons by creating hospital networks using 5G technology

Research is underway to equip Japan's first surgical robot with 5G in the future.

Using the next-generation, promising technology, what will we achieve?

We asked about that vision.



Yamaguchi Raizo × **Aburakawa Yuji** × **Okumura Yukihiro**

Vice Director

Kobe University Hospital
International Clinical Cancer
Research Center (ICCRC)

Senior Manager, Ph. D.

6G Laboratories
NTT DOCOMO, INC.

Senior Technology Architect, Ph. D.

R&D Strategy Department
NTT DOCOMO, INC.

Why does a surgical robot need 5G?

Dr. Yamaguchi : In today's Japan, the number of surgeons is on the decline, and at the same time, the number of instructors to teach young surgeons is also decreasing. An additional problem is that even if large urban hospitals have instructors, in some instances, the rural hospitals do not, which makes the younger generation reluctant to go to rural areas. If we become able to provide remote guidance and surgical support, it would be possible for young doctors in rural areas to be provided with surgical guidance by veteran doctors in other hospitals. Therefore, we consulted with NTT DOCOMO and decided to conduct a demonstration experiment using 5G as a method of enabling remote surgical support and guidance.

Dr. Aburakawa : When conventional communication methods are used to provide surgical support remotely, although the quality of the network connecting base stations may be fast and stable, the quality of the networks directly connecting the base station and each hospital varies from hospital to hospital, making it difficult to ensure the required level of quality for remote surgical support. Although there is the option of installing dedicated optical lines between hospitals, it is impractical in terms of cost. Since 5G will enable a direct connection between the surgical robot and the nearest base station, I believe that it will

result in higher quality, low delays, and lower costs compared to the conventional methods.

Dr. Okumura : Another advantage of this is that the users can use connection lines flexibly and timely within a 5G area. Not only existing hospitals, but also hospitals in rural areas without optical lines, can easily install the equipment without extending the optical lines to the hospital if a 5G base station is available in the vicinity, not to mention the cost and potential to reduce the installation time.

Dr. Yamaguchi : In the future, we believe we can address the uneven regional distribution of physicians by establishing centers in every region that will serve as bases for remote surgical support, building a network with hospitals in those surrounding areas, and creating an environment capable of providing surgical support and guidance remotely.

What are the challenges in introducing this 5G technology?

Dr. Yamaguchi : Even just for image data, the surgical robot transmits and receives an extremely large volume of data in the form of 4K 3D images. In addition, the communication must be at a low-latency level capable of supporting surgery. Further, since human lives are involved, the stability of communication is also important, and the highest level of security is also required since, of clinical information, surgical information is of the utmost importance.

Dr. Okumura : We must achieve a wireless

communication system capable of meeting all these requirements with 5G technology. In the past few years, NTT DOCOMO has been conducting demonstration tests of remote examinations and remote diagnosis using 5G; however, a higher level of support for remote surgery is required. In order to meet these requirements, we plan to conduct demonstration experiments here at the ICCRC.

In moving forward with this project, what are the merits of adopting the Kobe Vision for the Healthcare of Tomorrow?

Dr. Aburakawa : From the development side, we have been, and even now still are, actively involved in the remote medical care field; however, the hurdles seemed extremely high since we did not know what kind of requirements and conditions there were when it comes to surgical robots, among other things. Nonetheless, I believe that the adoption of the Vision has great significance since it has created a friendly environment for demonstration experiments and has given us the opportunity to directly inquire about needs from the medical workplaces.

Dr. Yamaguchi : In addition, since providing surgical support remotely is difficult under the current laws, the introduction of new laws and loosening of regulations are needed. I think that the adoption of this Vision for a project led by the Cabinet Office will make it easier to discuss these issues.



Development of an individualized prognostic prediction model for supporting precision surgery

Blood alone tells us so much. Liquid biopsy will transform the future of medicine

Research of liquid biopsies using blood sample has advanced significantly in recent years.

