

**Access**

- Train**
- From JR Shin-Osaka Station (Tokaido Line, Shinkansen): Change to the subway Midosuji Line (Kita Osaka Kyuko Line) and get off at Senri-Chuo Station. Take the Hankyu Bus from Stop No. 5 (or No. 6) and get off at the Junkankibyō Center Mae Stop
  - From Hankyu Railway Kitasenri Station (Senri Line): Take the bus from Stop No. 5 and get off at the Junkankibyō Center Mae Stop
  - From Osaka International Airport (Itami Airport): Take the Osaka Monorail to Senri-Chuo Station. Take the Hankyu Bus Stop No. 5 (or No. 6) and get off at the Junkankibyō Center Mae Stop
- Car**
- From Meishin Expressway Suita IC: Approx. 10 minutes
  - From Meishin Expressway Ibaraki IC: Approx. 20 minutes

**Shuttle bus (free)**

From/to Senri-Chuo Station (subway, Osaka Monorail), Kitasenri, Ibaraki-shi, Ishibashi and Mino Stations (Hankyu Railway), and Ibaraki Station (JR). (Runs daily except for weekends and national holidays)

5-7-1 Fujishiro-dai, Suita, Osaka, 565-8565  
 TEL: +81-6-6833-5012 Fax: +81-6-6833-9865  
<http://www.ncvc.go.jp/english/>



The symbol of the National Cerebral and Cardiovascular Center (NCVC) communicates that the NCVC is a place of creativity that generates new healthcare models. NCVC's new creations constantly combine with each other to circulate and interact infinitely. The blue and red hues represent veins and arteries, as well as cooperation between all of the various contrasting elements comprising the NCVC, such as practical healthcare and theoretical research, intellect and passion, and patients and doctors.

Published November 2014



# National Cerebral and Cardiovascular Center

## Taking clinical science beyond the cutting edge



# Our Founding Mission – Conquering Cerebral and Cardiovascular Diseases



**Nobuo Hashimoto, M.D., Ph.D.**  
**President, National Cerebral and Cardiovascular Center**

As one of the world's most advanced treatment centers for cerebral and cardiovascular diseases, the National Cerebral and Cardiovascular Center (NCVC) is attracting considerable attention from medical institutions around the world for its groundbreaking model. Since its inception as a national center for advanced and specialized medical care, the NCVC has set for itself the goal of conquering cerebral and cardiovascular diseases, including heart disease, stroke, diseases of the aorta and other blood vessels, and hypertension. The Center's mission is to safeguard human health in accordance with national healthcare policies.

What makes the NCVC truly unique is the integration of facilities for cardiovascular disease and stroke since they share a number of interrelated characteristics. Another unique feature of the NCVC is that the hospital and research units are fully integrated. Thus, issues encountered in clinical practice are directly relayed to the NCVC's world-leading clinicians and researchers, and their findings enrich and enhance the quality of clinical care we offer to patients. The third unique feature is the establishment of the Research and Development Initiative Center (RDIC) to ensure interdisciplinary collaboration between the Hospital and the Research Institute.

Taking advantage of these unique features in pursuit of its mission, the NCVC contributes proactively to the establishment of a platform for disease prevention, promotion of evidence-based healthcare, and ongoing initiatives for disease prevention.

The NCVC is the only national center in Japan that provides advanced and specialized medical care and conducts research focusing on the cardiovascular system.

#### **From prevention to rehabilitation: extending healthy life expectancy**

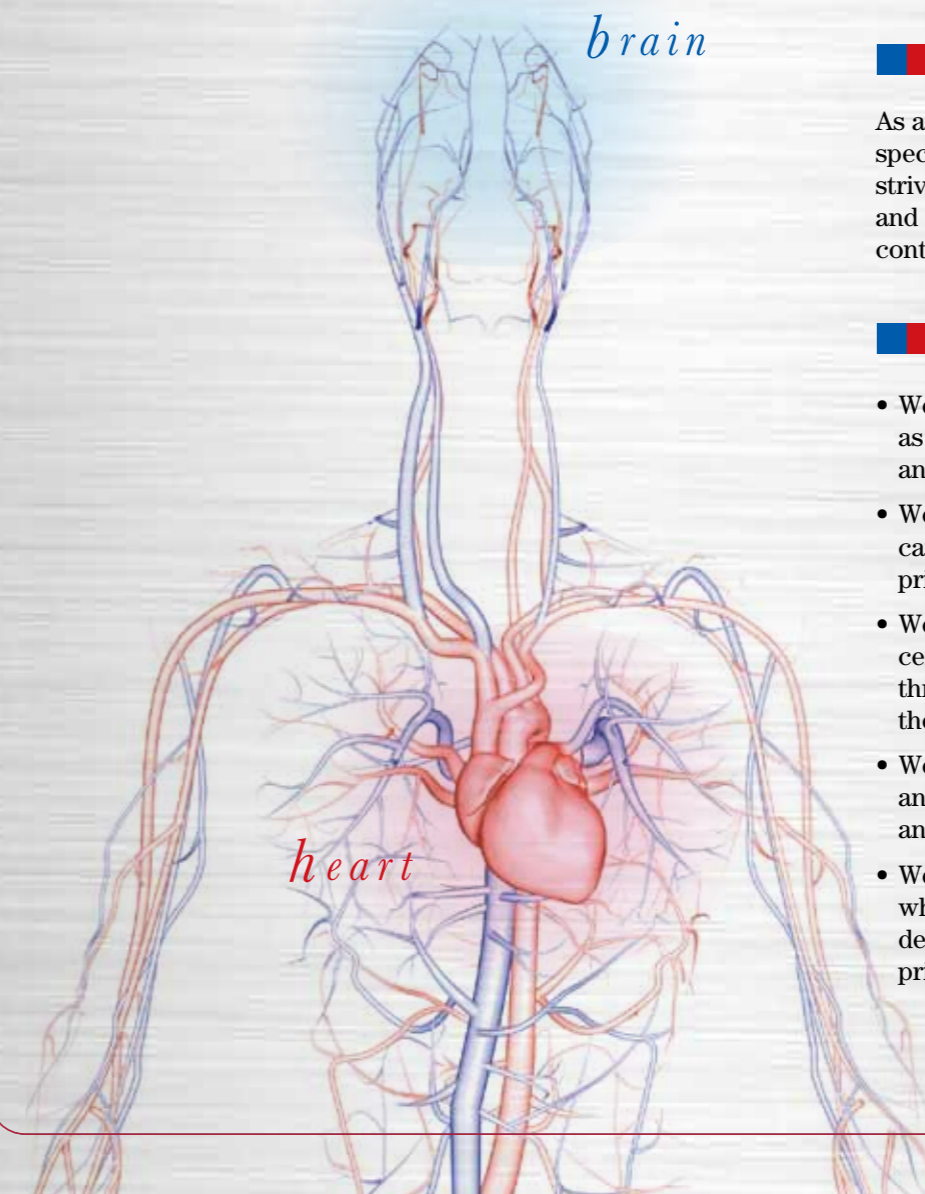
In addition to striving towards reducing the number of deaths from myocardial infarction and stroke, the NCVC takes an integrated approach toward extending healthy life expectancy, which encompasses prevention and early diagnosis of cerebral and cardiovascular diseases, hyperacute care after the onset of disease, and recovery from sequelae through appropriate rehabilitation. The NCVC is confidently moving ahead with the knowledge that its work continues to make significant contributions to society, even 20 or 30 years from now.

#### **Creating a community healthcare model and disseminating information**

Many cerebral and cardiovascular diseases involve the critical challenge of "fighting against time." The key to future success is the establishment of innovative therapies, including hyperacute care and a community healthcare model. To this end, the NCVC works closely with its host community to collect all relevant data. To create a safe and secure urban healthcare infrastructure, the NCVC has been conducting follow-up studies with urban residents (Suita Cohort Study), training students in cardiopulmonary resuscitation (CPR) at schools, and promoting inter-hospital collaboration. The results of such initiatives are shared worldwide.

#### **Educating leaders in recent advances in cerebral and cardiovascular disease treatment**

Engaged in cutting-edge medical practices, the NCVC knows intimately the challenges that confront medical professionals on a daily basis. With a world-class research institute addressing such challenges as an integral part of the institution, the NCVC has been devoted to training residents for more than 30 years. In this outstanding environment, the NCVC trains physicians who can take on these challenges and assume leadership positions that drive future advances in the treatment of cerebral and cardiovascular diseases.



#### **The Center's Objectives**

As a national center for advanced and specialized medical care and research, we strive to understand and control cerebral and cardiovascular diseases in order to contribute to human health and well-being.

#### **Principles of the NCVC**

- We provide a model medical care as well as pioneering medical care for cerebral and cardiovascular diseases.
- We provide safe, high-quality medical care guided by highly transparent, ethical principles.
- We conduct world-leading research on cerebral and cardiovascular diseases through the close collaboration between the hospital and the research institute.
- We nurture the next generation of experts and leaders in the treatment of cerebral and cardiovascular diseases.
- We create a working environment in which all staff can perform with a high degree of passion, professionalism, and pride.

Providing advanced medical care through and cerebrovascular departments while we are committed to taking cerebral and the cutting edge.

close collaboration between the cardiovascular integrating clinical care and research, cardiovascular disease treatment beyond

### **A one-of-a-kind medical research center with a holistic approach to the heart and the brain**

Many patients with heart disease are at increased risk for a stroke. Conversely, many stroke patients are at high risk of developing cardiovascular disease. Thus, both types of patients share a number of common, interrelated challenges. Consequently, the cardiovascular and cerebrovascular departments were both created within the NCVV hospital at its inception. Close collaboration between heart and brain experts ensures that patients benefit more and can experience a greater sense of security. With this unparalleled framework that combines two highly specialized fields, the NCVV continues to provide treatment of cerebral and cardiovascular diseases of the highest quality to patients all over the world.

### **The direct link between the hospital and the research institute continuously produces innovative medical results**

The unique fully integrated structure of the NCVV makes it possible to optimize the research enterprise for discovering solutions to issues encountered in clinical practice and to pass those research findings directly on to clinicians. Our goal is to effectively utilize the features common to cardiovascular and cerebrovascular research as well as medical and surgical treatment for these diseases, and to serve as a cutting-edge medical research and treatment facility. A number of bioactive substances discovered at the NCVV have already been in clinical use, and practical application of the world's smallest artificial heart and other medical devices is imminent.

### **The Research and Development Initiative Center Facilitating close collaboration between clinical practice and basic research**

The Research and Development Initiative Center (RDIC) was established in 2010 to further capitalize on the strengths of the NCVV as a center where clinical practice and research are directly linked. With the aim of fostering multidisciplinary clinical practice and research, the RDIC collaborates with the hospital and research institute to promote clinical research and epidemiological studies, make efficient use of intellectual assets, create a better information infrastructure to plan research projects, prepare a foundation for translational research, and advance collaboration among industry, academia, and government in "open innovation."



**Information**

Relocation to the former Suita Marshalling Yard site near the Shin-Osaka Station is slated for fiscal year 2018. The Hospital and Research Institute will be integrated in one building for further improvement.

Yard site near the Shin-Osaka Station is slated for fiscal year 2018. The Hospital and Research Institute will be integrated in one building for further improvement.

**Leading the world in the development of cutting-edge medical care and technology through open innovation**

Today, advancing partnerships with industry and academia is the key to developing new pharmaceutical products and medical devices. At the new NCVC, we will further advance translational research through the leadership of the RDIC, creating a new structure that allows participation of the research divisions of private companies and universities alike.

**Forming a global biomedical innovation cluster**

We will form a biomedical innovation cluster centered around the new NCVC, where we build up comprehensive partnership with companies and other research institutions. While providing advanced medical care, our goal is also to conduct solution-oriented research and commercialize the fruits of research to bring together related industries to Suita. Through this process, we will be able to form a biomedical innovation cluster.

**Outline of the new NCVC**

The latest plans call for a 50% increase in the total floor area; the new space will be approximately 115,000 m<sup>2</sup>. Access to the Center will improve considerably. The Center will be directly connected to the Kishibe Station, close to the Shin-Osaka Station, on the JR Tokaido Line, and it will take no more than 5 minutes for an ambulance to arrive at the new NCVC directly from the Suita Service Area via the Meishin Expressway. The Suita Municipal Hospital will also be relocated to a site adjacent to the new NCVC. The amenities available to patients and staff will be improved by the construction of accommodations and commercial facilities between the municipal hospital and the new NCVC.

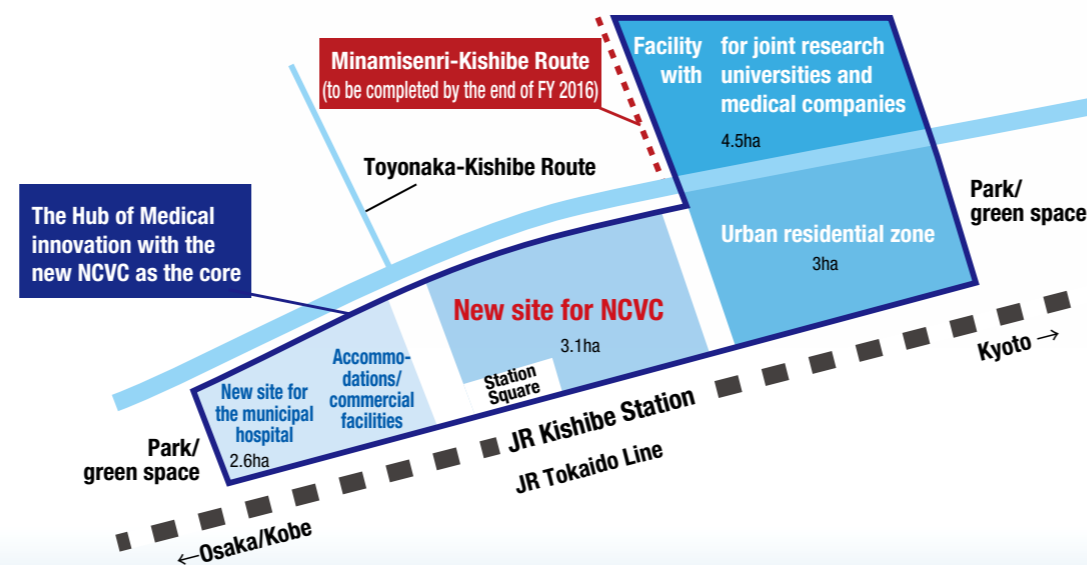
**New Location**

Block No. 5 (approx. 31,000 m<sup>2</sup>)  
Land Rezoning Project for the former Suita Marshalling Yard site,  
Northern Osaka Urban Development Project

**Outline of the New Building (provisional)**

Number of hospital beds: 550  
Number of outpatients: 700 per day (estimate)