What does it mean to utilize liquid biopsies in robotic surgery?

Also, how will the future of medicine change?

We talked to researchers actively involved in the frontlines.



Matsuoka Hiroshi ✕

Ajiki Tetsuo ✕

Sato Toshiyuki

Director
Kobe University Hospital
Bioresource Center

Director
Kobe University Hospital
International Clinical Cancer
Research Center (ICRC)

Executive Researcher
Central Research Laboratories
Sysmex Corporation

What does it mean to utilize liquid biopsies in robotic surgery?

Dr. Ajiki : Until now, the prognosis for cancer patients has been predicted using surgical specimens, but with liquid biopsy, it is now possible to predict the prognosis using pre-operation blood samples. If we can make these predictions, we can make decisions, for example, to reduce the extent of the resection in patients who are expected to have a good prognosis.



Dr. Matsuoka : Since robotic surgery has a magnification feature that makes surgery more precise than surgery performed by humans, the extent of the resection can be determined very precisely. However, conventional examination techniques have not yet been able to make prognostic predictions precise enough to utilize this precision. We believe that advances in research on liquid biopsies will lead to even more precise prognoses prediction and less invasive surgery depending on the patient's condition.

Specifically, how will you improve the accuracy?

Dr. Ajiki : First, since the information that can be obtained from the present liquid biopsies is limited, we would like to be able to obtain even more tumor marker types and genetic information going forward. However, since there are so many variables to handle, we need to use artificial intelligence (AI) to perform mathematical algorithm analyses to identify related markers.

Mr. Sato : Unlike surgical specimens, blood samples must be tested for mutated cells or DNA among innumerable normal cells and DNA. This requires highly sensitive and highly accurate testing, and we, at Sysmex, are collaborating with Kobe University in this area to advance the research.

Dr. Matsuoka : In addition to improving the accuracy of liquid biopsies, we also monitor the prognosis of actual patients and give feedback to Sysmex. We believe that we can improve the prognostic prediction model and improve its accuracy by continuously following up, collecting data, and analyzing it with AI.

Mr. Sato : In the course of following up with the patient, the results of the preoperative liquid biopsy will be compared with the results of the examinations using the surgical specimen. Surgical specimens are rich in tumor cells and enable us to conduct more comprehensive examinations. We will use that data to go back and see if we have that data for liquid biopsy. We can

use that as a marker for post-operative liquid biopsy, and we can improve the accuracy of the interpretation of the preoperative examination results.

How will this advance in prognostic prediction models change healthcare?

Dr. Matsuoka : Up to now medical care has evolved under randomized controlled trials (RCT). RCT is a trial that gathers as many homogenous patients as possible and compares conventional medical techniques with new treatment techniques, which has one improvement over conventional medical techniques. However, recruiting patients for the trials also takes time, and the trials themselves also take time and can be conducted only under conditions that are somewhat deviated from real-world data (RWD)*. As a result, it is sometimes difficult to use the trial results as a reference in actual patient care. On the other hand, analyzing many variables in actual patients using AI and improving the model case-by-case is a new way of thinking that is different from methods to date, which I believe can be utilized in medical fields other than cancer.

*Anonymized, individual patient data that can be obtained from the clinical site.

Development of future medical devices

Creation of medical devices of the future that will further advance robotic surgery

What are the “medical devices of the future” that will further advance surgical robots?

We asked Professor Mukai about what is behind their development and the future of fostering the medical-engineering professionals.

Mukai Toshiji

Director

Center for Advanced Medical Engineering Research & Development
Kobe University



Please tell us about the research you are doing in your project on the 3 fields of hyper-sense / hyper body-system, biodegradable devices, and micro-sensing.

In our research on hyper-sense / hyper body-system, we are working on the development of a robotic hand, which allows for more detailed movements than manual surgery, and a system that provides the surgeon's hand with haptic sensation during remote surgery. Some surgeons verify a patient's condition by their sense of touch by touching the affected area with the forceps, so we can support them by providing them with as detailed and realistic touch as possible.