Facility	Planned Floor Space
Research Institute	35,700 m <sup>2</sup> (currently 20,204 m <sup>2</sup> )
Research and Development Initiative Center	
Hospital	79,000 m <sup>2</sup> (currently 56,942 m <sup>2</sup> )
Total	114,700 m <sup>2</sup> (currently 77,146 m <sup>2</sup> )

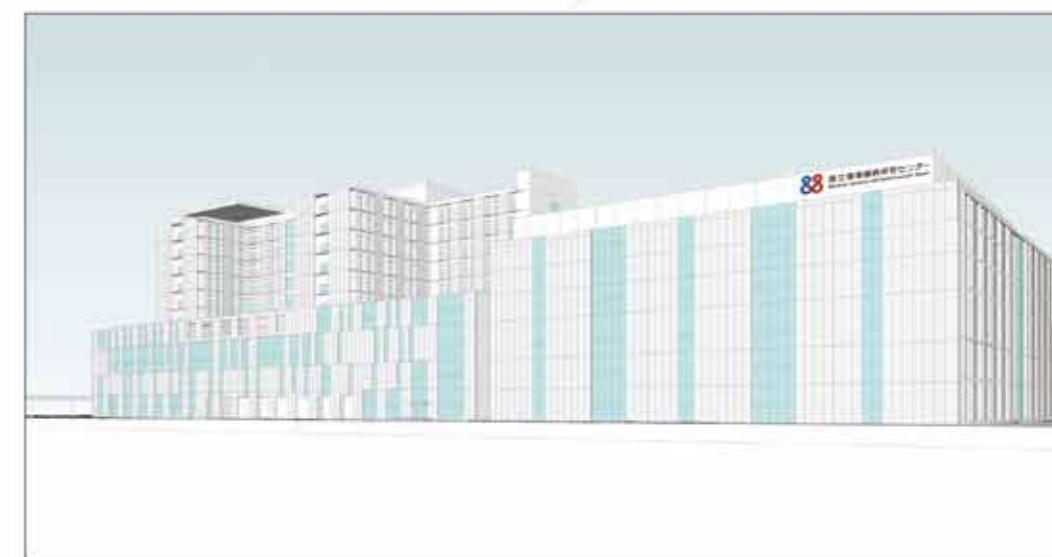


**New NCVC (image)**

View from the south



Exterior View from the JR Tokaido Main Line (image)



# Hyperacute care cutting-edge treatment

Establishing the world's leading medical care system  
To save more precious lives

A team of experts in leading-edge cardiovascular and cerebrovascular medicine races against time

**The earlier the initial treatment, the better the chance of survival from life-threatening cardiovascular diseases**  
**The innovative chain of survival begins even before patients arrive at the Center**

Acute myocardial infarction and stroke rank among the most common causes of death in Japan. Since cardiovascular and cerebrovascular diseases have common pathology and therapeutic strategies, these two departments at the NCVC have formed a tag team in the emergency department for hyperacute care. Improving patient survival rates depends on how quickly the initial treatment is started as the patient is being transported by ambulance.

Every year, more than 3,000 patients with cardiovascular or cerebrovascular diseases are transported to our Center by ambulance. More than half are in serious condition and require hospitalization. In order to ensure timely treatment of patients through understanding their disease state, the NCVC now operates a "doctor car," a high-performance ambulance staffed with doctors, akin to a "mobile ICU." The first of its kind in the world, this vehicle is capable of transporting a wide range of patients, from newborns to adults. Starting necessary medical treatment in the pre-hospital phase can improve survival and prognosis.



**Doctor car**  
Mobile ICU for treating emergency patients ranging from newborns to adults

**Creating an environment to ensure 24-hour, 365-day treatment with cutting-edge surgical equipment and reliable surgical techniques**

With a cardiovascular care unit (CCU) since its inception, the NCVC has successfully reduced the mortality of patients with myocardial infarction from the initial rate of over 20% to approximately 5%. The CCU, which was expanded and enhanced in 2010, is now capable of accommodating all emergency cardiovascular cases with a high risk for mortality and providing advanced emergency treatment around the clock. Our medical division provides advanced, minimally invasive catheter-based treatment. The NCVC leads the way in the treatment of cardiac disease in Japan, with advanced technologies such as coronary artery stenting for acute myocardial infarction, catheter-based ablation using 3-D mapping and other cutting-edge devices for arrhythmias and cardiac dysfunction, and balloon pulmonary angioplasty for pulmonary thromboembolism.

While cardiac surgery is usually performed with cardiopulmonary bypass (CPB), coronary artery bypass surgery without CPB accounts for more than 95% of procedures performed at our Center. We also perform minimally invasive surgeries, including those assisted by the da Vinci Surgical System, as well as the innovative transcatheter aortic valve implantation (TAVI) procedure. In the field of vascular surgery, we are internationally known for excellent results in vascular prosthesis implantation and stent-graft placement.



**PCI (percutaneous coronary intervention)**  
Advanced technology offers less invasive treatments to patients



**Robotic surgery support system**  
Robotic surgery (left) and remote surgery (right)

**Pursuing optimal treatment for stroke and promoting equal accessibility**

The NCVC became the first institution in Japan to establish a stroke care unit (SCU) in 1978, when there was little public awareness in Japan or other countries that stroke patients require treatment by specialists in dedicated settings. In the SCU, specialists in cerebrovascular medicine and neurology treat patients in cooperation with various other medical professionals. As a flagship medical facility in Japan, we have labored to achieve advances in intravenous thrombolysis using tissue plasminogen activator (t-PA) and endovascular thrombectomy in hyperacute ischemic stroke care. Consequently, we have contributed to considerable progress in emergency stroke care in Japan. Our neurosurgical team has abundant expertise and experience in various surgical procedures for occlusive and hemorrhagic cerebrovascular diseases. We always keep in mind our goal of providing the best stroke care to our patients, with close collaboration between neurosurgeons and vascular neurologists. Our Center has been one of the leaders in stroke management both in Japan and overseas, playing a central role in establishing and disseminating diverse treatment methods. We will continue to pursue optimal and complete stroke treatment ranging from prevention to medical treatment and nursing care that helps patients resume their normal lives. We will also maintain our efforts to achieve equal accessibility so that everybody can benefit from progress in hyperacute care and seamless medical and nursing care wherever he or she lives in Japan.



The SCU provides intensive care for various stroke patients.



**Neurosurgical procedure**  
Our neurosurgeons are experts in microsurgery, endovascular surgery, and stereotactic radiosurgery.



## The Voice of the Leaders



**Junjiro Kobayashi, M.D., Ph.D.**  
Deputy Director General, NCVC; Director, Department of Cardiovascular Surgery

Our cardiac surgeons are actively performing coronary artery bypass surgery without cardiopulmonary bypass, robot-assisted surgery, and minimally invasive mitral valvuloplasty. Our aortic surgeons in the Vascular Surgery Department are treating challenging cases, providing hybrid treatments that combine stents and grafts with surgery.



**Satoshi Yasuda, M.D., Ph.D.**  
Director, Department of Cardiovascular Medicine

Our Department consists of approximately 90 expert physicians in five divisions: Coronary Artery Disease, Vascular Disease, Heart Failure, Pulmonary Circulation, and Arrhythmias. We provide high-quality treatment with cutting-edge technology including catheter intervention, ablation, and device therapy. As a Center hospital of Japan, the goal of our Department is to integrate medical care from disease prevention to cardiovascular disease treatment.



**Kazunori Toyoda, M.D., Ph.D.**  
Director, Department of Stroke and Cerebrovascular Medicine

Our Department consists of the Divisions of Cerebrovascular Medicine, Neurology and Neurosurgery, with approximately 65 medical expert neurologists and neurosurgeons. The hyperacute reperfusion therapy program in our department, which performs procedures such as intravenous thrombolysis and mechanical thrombectomy, has the best performance record in Japan. Our neurosurgical team treats severe patients using the most advanced techniques. We have also been disseminating new strategies for stroke rehabilitation and cooperation to a wide network of medical centers.

# Heart transplantation and artificial hearts

The NCVC is taking up the challenge of performing heart transplants and developing artificial hearts that will dramatically improve the quality of life (QOL) of patients with severe heart failure



Saving the lives of those who would not otherwise be able to survive and improving the lives of those who are able to survive

## The NCVC: responsible for the heart transplants in Japan

Heart transplants and artificial hearts are the two ultimate methods for treating patients with severe heart failure. Since the first operation in 1999, the NCVC has performed over 60 heart transplant procedures in Japan. After the amendment of the Act of Organ Transplantation in 2010, the number of heart transplants in Japan has increased dramatically. The NCVC has been playing a key role as a pioneer in heart transplantation while committing itself to research and development of artificial hearts since the late 1970s, shortly after the Center's inception. In 1990, the NCVC-type VAS was granted governmental approval to be manufactured under the Pharmaceutical Affairs Act, which led to the world's first success in commercializing such a system. The NCVC has also formed a special project team for pediatric heart transplantation. We have also created clean rooms and other new facilities in the pediatric ward. The research and development team is also vigorously working on the development of artificial hearts for children.



A multi-disciplinary team approach is essential in heart transplantation. Team members make concerted efforts toward a common goal.

## Special ward for patients with severe heart failure awaiting heart transplants and post-transplant patients, combined with a training center for VAS implantation surgery: one of the few such facilities anywhere in the world

In 1997, the NCVC established a Heart Transplant Office before many other institutions, creating an early framework for multidisciplinary collaboration that involved not only cardiology and cardiovascular surgery but also nursing, transfusion medicine, infection control, nutrition management, and rehabilitation, as well as laboratory and administrative departments. In 2001, the NCVC created a special ward for severe heart failure patients awaiting heart transplants and post-transplant patients, one of the first of its kind in the world. The ward, which is capable of simultaneously accommodating more than 20 patients in total, has 20 rooms, including three clean rooms, which are all equipped with individually controllable air-conditioning systems. In the field of artificial hearts, the NCVC, in collaboration with relevant academic societies, has launched an accreditation system for medical professionals who manage patients with implantable VAS, with the aim of helping patients resume their daily lives at home after implementable VAS implantation. The NCVC also established a training center where physicians can hone their techniques in performing accurate VAS implantation. As a leading facility with a wealth of experience in innovation, the NCVC always adopts a proactive approach in anticipation of what lies ahead.



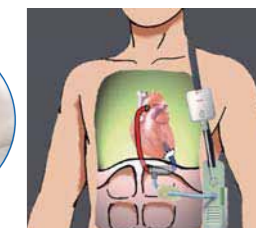
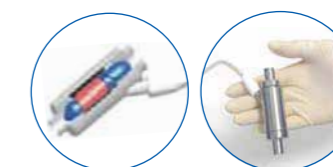
Rehabilitating patients waiting for transplants. We provide them with comprehensive training for developing physical strength to overcome surgery.

## Ultra-small implantable VAS created through collaboration between the hospital and research institute

Progress in a pneumatic VAS has enabled some patients to use the system for more than 4 years before receiving a heart transplant. However, a paracorporeal device with a large, heavy driver necessitates lengthy hospitalization for the patient. Meanwhile, the ultra-small implantable axial-flow VAS, which the NCVC is currently developing, is expected to improve QOL by enabling patients to stay at home and facilitating their return to society. Development efforts are underway to enhance its durability so that it can work without any malfunctions or complications for 5 years.

Heart transplantation and VAS development typically require a multidisciplinary team approach. With its hospital and research institute frequently exchanging data, the NCVC has established a cycle for expediting healthcare innovation with more reliability and rapidity.

Ultra-small implantable axial-flow VAS



As compact as a C-size battery, this VAS can be used in children and adults.

## The Voice of the Leaders



**Takeshi Nakatani, M.D., Ph.D.**  
Director, Department of Transplantation  
Director, Department of Clinical Nutrition

After the amendment of the Act of Organ Transplantation in 2010, the number of heart transplants has gone up dramatically in Japan. We have performed over 60 heart transplants in Japan, accounting for approximately one-fourth of all the cases in the country. In 2011, implantable ventricular assist systems (VASs) began to be covered by medical insurance, which brought about more treatment options for patients with severe heart failure. This has led to improvements in the QOL of patients awaiting transplants. VASs are generally used for maintaining circulation while waiting for heart transplantation. Heart transplant recipients have had good QOL for up to 15 years after transplant, and many recipients have returned to productive, fulfilling lives in society.



**Eisuke Tatsumi, M.D., Ph.D.**  
Director, Department of Artificial Organs

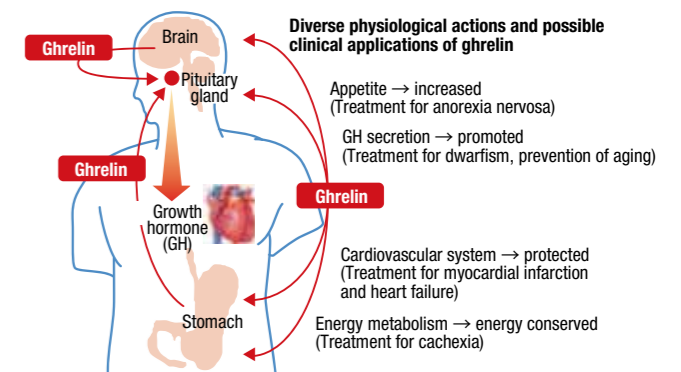
Mechanical circulatory support systems (MCSSs) play an important role in the treatment of patients with severe heart failure. We have been developing various innovative MCSSs, always with their clinical application uppermost in our mind. To date, we have launched the NCVC-type pneumatic ventricular assist system (VAS), portable VAS driver (Mobar-NCVC®), ultra-durable and thrombo-resistant artificial lung (PlantinumCube-NCVC®), and all-purpose mock circulation system (LabHeart-NCVC®), among others. Our current development targets are: 1) an ultra-small axial flow-type implantable VAS and 2) a portable extracorporeal membrane oxygenation (ECMO) system using the world's first hydrodynamically-suspended disposable centrifugal blood pump (BioFloat-NCVC®). We expect these cutting-edge devices will be tested in clinical trials within a couple of years. We are also taking on new challenges in constructing a platform for promoting research and development, clinical application, and production of promising but high-risk medical devices, as well as establishing guidelines for evaluating such devices for pharmaceutical approval.