In our research on biodegradable devices, we are developing such devices as magnesium-based clips that dissolve inside the body and biodegradable staples. These devices are typically made of titanium, a stable metal, that can remain in the body. In some cases, titanium-based devices may cause complications, and in the case of children, they may inhibit the growth of internal organs and the like, so it may be necessary to extract them. If these devices are made of magnesium, they do not need to be extracted. Furthermore, since its X-ray absorption rate approximates that of the human body and it is not magnetic, it also has the advantage of not



interfering with CT or MRI examinations.

In our micro-sensing research, we are developing a micrometer-scale sensor (about 300 μ m) that is attached to the tip of a catheter's guide wire or a robotic hand. Since the sensor can detect three-dimensional forces on the X-axis, the Y-axis, and the Z-axis, we believe it is capable of wide application such as providing the haptic sensation by attaching it to the end of the robotic hand to measure the strength.

Please tell us about the current issues and how you will proceed with future development.

First, regarding the hyper-sense / hyper body-system, we are working to improve haptic control, which is the degree of realistic haptic sensation that can be returned when the affected area is pressed by a robotic hand. Since an incomplete sensation will actually confuse the surgeon's sense of touch, we are working on the development by aiming for a sensation that is similar to actually touching with the fingertips.

In our research on biodegradable devices, the phases up to the animal experiments have been completed, and we are moving forward to obtain approvals from the Pharmaceuticals and Medical Devices Agency (PMDA), an independent regulatory agency, and to commercialize the devices. However, in parallel with that, we are also considering materials other than magnesium since the current materials pose such problems as degradation by gastric juices, possibly leading

to stones if devices made of the current materials are used in the urinary organs.

As for micro-sensing, since we have succeeded in the phases up to the development of a micrometer-scale sensor, we are considering how to address various challenges, including how to mount a micrometer-scale sensor on a guide wire or the robotic hand and how to reduce related costs.

How will the adoption of the Kobe Vision for the Healthcare of Tomorrow affect future development?

Until now, we have been conducting research in collaboration with surgeons and companies individually. However, once a research hospital is established in the ICCRC, researchers and healthcare professionals will become able to discuss issues around one table, we anticipate that development will be even further accelerated.

In addition, since there are currently few integrated medical-engineering professionals in Japan, it is difficult to develop medical devices made in Japan. In order to cultivate such professionals, it is necessary for them to see the actual workplace and accurately grasp its needs; however, to date, engineering researchers have only very rarely actually visited a surgical theater. If the project of establishing a research hospital is realized, engineers will be afforded the opportunity to become familiar with the surgical workplace, an experience that engineers have hitherto not had. I believe that this will play an important role in fostering these medical-engineering professionals.

A project to foster professionals:
“Development of Global Entrepreneur Program”

Changing the economy of Kobe City by creating start-ups with high-growth potential

Professor Kutsuna indicates that entrepreneurs capable of connecting technology to business are essential to aim for the revitalization of Kobe City in the Kobe Vision for the Healthcare of Tomorrow.

We asked about the reason and professional development.



Kutsuna Kenji

Professor
Kobe University
Graduate School of Business Administration

We heard that you are working on professional development in this Vision. What kind of approach are you taking?

We provide training in order to generate entrepreneurs and venture companies. Specifically, we conduct the “Development of Global Entrepreneur Program” to foster entrepreneurs capable of playing an active role globally. We plan to bring together, among others, seed-stage and early-stage entrepreneurs as well some students and have lectures conducted by leading talent on the cutting-edge. In this program, we also plan to include a program for learning about businesses focused on healthcare.

Why did you think about generating entrepreneurs and venture companies in this Vision?

This is due to the significant importance of start-up companies’ existence to the economy and, in particular, to employment. More than 70 percent of new jobs are created by rapid-growth start-ups within 4 years of their start of business. However, not all of these start-ups contribute to employment. Only the contribution of the top 4-5% of them to employment is very high. For that reason, it is important how to generate start-ups with high-growth potential.