## Tireless efforts in basic research and clinical applications, in search of potential new drug discoveries

Only those at the cutting edge can discern what cannot be solved using the current state-of-the-art technology

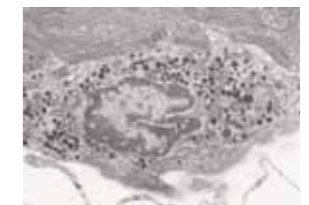
### Tackling issues that need to be addressed now with an eye towards future clinical applications

The NCVC is pursuing a broad spectrum of research initiatives, ranging from projects that will soon reach the market to basic research projects that look ahead to 10 years later. However, all our research efforts share the same goal of translating research into clinical applications for treating cerebral and cardiovascular diseases. The Center's integrated structure enables its hospital and research institute to collaborate closely on discovery of "potential new drugs," elucidating their functions and introducing them into clinical practice. A number of projects in different stages are underway, progressing towards clinical application. In 2010, the RDIC was established to serve as a "conductor" that channels research findings into clinical practice. Under the banner of "from discovery to clinical application," all of the teams are acting in unison to improve the quality of treatment for cerebral and cardiovascular diseases.

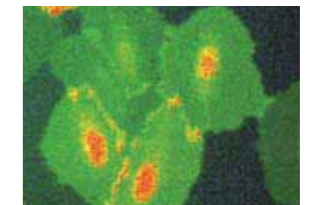


### Discovery of ghrelin: a revolutionary bioactive peptide for the treatment of cerebral and cardiovascular diseases

Among the discoveries made by the NCVC's basic research team, the peptide hormone ghrelin is drawing the most attention. This peptide hormone found in the stomach has a broad range of physiological roles, including promoting the secretion of growth hormone, increasing appetite, and regulating energy metabolism and circulation. Unlike current pharmaceutical products that only perform one specific function, this remarkable multifaceted substance is free from adverse effects because it is an endogenous peptide. More than one-third of bioactive peptides discovered in the world to date have been identified by Japanese researchers, and half of these discoveries are the results of the NCVC's research efforts spanning more than 30 years. The clinical use of ghrelin therapy is expected to start in the next few years. Given that the aging of the world's population is expected to further accelerate, ghrelin has the potential not only to improve cerebral and cardiovascular disease treatment but also to enhance of QOL in an aging global society.



Electron microscope image of ghrelin-producing cells in the stomach

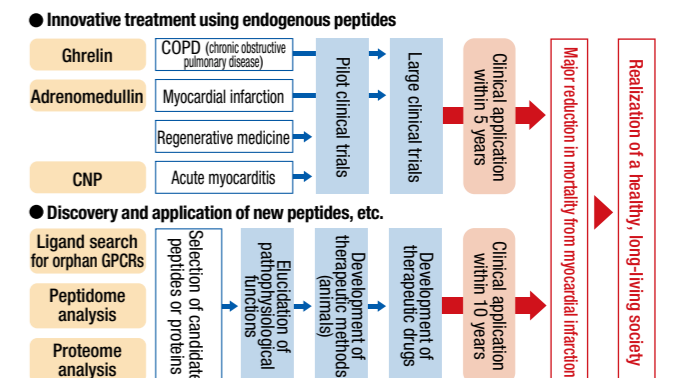


Molecular imaging of vascular endothelial cells: visualizing molecules in living cells to determine their function

### Translational research opening up the future of medicine and drug discovery

The NCVC Research Institute has discovered many novel bioactive peptides, including adrenomedullin and members of the natriuretic peptide family (ANP, BNP, and CNP), thereby shedding light on the existence of a previously unknown circulatory regulation system and its physiological significance. ANP and BNP have already come into widespread clinical use as therapies and diagnostic agents for heart failure. Adrenomedullin, known to have diverse physiological effects in the circulatory system, is expected to become a new therapeutic option in the treatment of myocardial infarction and heart failure as well as regenerative medicine. Determining the safety and efficacy of substances identified and discovered in basic research, assessing their therapeutic effects in the clinical setting, and identifying those with a potential for use in the treatment of cerebral and cardiovascular diseases: these are the functions of the NCVC. Even after the completion of the sequencing of human genome that has as many as three billion base pairs, the mysteries of the human body continue to emerge, yet the clues to solve all these mysteries lie within our bodies.

Development of revolutionary preventive and therapeutic methods without adverse effects from endogenous peptides



### The Voice of the Leaders



**Kenji Kangawa, Ph.D.**  
 Director General, NCVC Research Institute

Peptides hormones are secreted in small amounts in the human body. Since they are endogenous in nature, the use of peptide hormones in medical and pharmaceutical products may be free from severe adverse effects. More than one-third of the discoveries of endogenous bioactive peptides to date have been made by Japanese researchers. Researchers at the NCVC Research Institute have been involved in half of these discoveries. In October 2012, NCVC researchers discovered that atrial natriuretic peptide (ANP) has preventive and inhibiting effects on metastasis of various types of cancers. While ANP is not currently ready to be used in the treatment of cancer, in the future its use is expected to help significantly advance cancer treatment.



**Masafumi Kitakaze M.D., Ph.D.**  
 Director, Department of Clinical Medicine and Development (RDIC)

Our department plays a translational role, conveying the results from basic research at the Research Institute to clinical researchers at the Hospital. We help to make the fruitful results of clinical research applicable to clinical practice in Japan and worldwide. For example, ANP, which was discovered at NCVC, has been used as a treatment for hundreds of thousands of patients with heart failure with almost no side effects. We continue to work on translational research create to more similar success stories.

Improving QOL throughout the entire lifespan,  
 from fetus to adult

## Keeping tiny lives alive, making the most of our advanced diagnostic and therapeutic approaches



### Establishing advanced surgical techniques

The surgical treatment of congenital heart diseases has seen outstanding progress. The NCVC has been playing a pioneering role in the treatment of pediatric cardiovascular diseases, achieving the highest level of results in Japan. The NCVC has made very significant contributions to establishing techniques used in the double switch operation and the Ross procedure.

The double switch operation is performed in patients with congenitally corrected transposition of the great arteries (TGA), while the Ross procedure is used to replace a diseased aortic valve with the patient's own pulmonary valve. Both procedures require a high level of technical skill and can be performed only at a limited number of medical facilities in Japan.

Since its inception, the NCVC has also been actively performing the Fontan procedure. We have performed this procedure in more than 400 patients. We have been following up the patients after Fontan procedure for more than 20 years. The Fontan procedure has greatly changed: it is now performed at a younger age because the data from our long-term follow-up study showed that earlier surgery would result in better outcomes in the adulthoods. While the Fontan procedure is currently performed at a large number of medical facilities, the NCVC has adopted a method that does not use cardiopulmonary bypass, which is still rare around the world. Performing the operation without cardiopulmonary bypass is less invasive to the lung and other organs.



Surgery for severe congenital heart disease

### Determined to be the last bastion for the treatment of pediatric cardiovascular diseases, we never refuse or give up on patients with severe disease

Approximately one in one hundred newborn babies in Japan is born with some sort of congenital heart disease. Since more than one million babies are born annually, as many as approximately ten thousand babies—a substantial number—are born with congenital heart disease every year in Japan. While nearly half of them have mild abnormalities that may resolve spontaneously, the rest need surgery or catheter-based intervention. In addition, many of our patients have reached adulthood and face newly emerging problems.

The NCVC has accepted the most serious cases of neonatal congenital heart disease from all over Japan since its establishment. We have been a pioneer in Japan, not only in terms of improving diagnostic procedures, but also in developing cutting-edge therapeutic methods such as catheterization. To prevent infant lives from being lost, we continue to work on developing minimally invasive diagnostic and therapeutic methods. Developing such therapeutic methods not only saves lives but maintains a high quality of life as patients grow up.



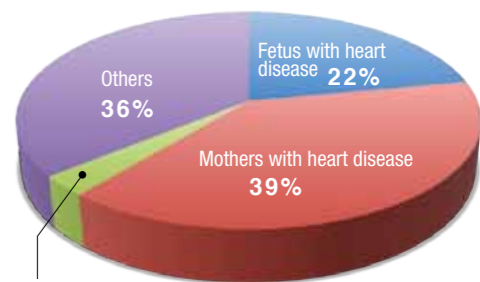
The Pediatric ICU treats babies with severe congenital heart disease

### We help continue the succession of generations by assuring safe and secure pregnancy and delivery

The treatment and management of heart disease has seen outstanding improvements in recent years. The chances for pregnancy in women with heart disease who in the past would have given up the possibility of pregnancy from the outset are now growing. We offer counseling to patients before pregnancy, carefully explaining the changes pregnancy will bring to the mother's body and how it affects the mother's heart condition based on past experience. If the patient chooses pregnancy, we ask her to fully understand and accept our medical advice. We respect the patient's wish as well as her family's preferences, and will provide intensive care and management in cooperation with other divisions.

We envision that baby girls with heart disease that are born at the NCVC will grow up under our continuous care, conceive, and deliver their own babies at the NCVC. Our vision is for the NCVC to help maintain the succession of life for generations.

Pregnant patients in 2012



### The Voice of the Leaders



**Isao Shiraiishi, M.D., Ph.D.**  
 Director, Department of Perinatal and Pediatric Cardiology

Our department provides care throughout the stages of life, from fetus to adult, ranging from diagnosing congenital heart disease to treating the sequelae of Kawasaki disease. We are leaders in the field in pediatric cardiology in Japan, providing early-stage treatment based on accurate diagnostic imaging and minimally invasive catheterization. We also commit ourselves to solving issues encountered in pediatric cardiology, such as infant heart transplantation and adult congenital heart disease.



**Hajime Ichikawa, M.D., Ph.D.**  
 Director, Division of Pediatric Cardiovascular Surgery

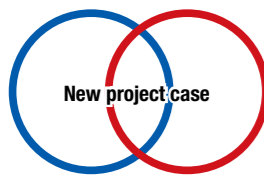
Our division has performed almost 10000 open heart surgeries for congenital heart disease, including the most severe type of single ventricle defect in a neonate. We treat various types of congenital heart disease, ranging from a single ventricle in a neonate (e.g. HLHS, atrial isomerism) to adult congenital heart diseases. In cooperation with the Division of Pediatric Cardiology, we are creating an environment that ensures treatment 24 hours a day, 365 days a year. We also provide long-term care after patients leave the hospital.



**Jun Yoshimatsu, M.D., Ph.D.**  
 Director, Division of Perinatology and Gynecology

Our division is committed to managing pregnant patients with cerebral or cardiovascular disease and those with a fetus suffering from heart disease during their labor and delivery. In particular, we take care of approximately 100 pregnant women with cardiovascular disease each year, the highest number in Japan and third in the world.





# New projects at the NCVC

## Taking on challenges to lead medical care in the next 10 or even 20 years, capitalizing on our long-standing intellectual assets

### Extending healthy life expectancy and creating a vibrant society

The NCVC has been taking a strategic approach to achieve even better results in prevention, cutting-edge therapy, hyperacute care, and rehabilitation by capitalizing on its long-standing intellectual assets and carefully evaluating medical care in the next 10 or even 20 years. The low-salt project and early exploratory clinical trials that facilitate development initiatives represent forward-looking steps taken by the NCVC. The former works on a strategy to lower the blood pressure of the entire Japanese population, thereby reducing the number of patients with cerebral and cardiac disease patients more extensively. The latter creates a new system for advancing drug discovery and medical device development. Both these projects could not have been started without the expertise and experience the NCVC has gathered since its inception in 1977.



Striving to improve patient QOL

### Karushio (A tasty low-salt diet)



#### Various initiatives for promoting a low-salt diet to decrease the daily salt intake of Japanese individuals

The main goal of the NCVC is to eradicate cerebral and cardiovascular diseases in Japan and realize a society where each and every person can lead a healthy life. A vital step to achieving this goal involves the diet. Globally speaking, the Japanese among the heaviest salt-takers, with an average daily intake of more than 10 grams. In addition, 40% of adults and two-thirds of elderly individuals in Japan are diagnosed with hypertension. In 2005, the NCVC Hospital started serving inpatients low-salt meals with approximately 2 grams of salt per serving and below 6 grams per day. While low-salt dishes are generally considered tasteless, our low-salt meals that bring out the good taste of the ingredients are receiving a positive reputation as tasty and delicious. In order for many more people to enjoy tasty low-salt dishes on a daily basis, we have been promoting a low-salt diet through various initiatives. For example, we published a low-salt cookbook in December 2012 and are providing cooking classes for local residents. We are also working with private companies to distribute low-salt recipes and sell low-salt lunch boxes (obento). In addition, in 2013 we started the NCVC S-1g Grand Prix - Local Karushio (Low-salt) Specialty Recipe Project to create low-salt versions of recipes for local specialties across Japan, which has so far been very successful.

### Early exploratory clinical trial center development initiatives

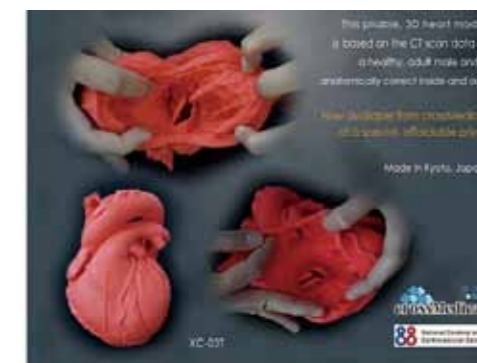


#### Building models of medical device development for the future

The NCVC was selected as one of the five facilities in Japan for the Early and Exploratory Clinical Trial Center Development Initiative, which was launched in fiscal year 2012 as an initiative of the Ministry of Health, Labour and Welfare, for the purpose of creating innovative pharmaceutical products and medical devices in Japan. Among the five facilities, we are the only one that is involved in the development of medical devices. Since our selection, we have been fostering necessary capabilities and improving our facilities so that we can perform first-in-human clinical trials led by physicians, not private companies. In the medical device development sector, concerns over risks on safety, profitability, and regulations have been limiting the entry of domestic companies into the market, resulting in continuous dependency on imported devices. The NCVC aims to create model systems for facilitating medical device development, successively bringing promising ideas into practical application and commercialization.



Medical Device Innovation Circumstances Improvement Project



A cardiac simulator that faithfully reproduces the complicated shape of the heart down to its finest details was developed jointly with a private company and commercialized.



The NCVC Local Karushio (Low-salt) Specialty Recipe Project  
S-1g means reducing 1 g of salt per meal.  
Grand Prix 2013



#### Key person



Yuhei Kawano, M.D., Ph.D.  
Director, Division of Hypertension and Nephrology

The target daily intake of salt for Japanese individuals with hypertension is less than 6 g, less than 9 g for healthy men, and less than 7.5 g for healthy women. However, the average daily intake of salt in Japan is more than 10 g, far exceeding the target value. The meals that the NCVC Hospital is serving to its inpatients contain less than 6 grams of salt per day, yet they are receiving a good reputation of being tasty by bringing out the natural taste of the ingredients. Subsequently, we have published two low-salt cookbooks that have sold more than 330,000 copies. In order to constantly update our low-salt diet initiative, we also started a low-salt recipe contest in 2013.