So then, what kind of industry can generate rapid-growth start-ups? Thinking about that, rather than already matured seeds, the likelihood

of generating rapid-growth start-ups is higher with the use of the regional advantage combined with an approach based on cutting-edge scientific technology. With the cutting-edge scientific technology of the Kobe Vision for the Healthcare of Tomorrow and the unrivaled medical treatment base of the Kobe Biomedical Innovation Cluster, Kobe has an extremely favorable environment for generating such start-ups.



What are the challenges in generating rapid-growth start-ups in Kobe?

First is the issue of funding. Most of the investment by Japanese venture capital firms (VCs) flows to Tokyo, making it difficult for private VCs to invest heavily in the high-risk medical industry in the Kansai region. For example, it is necessary to move ahead with demonstration experiments while using subsidies and grants, POC (Proof of Concept) funding, university-launched VCs, etc., and then to use the success of these experiments as incentive to attract private funding.

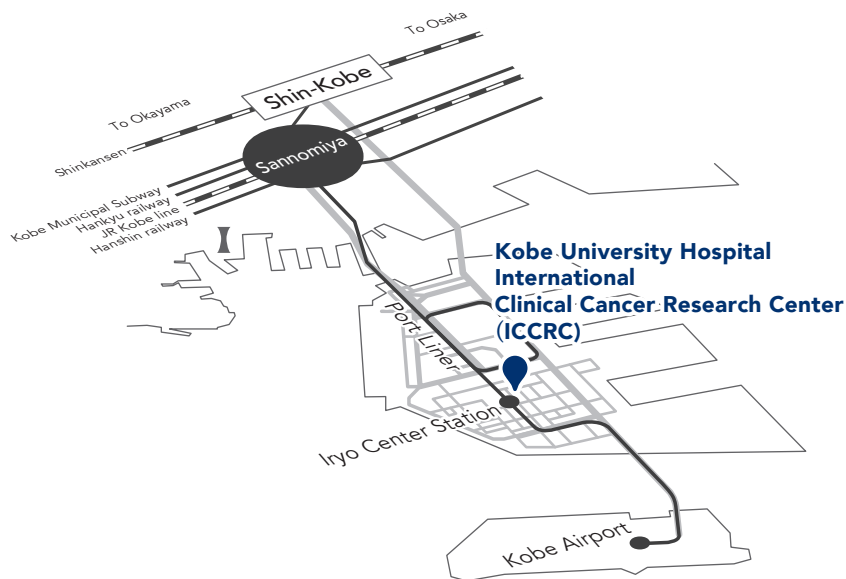
In addition, it is also important to secure professionals who can be assigned as a CEO (Chief Executive Officer) capable of determining whether or not the research can turn into a business or as a CFO (Chief Financial Officer) capable of supervising the financial aspects. It will also be necessary to recruit professionals using recruiting networks or train them as a CEO or CFO.

What kind of training does the Development of Global Entrepreneur Program provide for the development of such professionals?

In addition to conducting lectures about, among other things, creating business plans, finance, intellectual property, and the law, the top six winners of the final presentations will be sent to the University of California, San Diego for an intensive program. This program will be mentored by local angel investors who will become members and will provide guidance on business plans. Participants take the stance that if their plan is highly feasible, they can actually get funding and they can also receive very practical advice. Through these efforts, Kobe University hopes to support entrepreneurs in brushing up their business plans and achieving rapid growth.

Development of Global Entrepreneur Program
<https://www.b.kobe-u.ac.jp/~geep/>

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T.+81-78-322-6374 F.+81-78-322-6010

Kobe City Hall Bldg. No. 1 (23F)
6-5-1 Kano-cho, Chuo-ku, Kobe, Japan

E-mail kobe_mc@office.city.kobe.lg.jp

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