Low-salt cooking class were well received by local residents



The NCVC Tasty Low-salt Cookbook  
A bestseller: the original and its sequel sold 330,000 copies

#### Key person



Haruko Yamamoto, M.D., Ph.D.  
Specially appointed Assistant to the President  
Director, Department of Advanced Medical Technology Development

Established in October 2011, the Department of Advanced Medical Technology Development is a relatively new division committed to education and support of researchers conducting clinical research. The NCVC is among five facilities designated in the Early and Exploratory Clinical Trial Center Development Initiative launched in fiscal year 2012, and the only one that is involved in the development of medical devices. We are promoting clinical trials led by physicians and improving the environment for medical device development in Japan. Our goal is commercialization of our research and development results, assisting researchers in their consultation with the government, preparation of plans and reports, management of trial progression, and various clerical procedures.

# Hospital

A team of specialists at the cutting edge of medical care makes all-out efforts to conquer cerebral and cardiovascular diseases

The NCVC Hospital is one of the innovative medical institutions in the world, providing advanced treatment of cardiovascular and cerebrovascular disorders with a sense of safety and security. It is the only national center for advanced and specialized medical care and research in Japan that focuses on cerebral and cardiovascular diseases. Through close collaboration with the NCVC Research Institute and the Research and Development Initiative Center, we are developing new world-class preventive and therapeutic methods.



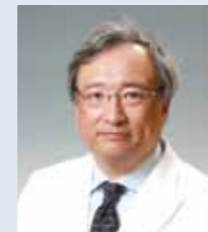
Hiroaki Naito, M.D., Ph.D.  
Director General



Kazuo Minematsu, M.D., Ph.D.  
Deputy Director General



Hisao Ogawa, M.D., Ph.D.  
Deputy Director General



Junjiro Kobayashi, M.D., Ph.D.  
Deputy Director General



Fumiyo Ito  
Director, Department of Nursing

## Hospital Themes

### Medical care

Emergency care  
Invasive care / intervention  
Managed / preventive care  
Advanced and cutting-edge medical care

### Research

Development of next-generation medical care

### Education and human resource development

Education of medical specialists  
Education of health professionals  
Advanced medical training

### Provision of information

Provision of medical care models  
Enlightenment / education on diseases

## Hospital Organization

### Department of Cardiovascular Medicine

Arrhythmia and Electrophysiology  
Heart Failure  
Coronary Disease  
Vascular Disease  
Pulmonary Circulation  
Adult Congenital Heart Disease  
CCU/HCU

### Transplantation

### Department of Cardiovascular Surgery

Adult Cardiac Surgery  
Vascular Surgery

### Department of Stroke and Cerebrovascular Diseases

Cerebrovascular Medicine  
Neurology  
Neurosurgery  
SCU

### Department of Perinatal and Pediatric Cardiology

Pediatric Cardiology  
Pediatric Cardiovascular Surgery  
Perinatology and Gynecology

### Department of Lifestyle-related Diseases

Hypertension and Nephrology  
Endocrinology and Metabolism  
Preventive Cardiology

### Department of Essential Core Services

Operation  
ICU  
Clinical Engineering  
Radiology  
Pathology  
Laboratory Medicine  
Respiratory and Infectious Diseases  
Outpatient Clinic  
Bed Management  
Medical Cooperation Support  
Stroke and Cardiovascular Rehabilitation  
Clinical Nutrition  
Medical Information Technology  
Quality Management and Patient Safety  
Clinical Education and Training

### Department of Nursing

### Department of Pharmacy

## Resident Education Nurse Education

We are developing talented individuals who will lead the field of cerebral and cardiovascular care in the future

We provide a three-year specialist training course on cerebral and cardiovascular diseases for residents with more than two years of clinical experience after graduation from medical school, and a two-year course for senior residents with more than five years of clinical experience. To date, more than 1,300 medical doctors from all parts of Japan have participated in our courses since our resident education program started in 1978.



We are developing nurses who can think independently and act at the forefront of medical care

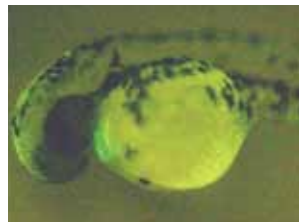
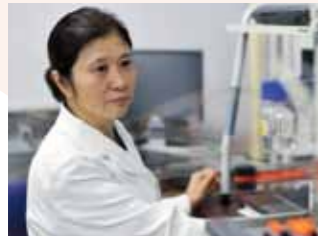
We have instituted the Cerebral and Cardiovascular Expert Nurse (CVEN) accreditation system to assess and accredit nurses who have acquired excellent skills through their clinical nursing experience in cerebral and cardiovascular medicine, with the aim of improving the quality of nursing. Since the system was initiated in 2002, 140 nurses have been accredited as CVENs to date.



# Research Institute

World-class scientists are engaged in first-rate research in the quest to develop effective cerebral and cardiovascular care for future generations

The most distinctive feature of the NCVI Research Institute is its ability to address the real issues facing clinicians and disseminate research findings back to clinicians. We remain actively committed to the development of the world's smallest artificial VAS in collaboration with the NCVI Hospital as well as the clinical application of newly discovered peptides and various other bioactive substances. The NCVI Research Institute is accelerating its research activities toward the ultimate goal of conquering cerebral and cardiovascular diseases.



**Kenji Kangawa, Ph.D.**  
Director General

## Research themes

### Peptide/protein research

We discovered ghrelin and other bioactive peptides that act on the circulatory system. Efforts to discover new drugs and pathological studies are underway.

### Genetics/genomics research

Our ongoing research attempts to identify changes in genes that are responsible for cerebral and cardiovascular diseases, with the objective of providing personalized diagnosis and therapy.

### Regenerative medical science and development of artificial organs

We are conducting pioneering research towards the development of artificial organs and the application of regenerative medicine to cerebral and cardiovascular organs or tissues including cardiac valves, cardiac muscles, blood vessels, and ischemic brain tissue.

### Nanomedicine research

We are conducting advanced research in clinical applications for nanotechniques that allow for manipulation on the atomic or molecular scale.

### Diagnostic molecular imaging

PET/SPECT imaging provides information essential to understanding the pathophysiological status of cerebral and cardiovascular diseases. We are developing methodologies for clinical diagnosis and evaluation of treatment responses, from bench to bedside.

## Organization (Departments and Laboratories)

### Basic Medical Science

Bioscience and Genetics  
Biochemistry  
Molecular Physiology  
Molecular Pharmacology  
Cell Biology  
Basic Medical Research Projects

### Applied Medical Science

Molecular Pathogenesis  
Genomic Medicine  
Vascular Physiology  
Cardiac Physiology  
Molecular Innovation in Lipidology  
Pathogenesis Research Projects

### Advanced Medical Engineering

Artificial Organs  
Cardiovascular Dynamics  
Biomedical Engineering  
Investigative Radiology  
Regenerative Medicine and Tissue Engineering  
Medical Engineering Projects Development

### Research Support

Research Promotion and Management  
Animal Experiment and Medicine Management  
Biomedical Sciences and Information Management  
Occupational Safety and Health Management

### Fund-supported Project

Pulmonary Hypertension Advanced Medical Research  
Integrated Imaging Center for Strokes

# Research and Development Initiative Center

Serving as a hub for collaborations between medicine and engineering, as well as industry, academia, and government, the Research and Development Initiative Center will shape the future of medical sciences through integration of research, commercialization, and clinical practice

Japan has great potential for developing cutting-edge medical technologies while the needs envisaged in clinical practice remain unfulfilled. The Research and Development Initiative Center aims to match such potential with corresponding needs. Its open platform makes it possible to offer a one-stop solution covering all phases from fundamental or clinical studies to commercialization by tapping into the outstanding intellectual assets that NCVI has amassed over the years, including a wealth of experience in research and treatment, excellent human resources, and advanced facilities and equipment.



**Yoshiyuki Taenaka, M.D., Ph.D.**  
Director General

## Organization

Intellectual Asset Management  
Educational Promotion  
Advanced Medical Technology Development  
Clinical Research and Development  
Preventive Medicine and Epidemiologic Informatics  
Training Center  
Cell Processing Center (CProC)

## Countless innovations created through drawing upon intellectual assets built up over 30 years

**Initiative 1** Sharing artificial heart implantation expertise with as many staff members as possible: Training Center

Cutting-edge medical devices require surgeon training for maximum effectiveness. For instance, artificial hearts cannot work properly without the surgeon's expertise in accurately implanting them. Accordingly, the Research and Development Initiative Center established Japan's first training center for artificial heart transplantation, providing an opportunity for staff members from other medical institutions to acquire the necessary surgical expertise. In Japan, numerous patients are awaiting artificial heart transplantation. To shorten this "waiting time for life," staff members at the training center are working tirelessly to disseminate the skills to as many medical professionals in Japan as possible.



Training session



Hybrid Operation Room/Laboratory

**Initiative 2** Developing devices to advance regenerative medicine: Cell Processing Center (CProC) x Department of Clinical Research and Development

Regenerative medicine is one cutting-edge area of medical science that is currently attracting the greatest attention. The CProC is working to actualize regenerative medicine by advancing its clinical research in stem cells and conditioning cells to make them available for clinical applications. The CProC also works closely with the Department of Clinical Research and Development, which has direct patient contact. One of the fruits of such efforts was the development of a new device that has made it easier and faster to sort cells, a previously difficult and specialized process, which has subsequently improved healthcare quality. The CProC, working in a seamless process from research to commercialization based on the needs of medical professionals, is expected to help advance the frontiers of medical care through close collaboration with businesses that possess superior technologies.



Sorting cells at the CProC

# NCVC Biobank

## Biobank

The NCVC Biobank is committed to enhancing research based on a careful assessment of future healthcare needs

The NCVC Biobank was started to preserve and manage blood, tissues, and other biospecimens derived specifically from patients with cardiac and cerebrovascular diseases so that they can be effectively utilized for academic research and drug discovery. Biospecimens and medical datasets are being provided not only to researchers within the NCVC but also to those in and outside of Japan while maintaining patient anonymity.



**Hatsue Ishibashi-Ueda,**  
M.D., Ph.D.  
Director, Biobank



### Organization

Bioresource Section  
Data Resource Section  
Personal Information Section  
National Center Biobank  
Network (NCBN) Joint  
Research Arrangement  
Section

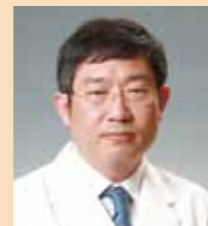


# Center for Cerebral and Cardiovascular Disease Information

## Center for Cerebral and Cardiovascular Disease Information

We are developing countermeasures against cerebral and cardiovascular diseases in line with actual settings

Cerebral and cardiovascular diseases are common in Japan, accounting for approximately one-third of deaths in the entire population. In addition, these diseases constitute a major cause of an almost 10-year gap between average life expectancy and healthy life expectancy. Moreover, cerebral and cardiovascular diseases account for approximately 20% of national health care expenditures, far more than the 13% spent on cancer in Japan. In order to develop preventive and therapeutic procedures for cerebral and cardiovascular diseases, it is essential to accurately grasp what is really going on with these diseases. The Center for Cerebral and Cardiovascular Disease Information was inaugurated on April 1, 2014 with the objective of collecting national-level data on cerebral and cardiovascular diseases with the following objectives.



**Yoshihiro Miyamoto**  
M.D., Ph.D.  
Director

### Main Objectives

- 1 Gathering nationwide data on cerebral and cardiovascular diseases and accurately assessing morbidity and other outcomes.
- 2 Enhancing the in-hospital registration system for collecting detailed information on cerebral and cardiovascular diseases.
- 3 Making the data collected widely available for research on prevention and treatment and returning the benefit of research findings to the nation.
- 4 Collecting and storing data on stroke and cardiovascular diseases in one centralized database, with data on numerous risk factors.

### History

1977	June	Dr. Tsuneo Yoshida installed as the first president
	July	National Cardiovascular Center inauguration ceremony held
	August	Hospital and Research Institute operations began
		Three general wards and ICU opened
	October	One special ward (Coronary Care Unit (CCU)) opened
1978	April	Residency system began
	May	Six general wards and two special wards (Infants' and Stroke Care Unit (SCU)) opened
1979	May	Two general wards and one special ward (Neurosurgical Care Unit (NCU)) opened
1980	April	One general ward opened
1981	March	Library construction completed
1982	January	A special ward for perinatal care opened
1983	August	Dr. Hisao Manabe installed as the second president
1986	February	The National Cardiovascular Center was designated as a WHO Collaborating Center for Research and Training
	June	Construction of the Research Institute annex completed
1987	May	Department of Pharmacy established in the Hospital
	November	Tenth anniversary ceremony held
1990	March	Construction of the radioisotope ward completed
	April	Dr. Teruo Omae installed as the third president
1992	March	Construction of the rehabilitation ward completed
1993	September	The National Cardiovascular Center was approved as a specialty hospital
1995	April	Dr. Yasuo Kawashima installed as the fourth president
1996	March	Nationwide network offering integrated medical support for cerebral and cardiovascular diseases (JUN Net) established
	October	Dr. Haruhiko Kikuchi installed as the fifth president
1997	October	Heart Transplant Office established
	November	Twentieth anniversary ceremony held
1998	July	Organ and Tissue Donation Task Office established
1999	March	Division of Clinical Trial Management established
2000	March	Construction of the biotechnology ward completed
	July	Dr. Takenori Yamaguchi installed as the sixth president
2001	March	Severe heart failure/transplantation ward opened
	April	Dr. Soichiro Kitamura installed as the seventh president
2002	February	Construction of the gamma knife ward completed
2004	October	Advanced Medical Engineering Center opened
2005	October	Clinical Research Center opened
2006	March	Ten-year Strategy for Conquering Cerebral and Cardiovascular Diseases formulated
2007	December	Thirtieth anniversary ceremony held
2008	April	Dr. Nobuo Hashimoto installed as the eighth president
2009	April	Cell Processing Center established
2010	April	Reorganized as an institution with an independent administration
	April	Dr. Nobuo Hashimoto inaugurated as first president of the new entity
	April	Research and Development Initiative Center opened
	July	Clean room for infant transplantation completed
	October	New Cardiovascular Care Unit (CCU) opened
2011	January	Hybrid operation room system introduced
	July	The NCVC was designated as an Early and Exploratory Clinical Trials Facility
	August	A childcare facility was established
	October	Medical care cluster ward opened
	November	BioBank established
2012	January	Electronic medical record system introduced
	May	"Doctor Car" ambulance system introduced
	December	NCVC's Healthy Low-salt Cookbook published
2013	June	Relocation to former Suita Marshalling Yard site announced
	December	NCVC's Healthy Low-salt Cookbook, Volume II published
2014	March	Handover of relocation site completed
	April	Center for Cerebral and Cardiovascular Disease Information opened
	May	Medical Care Cluster Formation Council established